Chapter 31
Leiomyomata Uteri and Myomectomy

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DEFINITIONS

Intravenous leiomyomatosis—Smooth muscle tumor that consists of polypoid intravascular projections into the veins of the parametrium and broad ligaments.

Leiomyomatosis peritonealis disseminata—A benign reparative process in which fibroblasts replace soft peritoneal decidua on subperitoneal surfaces of the uterus and other pelvic and abdominal viscera resulting in nodules with a pseudoleiomyomatous pattern.

Menorrhagia—Prolonged (>7 days) or heavy (>80 mL) menstrual bleeding occurring at regular intervals.

Metrorrhagia—Uterine bleeding occurring at irregular intervals, sometimes of prolonged duration.

Menometrorrhagia—Heavy, prolonged bleeding occurring at irregular intervals.

Submucosal—Present within the uterine myometrium just below the basal layer of the endometrial lining.

Subserosal—Present within the uterine myometrium just below the serosal or peritoneal covering of the uterus.

Leiomyomata are the most common tumors of the uterus and the female pelvis. This chapter discusses the pathologic and clinical features of uterine leiomyomata, the choice of treatment, and the indications and techniques for myomectomy.

Hysterectomy is sometimes required for the management of leiomyomata. It is also performed for many other indications, but leiomyomatous uteri are the most common indication for hysterectomy. Refer to Chapter 32 for a complete discussion of hysterectomy.

Advances in gynecologic surgery in the early 1900s finally brought this common, sometimes fatal, disease of women under reasonable control. Before the 20th century, no effective treatment was available. Uterine leiomyomata often grew to enormous size and caused great suffering from bleeding, pain, and emaciation (**Fig. 31.1**). Death from this benign disease was not uncommon. Progress in gynecologic surgery and anesthesia finally allowed the safe removal of these tumors by skilled gynecologic surgeons.

No one played a more important role in this endeavor than Drs. Kelly and Cullen. Working together at Johns Hopkins Hospital, they gradually developed surgical techniques that were successful in preventing and controlling intraoperative hemorrhage. Several illustrations from their magnificent treatise, *Myomata of the Uterus,* published in 1907, are included in this chapter. In the preface, Cullen wrote:

> It was my good fortune to come to Baltimore in 1891, shortly after the hospital opened. At that time many cases of myoma were considered inoperable, and even when hysterectomy was undertaken it was only in the cases in which a stout rubber ligature could be temporarily tied around the cervix and when, as happened in some cases, this ligature slipped, alarming hemorrhage followed. Then came the systematic controlling of each of the cardinal vessels; later the bisection, and finally the transverse severance of the cervix as a preliminary feature of the operation in

exceptionally difficult cases, until at present a myomatous uterus that cannot be removed is almost unheard of. I have watched the gradual simplification of the surgical procedures with the greatest interest. Many American surgeons have had much to do with the wonderful advance in this direction, but I know of no other man, either here or abroad, who has done as much toward this advancement as Howard A. Kelly.

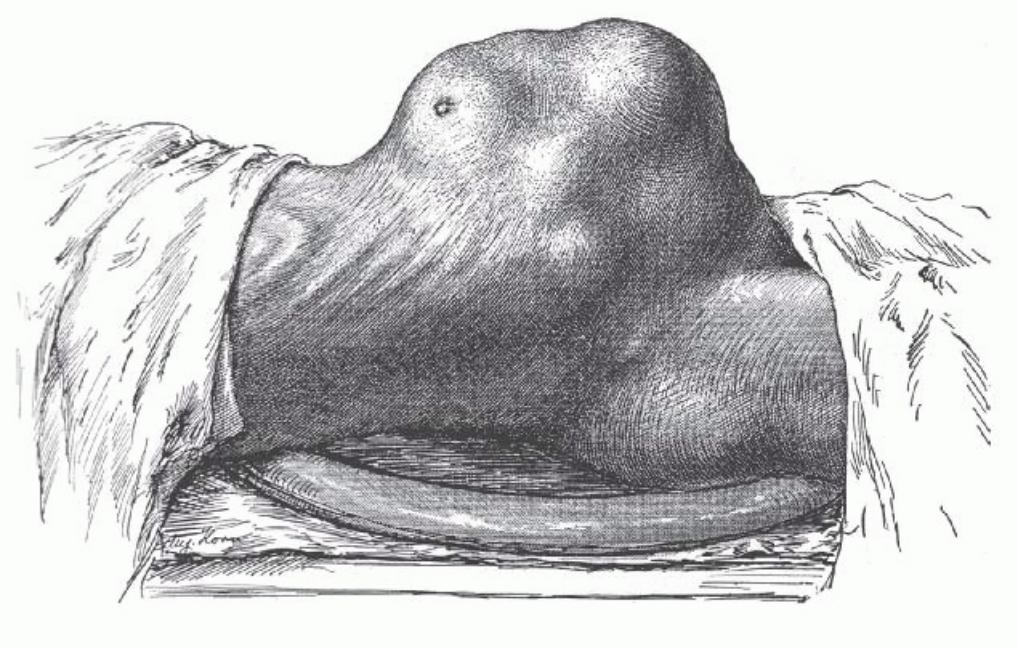

FIGURE 31.1 The patient is thin and emaciated, the outline of the ribs being prominent. Such advanced and neglected cases of multiple uterine leiomyomata are rarely seen today.

The mortality rate for 1,373 operations performed for uterine leiomyomata at Johns Hopkins Hospital between 1889 and 1906 was 5.75%; it was less than 1% for 238 operations performed between 1906 and 1909. In 55 patients, no operation was attempted because of patients' refusal or weakened condition. Among these patients, 21 deaths occurred in the hospital. Death from uterine leiomyomata rarely occurs today. The near elimination of mortality secondary to uterine fibroids represents a major milestone in the health care of women.

During the past century, hysterectomy and myomectomy by the traditional and classic techniques have been the main treatment for women with uterine leiomyomata and significant symptoms; they continue to be so today. Each year in the United States, more than 200,000 hysterectomies are performed with uterine leiomyomata as the primary indication. However, this traditional management is currently evolving toward more conservative, less invasive techniques for several reasons:

1. Concern regarding the increasing costs of health care has focused on the need to use effective but less expensive methods of management of uterine leiomyomata.
2. Advances in surgical technology now allow certain patients to be treated with new, minimally invasive techniques, including robotic hysterectomy, laparoscopic hysterectomy, laparoscopic-assisted vaginal hysterectomy, robotic myomectomy, laparoscopic myomectomy, laparoscopic myoma coagulation (myolysis), and hysteroscopic resection of submucous myomata. Under proper circumstances, these procedures can be safe, effective, and less costly.
3. Interest in nonsurgical management also appears to be increasing with more data available regarding minimally invasive procedures, including uterine artery embolization (UAE). This procedure has emerged from an investigational realm to common clinical practice. As more long-term data become available,

outcomes and prognosis are becoming more clearly delineated.

4. A medical approach to the management of patients with leiomyomata is now available. Gonadotropin-releasing hormone (GnRH) analogs, administered for 3 to 6 months, cause most uterine leiomyomata to shrink. However, the myomata regain their original size several months after the GnRH analog is discontinued. This medical regimen has

been useful as an adjunct to surgical management. Women who become symptomatic with leiomyomata just before menopause can be treated temporarily with GnRH analogs and can possibly avoid surgical therapy.

5. Uterine leiomyoma are a major public health and women's health care problem. Society has a legitimate reason for interest and concern and has questioned the advisability of hysterectomy for the management of most cases of uterine leiomyomata. Many women insist on the preservation of uterine function for future childbearing and sometimes even when future childbearing is not desired or not likely to occur. A greater emphasis has developed on expectant management, medical management, minimally invasive surgical procedures, and conservational management of uterine leiomyomata in the future.

In the future, the traditional and classic techniques of hysterectomy and myomectomy will be required less often for patients with symptomatic leiomyomata. At present, however, these operations are still appropriate in many situations.

ETIOLOGY, PATHOLOGY, AND GROWTH CHARACTERISTICS OF UTERINE LEIOMYOMATA

A leiomyoma is a benign tumor composed mainly of smooth muscle cells but containing varying amounts of fibrous connective tissue. The tumor is well circumscribed but not encapsulated. Various terms are used to refer to the tumor, such as *fibromyoma, myofibroma, leiomyofibroma, fibroleiomyoma, myoma, fibroma,* and *fibroid*. The latter designation is the one most commonly used, but it is the least accurate and acceptable. The term *leiomyoma* is a reasonably accurate one that emphasizes the origin of this tumor from smooth muscle cells and the predominance of the smooth muscle component. The tissue culture work of Miller and Ludovici suggested an origin from smooth muscle cells, and the studies of Townsend and associates affirm a unicellular origin for leiomyomata.

Leiomyomata are the most common tumors of the uterus and female pelvis. It is impossible to determine their true incidence accurately, although the frequently quoted incidence of 50% found at postmortem examinations seems reasonable. Leiomyomata are responsible for about one third of all hospital admissions to gynecology services. It is well recognized that the incidence is much higher in African American than in Caucasian women. In a careful study of leiomyomata among women in Augusta, Georgia, Torpin and associates found the incidence among African American women to be three and one third times that among Caucasian women. There is no known explanation for this racial difference. Leiomyomata also are larger and occur at a younger age in African Americans. In fact, many African American women develop leiomyomata before 30 years of age. However, development prior to age 20 is extremely rare, regardless of race. Patients with uterine leiomyomata often have a positive family history of uterine leiomyomata. This suggests the presence of a gene, which has yet to be discovered, encoding for their development.

About 40% to 50% of leiomyomas show karyotypically detectable chromosomal abnormalities that are both nonrandom and tumor specific. Identified chromosomal abnormalities include t(12;14) (q15;q23-24), del(7) (q22q32), rearrangements involving 6p21, 10q, trisomy 12, and deletions of 3q. Interestingly, a recent study of 217 myomas found a positive correlation between the presence of a cytogenetic abnormality and the anatomic

location of the myoma. In this study by Brosens and colleagues, submucous myomas were consistently shown to have fewer cytogenetic abnormalities when compared with intramural and subserous lesions (12% vs. 35% and 29%, respectively). An increased prevalence in certain races, twin studies indicating higher correlation with hysterectomy in monozygotic twins, and increased incidence in first-degree relatives all seem to support an inherited predisposition. The true genetic contribution to the development of uterine leiomyoma remains to be defined.

Most of the data concerning the incidence of uterine leiomyomata are based on gross examination of the uterus, routine pathology reports, or the clinical diagnosis of uterine leiomyomata. Cramer and Patel subjected 100 uteri to gross serial sectioning at 2-mm intervals. They found 649 leiomyomata, roughly threefold the number identified by routine pathologic examination. Admittedly, some were only a few millimeters in diameter, but all were grossly visible. In 48 uteri with no mention of leiomyomata in the routine report, 27 were found to have small tumors. The incidence of leiomyomata was the same in premenopausal and postmenopausal uteri, although the average number of leiomyomata and the average size of the largest leiomyoma were greater in the premenopausal women. This work has important implications for future epidemiologic studies. It also suggests that it is almost never possible to surgically remove all leiomyomata when a myomectomy is performed.

The growth of leiomyomata is dependent on estrogen production. The tumors thrive during the years of greatest ovarian activity. Continuous estrogen secretion, especially when uninterrupted by pregnancy and lactation, is thought to be the most important underlying risk factor in the development of myomata. After menopause, with regression of ovarian estrogen secretion, growth of leiomyomata usually ceases. Actual regression in the tumor size may occur. There are rare instances, however, of postmenopausal growth of benign leiomyomata, suggesting the possibility of postmenopausal estrogen production either in the ovary or elsewhere. Postmenopausal ovarian cortical stromal hyperplasia may be associated with an increase in estrogen secretion by the ovary. The postmenopausal ovarian stroma in a variety of presumably inactive ovarian tumors, including mucinous cysts and Brenner tumors, can also produce estrogen. When a central pelvic tumor presumed to be uterine leiomyomata enlarges after menopause, one should think of the possibility of malignant change in the leiomyoma itself or in the adjacent myometrium, or of the growth of a new pelvic tumor of extrauterine origin.

Older nulliparous women have an increased risk of developing leiomyomata. However, in multiparous women, the relative risk decreases with each pregnancy. A woman who has had five term pregnancies has only one fifth the risk of a nulliparous woman of developing myomata. The risk is reduced in women who smoke and is increased in obese women; this is possibly related to the conversion of androgens to estrogen by fat aromatase.

The observation that leiomyomata may show significant enlargement during pregnancy provides further clinical evidence of the relation of estrogen and progesterone to the growth of these tumors. However, a better blood supply during pregnancy might also encourage their growth. In a prospective ultrasonographic study of 29 pregnant patients with uterine leiomyomata, Aharoni and associates found no evidence of enlargement of the myomata in 78%. Lev-Toaff and colleagues also confirmed that some but not all leiomyomata enlarge during pregnancy in response to estrogen and progesterone.

In the initial two decades following the introduction of oral contraceptives containing high-dose estrogen, there was a striking increase in the occurrence of large leiomyomata among young women of all racial backgrounds who took these pills. Although the growth of uterine leiomyomata is not invariably stimulated, oral contraceptives containing highdose estrogen should not be prescribed for women with these tumors. Oral contraceptives with low-dose estrogen are less likely to stimulate growth. According to Parazzini and associates, there is no significant relation between the occurrence or growth of leiomyomata and the newer oral contraceptives that contain much smaller amounts of estrogens and progestins, and some believe that the risk of developing myomata is reduced with these low-dose pills.

Scientific investigators have been intrigued by the observation that leiomyomata develop during the reproductive years, sometimes grow during pregnancy, and regress after menopause. Nelson, Lipschutz, and others have produced multiple leiomyomata artificially on the serosal surface of the uterus and other peritoneal surfaces in guinea pigs given prolonged estrogen injections. Spellacy and coworkers found that levels of plasma estradiol were the same in patients with and without leiomyomata. However, Wilson and associates found a significantly higher concentration of estrogen receptors in leiomyomata than in myometrium. Farber and colleagues reported that these tumors bind about 20% more estradiol per milligram of cytoplasmic protein than does the normal myometrium of the same organ. This observation was not uniformly true for all leiomyomata, suggesting that different cellular components with a leiomyoma may be associated with different biologic activity. Otubu and coworkers found the concentration of estradiol to be significantly higher in leiomyomata than in normal myometrium, especially in the proliferative phase of the menstrual cycle. Soules and McCarty reported that leiomyomata had more estrogen receptors than did normal uterine tissues in the first phase (days 1 through 9) and in the second phase (days 10 through 18) of the menstrual cycle. Gabb and Stone found that the ability to convert estradiol to estrone was similar in leiomyomata and myometrium. However, Pollow and associates found the conversion of estradiol into estrone to be significantly lower in leiomyomata than in myometrium. This difference in conversion rate could result in a relative accumulation of estrogen in a leiomyoma, causing a hyperestrogenic state within the tumor and surrounding tissues. The enzyme 17β-hydroxy dehydrogenase accelerates the conversion of estradiol to estrone. Leiomyomata have a low concentration of 17β-hydroxy dehydrogenase, which results in a relative accumulation of estradiol in leiomyomatous tissue. These findings may explain the myometrial hypertrophy that is invariably present with leiomyomata.

Other abnormalities in endocrine function have also been suggested. Ylikorkala and colleagues found that pituitary function may be abnormal in women with leiomyomata. Patients with leiomyomata had a low follicle-stimulating hormone level and a diminished follicle-stimulating hormone response to pituitary GnRH. There was an excessive prolactin response to thyrotropin-releasing hormone. Spellacy and colleagues found that the peak levels of human growth hormone reached during a hypoglycemic test were twice as high in patients with leiomyomata as in the control group. Reddy and Rose suggested the possibility that 5α-reduced androgens may play a role in the pathophysiology of uterine leiomyomata, because a significant increase in 5α-reductase has been found in leiomyoma tissue as compared with the myometrium and endometrium. Influenced by the experimental investigations of Lipschutz and associates, Goodman in 1946 treated patients with uterine leiomyomata with progesterone and noted a decrease in tumor size in all patients. However, Segaloff and colleagues reported no effect in their study. Goldzieher and coworkers produced histologic evidence of extensive degenerative changes in leiomyomata by administering high-dose progestin therapy (medrogestone in high doses for 21 days). Filiceri and associates have reported the regression of a uterine leiomyoma after longterm administration of a long-acting luteinizing hormone-releasing hormone agonist given to suppress ovarian estrogen secretion. Coutinho successfully used a potent 19-norsteroid antiestrogen-antiprogesterone to treat excessive uterine bleeding in 16 patients with uterine leiomyomata. A reduction in the size of the tumors was noted.

Although the exact etiology of uterine leiomyomata is not known, the puzzle may be solved bit by bit by the research of Kornyei and colleagues, Wilson and coworkers, Tamaya and associates, Buchi and Keller, Sadan and colleagues, and others who continue to investigate estrogen and progesterone as possible growth factors. Although some data are conflicting, evidence suggests that both estrogen and progesterone are involved in the growth of uterine leiomyomata. The possibility that progesterone may play a role in the growth of leiomyomata is suggested by the work of Kawaguchi and coworkers, who found a higher mitotic count in leiomyomata obtained in the proliferative phase of the menstrual cycle.

Anderson and associates have shown that medroxyprogesterone acetate, a progestin, causes a decrease in

connexin-43 messenger ribonucleic acid levels in primary cultures of human myometrium and leiomyoma. Connexin-43 is a gap junction protein whose formation is stimulated by 17β-estradiol.

According to the research data of Brandon and colleagues, progesterone receptor messenger ribonucleic acid is overexpressed in uterine leiomyomata, compared with normal adjacent myometrium, suggesting that amplified progesteronemediated signaling is instrumental in the abnormal growth of these tumors. It is possible that the increased amount of progesterone receptor is caused by an alteration of estrogen or estrogen receptors in leiomyomata. The work of Kastner and coworkers and Nardulli and associates has demonstrated that progesterone receptor expression is regulated by estrogen.

Research in recent years has also focused on polypeptide growth factors in the stimulation of growth of leiomyomata. Polypeptide growth factors that have been investigated include epidermal growth factor, transforming growth factor alpha and beta, insulin-like growth factor (IGF), platelet-derived growth factor, vascular endothelial growth factor, and basic fibroblast growth factor. Other growth factors may also be involved. Polypeptide growth factor research has been performed by Goustin and colleagues, by Hoffmann and coworkers, by Lumsden and associates, and by others. A brief review of this research has been written by Vollenhoven and associates, who have been involved in the study of IGFs in uterine leiomyomata.

Results from a study by Strawn and colleagues demonstrate that IGF-I stimulates leiomyoma growth in a dose-related manner over that of normal myometrial tissue in monolayer culture. This stimulatory effect, in the absence of sex steroid hormones or other growth factors, provides additional support that IGF-I may play an important direct role in the pathogenesis of these tumors, possibly by modulating the response of these tumors to various levels of sex steroids. Dawood and Kahn-Dawood were unable to find any significant elevation in peripheral levels of serum IGF-I in nonpregnant premenopausal women with uterine leiomyomata of 14 weeks gestational size. The authors state, “Nevertheless, the finding does not detract from the potential paracrine or autocrine role that

IGF-I produced by leiomyoma cells may have either on the growth of its own or adjacent myomas or on the vascular supply and blood flow of the uterus and myomas.”

Rein and coworkers have proposed a hypothesis to explain the pathogenesis of myomata. This hypothesis suggests a critical role for progesterone in the growth of myomata. They state:

> The initiation and growth of myomas likely involves a multistep cascade of separate tumor initiators and promoters. The initial neoplastic transformation of the normal myocyte involves somatic mutations. Although the initiators of the somatic mutations remain unclear, the mitogenic effect of progesterone may enhance the propagation of somatic mutations. Myoma proliferation is the result of clonal expansion and likely involves the complex interactions of estrogen, progesterone, and local growth factors. Estrogen and progesterone appear equally important as promoters of myoma growth.

To treat patients with uterine leiomyomata properly, the gynecologic surgeon must be familiar with their pathology, growth characteristics, and clinical features. Leiomyomata may be single, but most are multiple. They develop most commonly in the uterine corpus and much less often in the cervix. They may develop in the round ligaments, but this is rare. Because they arise in the myometrium, they are all interstitial or intramural in the beginning. As they enlarge, they can remain intramural, but growth often extends in an internal or external direction. Thus, the tumor can eventually become subserous or submucous in location. A subserous tumor can become pedunculated and occasionally parasitic, receiving its blood supply from another source, usually the omentum. A submucous tumor can also become pedunculated and may gradually dilate the endocervical canal

and protrude through the cervical os. Indeed, a submucous myoma may descend through the vagina. Rarely, chronic uterine inversion results if the prolapsing submucous leiomyoma is attached to the top of the endometrial cavity and pulls the uterine fundus downward through the cervix.

In general, subserous leiomyomata contain more fibrous tissue than submucous leiomyomata. However, submucous leiomyomata contain more smooth muscle tissue than subserous leiomyomata. Sarcomatous change is more common in submucous tumors.

The typical uterine leiomyoma is a firm multinodular structure of variable size. The largest tumor, reported by Hunt in 1888, weighed more than 65 kg. Tumors of 4 to 5 kg are not rare, but most are smaller. In the operating room, leiomyomata appear as nodular tumors of different sizes that distort the uterus in various ways, depending on their size, location, and direction of growth. Growth between the leaves of the broad ligament and origin from the cervix may make surgical removal difficult. Subserous and subserous pedunculated tumors, as well as intraligamentous tumors, may create problems in diagnosis because they are difficult to distinguish from tumors arising from the adnexal organs (**Fig. 31.2**). When tumors cause symmetric enlargement of the uterus, they may be mistaken for a pregnant uterus on bimanual examination.

FIGURE 31.2 The uterine corpus is almost completely replaced by small and large myomas in intramural, subserous, and submucous positions. Some are pedunculated. A pedunculated submucous myoma is dilating the endocervical canal. A pedunculated subserous myoma is adjacent to the left ovary and will interfere with its palpation.

The “normal” intramural leiomyoma on section protrudes from the surrounding compressed myometrium. Ordinarily, there is a clear distinction between the myoma and the myometrium so that dissection between the two is easy to accomplish. Myomata usually can be removed from surrounding myometrium with ease. Although these tumors are not encapsulated, a clear distinction can usually be made between a myoma and the myometrium that surrounds it. The cut surface appears as glistening pinkish white and gray. It is firm, and there is a whorllike arrangement of the muscle and the fibrous tissue. In contrast to this typical appearance, the myometrium may be thickened by a diffuse, ill-defined nodularity of smooth muscle. This so-called diffuse leiomyomatosis usually involves all parts of the myometrium and causes symmetric enlargement of the uterine corpus. The nodules of smooth muscle are not distinct, contain little collagen, and merge with one another and the surrounding hypertrophied myometrium.

The extracellular matrix of leiomyomata is composed mostly of collagen but also contains proteoglycans and fibronectin. According to Fujita, myomata contain 50% more collagen than does normal myometrium, and the ratio of collagen type I to collagen type III is increased in myomata. Proteoglycans provide hydrated spaces between myoma cells. Fibronectin is a glycoprotein that mediates adhesion between myoma cells and extracellular matrix.

The most common change in leiomyomata is hyaline degeneration. The cut surface of a hyalinized area is smooth and homogeneous and does not show the whorllike arrangement of the rest of the leiomyoma. Almost all leiomyomata, except the smallest, have scattered areas of hyaline degeneration. Eventually, these may become liquefied and form cystic cavities filled with clear liquid or gelatinous material

(Fig. 31.3). Sometimes, the cystic change is so great that the leiomyoma becomes a mere shell and is truly a cystic tumor. Softness of a tumor does not necessarily indicate cystic degeneration. Fleshy leiomyomata may be equally soft.

FIGURE 31.3 Multiple leiomyomata are present. A large subserous myoma has undergone partial cystic degeneration.

Over time, with continued diminished blood supply and ischemic necrosis of tissue, calcium phosphates and carbonates are deposited in myomata. Their presence is evidence of a continuum of degenerative changes. The calcium may be deposited in varying amounts. If it is deposited at the periphery of the tumor, the leiomyoma may resemble a calcified cyst. Other calcified leiomyomata may show an irregular or diffuse distribution throughout with a honeycomb or mulberry appearance. When the degenerative change is advanced, the leiomyoma may become solidly calcified. Such calcified tumors have been called “womb stones.” Calcified leiomyomata are seen most often in elderly women, in African American women, and in women who have pedunculated subserous tumors. They are easily seen radiographically (Fig. 31.4).

Leiomyomata may undergo changes as a result of infection. Submucous leiomyomata are most commonly infected when they protrude into the uterine cavity, or especially into the vagina (**Fig. 31.5**). The pedunculated submucous leiomyoma thins out the endometrium as it grows inward, and eventually, the surface becomes ulcerated and infected (**Fig. 31.6**). An intramural leiomyoma in an involuting puerperal uterus can also become infected when endometritis is present. Microscopic abscesses can be found, and gross abscesses occasionally occur, particularly if the leiomyoma descends as low as the cervical canal. Such infections are usually streptococcal and may be virulent. *Bacteroides fragilis* infections also occur. Parametritis, peritonitis, and even septicemia may result.

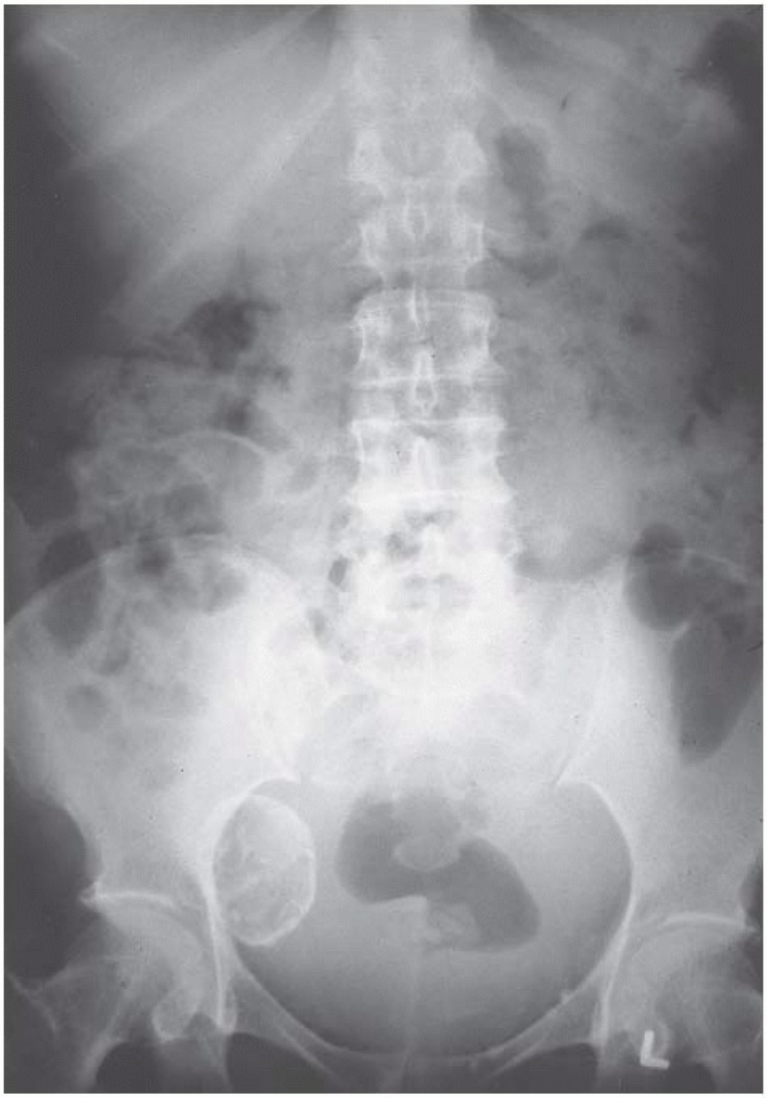

FIGURE 31.4 An abdominal radiograph shows typical calcification in a leiomyoma.

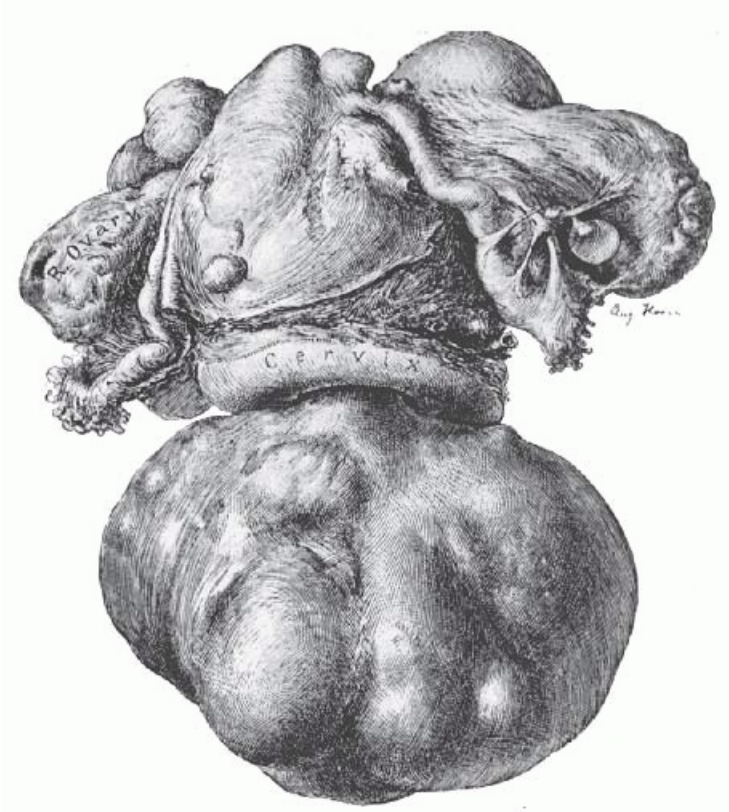

FIGURE 31.5 A large submucous pedunculated myoma has dilated the cervix and is now located in the vagina. Its pedicle is attached inside the uterine cavity. Morcellation of the myoma performed transvaginally allows clamping and ligation of the pedicle.

Necrosis of a leiomyoma is caused by interference with its blood supply. Occasionally, a pedunculated subserous leiomyoma twists, and if an operation is not done immediately, infarction results. Necrosis sometimes occurs in the center of

a large tumor simply as a result of poor circulation. Necrotic leiomyomata are dark and hemorrhagic in the interior. Eventually, the tissue breaks down completely. So-called red or carneous degeneration is seen occasionally, especially in association with pregnancy. This condition is thought to result from poor circulation of blood through a rapidly growing tumor. Thrombosis and extravasation of blood into the myoma tissue are responsible for the reddish discoloration (**Fig. 31.7**).

FIGURE 31.6 Pedunculated submucous myoma showing necrosis and ulceration.

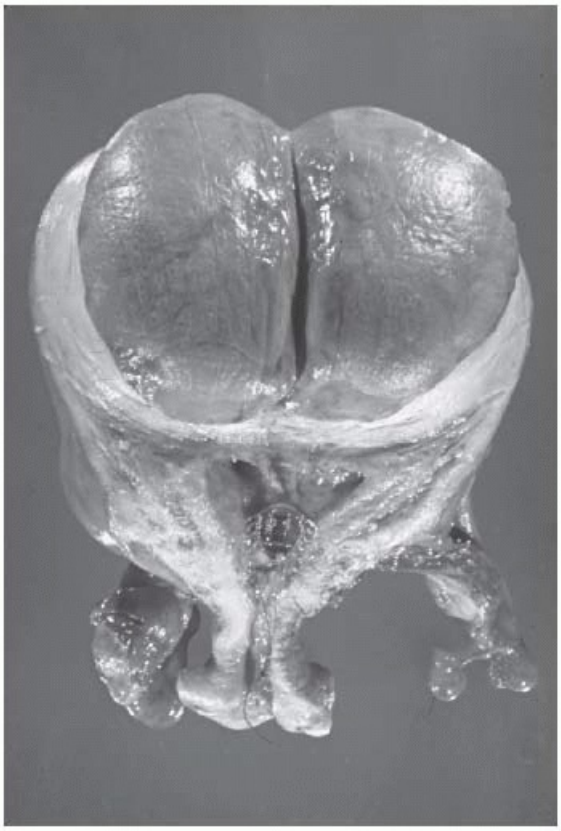

FIGURE 31.7 Degenerating leiomyoma showing carneous discoloration caused by thrombosis and extravasation of blood into the myoma tissue. A Dalkon shield can be seen in the endometrial cavity.

A subserous and especially a subserous pedunculated myoma may gradually outgrow its blood supply (**Fig. 31.8**). To keep the myoma tissue from undergoing complete ischemic necrosis, the omentum becomes adherent to the peritoneal surface of a pedunculated subserous myoma and provides whatever blood supply is needed. Eventually, the pedicle may disappear or twist, and the myoma will become completely free from the uterus, wander in the upper abdomen, and receive its "parasitic" blood supply from the omentum and other sources.

On occasion, fat occurs in leiomyomata as true fatty degeneration. The cut surface may have a yellowish discoloration. Infrequently, a deposit of true fat may form a fibrolipoma; however, the presence of fat in a leiomyoma is rare. Indeed, if fat is seen grossly or microscopically in a curettage specimen, one should not assume that it represents fatty degeneration of a leiomyoma. One should assume that the uterus has been perforated and that fragments of fat have been curetted from the mesentery or omentum.

The most important, but rare, change in a leiomyoma is sarcomatous degeneration. There is much variation in the reported incidence of sarcoma in leiomyomata. The incidence given by

Novak is 0.7%. However, a review of 13,000 myomata by Montague and associates at Johns Hopkins Hospital revealed 38 cases of malignant change, the incidence of sarcoma thus being 0.29%. Corscaden and Singh indicated by their study that the true incidence of sarcoma developing within uterine leiomyomata is no higher than 0.13% and is probably as low as 0.04%. It should be remembered that because most women with uterine leiomyomata do not undergo surgical removal, the true incidence of sarcoma in leiomyomata is probably much lower than 1 per 1,000 (0.1%).

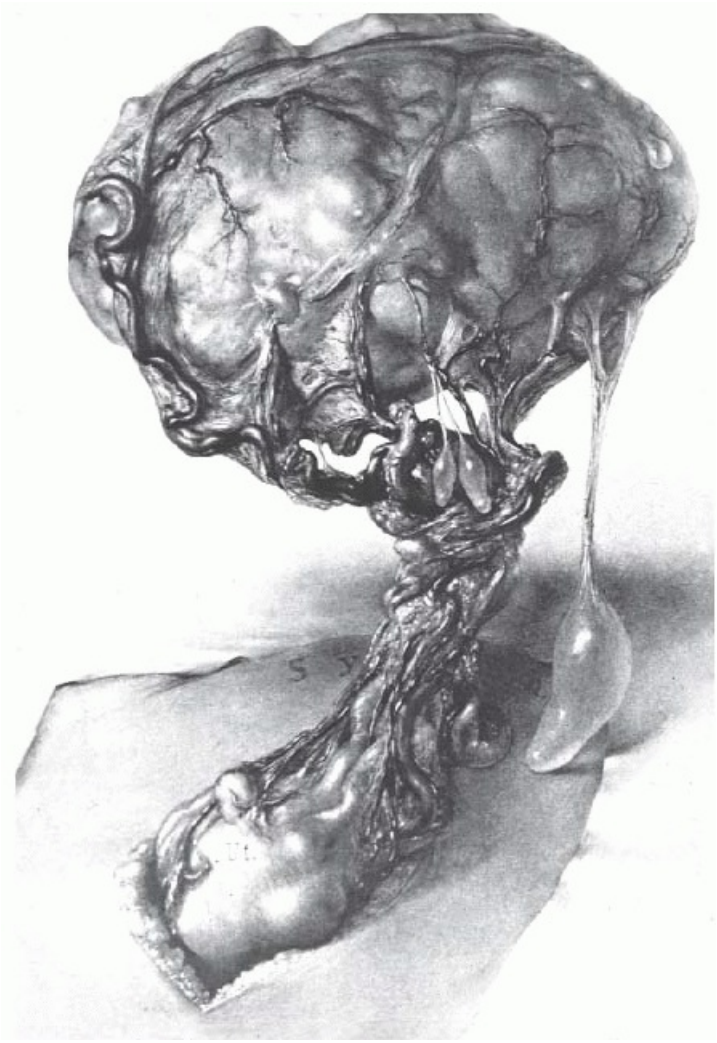

FIGURE 31.8 A subserous pedunculated myoma receives tenuous blood supply through its uterine pedicle. Such a myoma may wander in the upper abdomen and eventually receive its blood supply from other sources. It may also twist on its pedicle and undergo infarction.

After hysterectomy in 1,429 patients with presumed benign leiomyomata, the histologic diagnosis of leiomyosarcoma was made in seven (0.49%), according to a study by Leibsohn and coworkers. There was no evidence of malignancy in the endometrial sampling of any of these seven patients, and the diagnosis was suspected intraoperatively in only three. Uterine weights ranged from 120 to 1,100 g. In a woman between 41 and 50 years of age with presumed symptomatic leiomyomata, there is a 1 in 112 chance of a leiomyosarcoma being present, according to these authors. This information has important implications in the consideration of conservative or delayed treatment for these women. Parker and associates found that the total incidence of uterine sarcomas (leiomyosarcoma, endometrial stromal sarcoma, and mixed mesodermal tumor) among patients operated on for presumed benign uterine leiomyoma is lower (0.23%) than the 0.49% reported by Leibsohn and coworkers.

The difficulty in defining the true incidence of sarcomatous change is understandable if one is familiar with the histology of leiomyomata. Abundantly, cellular leiomyomata are relatively common, and at first glance, they suggest sarcoma; however, they lack a significant number of mitotic figures, and patients from whom such tumors are removed all remain well. Misinterpretation of the histologic picture of this type of cellular leiomyoma undoubtedly accounts for the increased incidence of leiomyosarcoma reported by some. When cutting into leiomyomata in the operating room, the surgeon finds that sarcomatous areas have a somewhat characteristic appearance, although the histologic diagnosis certainly cannot be made by gross examination. A sarcoma is likely to occur in a rather large leiomyoma and toward the center of the tumor, where the blood supply is poorest.

Instead of being firm fibrous tissue that grates when scraped with a knife blade, the tissue is soft and homogeneous and is described as resembling raw pork. Later, as necrosis of the malignant tissue occurs, it becomes more friable and hemorrhagic.

It has been difficult to understand uterine leiomyosarcoma, because pathologists do not agree on the criteria necessary for diagnosis. Some pathologists rely on the mitotic count. All tumors with less than 5 mitotic figures per 10 high-power fields are considered benign. All tumors with more than 10 mitotic figures per 10 high-power fields are called malignant. Those in between can be called smooth muscle tumors of uncertain malignant potential.

Other pathologists believe the mitotic count may have some significance but choose to rely instead on the presence of nuclear hyperchromatism, nuclear pleomorphism, or giant cells and other bizarre cell forms to make the diagnosis. Corscaden and Singh believe that no combination of histologic features is reliable and that only smooth muscle tumors that metastasize or recur are definitely malignant. We believe that all of these features should be taken into consideration for diagnosis and prognosis. When the tumor is confined to the uterus, both mitotic grade and histologic grade are important in the diagnosis and prognosis. A poor prognosis is associated with high mitotic counts and extremely atypical and anaplastic cytologic features. Bell and colleagues at Stanford University Medical Center assessed a variety of histopathologic features of 213 problematic smooth muscle neoplasms for which there were at least 2 years of clinical follow-up data. From the wide variety of light microscopic features assessed, the important predictors that emerged were mitotic index, the degree of cytologic atypia, and the presence or absence of coagulative tumor cell necrosis. Previously, the mitotic index was relied on exclusively to determine whether a uterine smooth muscle tumor was benign or malignant, but currently, an approach is used that incorporates additional histopathologic features.

A normal chromosome complement (46,XX) was observed by Meloni and coworkers in about 50% of leiomyoma cases. About 50% showed clonal abnormalities, such as those of chromosomes 1, 7, and 13, and t(12;14). Interstitial deletions of chromosome 7 were the ones most often involved, suggesting that this abnormality may be of primary importance in the cellular proliferation of leiomyomata. A relation between more aggressive histology and chromosomal abnormalities was also suggested.

Tumors that show obvious evidence of blood vessel invasion or spread to contiguous organs are rarely cured. The extent of the disease at the time of initial diagnosis is of even greater significance. In other words, when the diagnosis is suspected for the first time by the pathologist when he or she examines routine sections from a uterine leiomyoma, the patient almost always survives. However, if the diagnosis is made preoperatively by the gynecologist or is suspected during the operative procedure because of invasion of surrounding organs, the prognosis is grave.

An unusual atypical smooth muscle tumor was first described in the stomach by Martin and associates in 1960. Variously called *bizarre leiomyoma, leiomyoblastoma, clear cell leiomyoma,* and *plexiform tumorlet,* these atypical smooth tumors probably all belong together. The term *epithelioid leiomyoma* was adopted by the World Health Organization. Kurman and Norris have proposed that this term be used for all atypical leiomyomata. Histologically, the characteristic feature is the mixture of rounded polygonal cells and multinucleated giant cells present in epithelioid clear cell and plexiform patterns. Clinically, in the uterus most of these tumors are benign. They may rarely exhibit malignant potential. Malignancy is difficult to predict from histologic criteria because some metastases occurred from tumors that demonstrated very few mitoses. Kurman and Norris have suggested, however, that epithelioid neoplasms having more than 5 mitotic figures per 10 highpower fields should be called *epithelioid leiomyosarcomas* and that the term *epithelioid leiomyoma* should be applied when there is a lower level of mitotic activity. Although combination therapy (surgery plus radiation therapy or chemotherapy) may not be indicated for a patient with an epithelioid leiomyoma, follow-up should be considered

essential, as emphasized by Klunder and colleagues.

An unusual benign form of leiomyomata uteri, *intravenous leiomyomatosis,* was first recognized at the turn of the 20th century and has been reported sporadically since then. Before 1982, about 50 cases had been reported, according to Bahary and coworkers. Probably, at least that many have been reported since. Marshall and Morris presented the first detailed report of this entity in the American literature in 1959. The characteristic feature of this peculiar smooth muscle tumor is the extension of the polypoid intravascular projections into the veins of the parametrium and broad ligaments. Although there may be some difficulty in distinguishing such lesions from lowgrade sarcoma, they are distinctly different histologically from stromatosis uteri because the intravenous plugs are mainly smooth muscle in origin. In 1966, Edwards and Peacock collected 32 cases of intravenous leiomyomatosis, including two cases of their own, and reviewed the clinical experience with this condition. In approximately 50% of the cases, the intravenous tumor was confined to the parametrium; in 75%, it extended no further than the veins of the broad ligament. The observations of Edwards and Peacock suggest that the severed intravenous extensions are probably incapable of independent parasitic existence and remain dormant after removal of the uterus. However, the cases presented by Bahary and associates tend to refute this idea. Total surgical excision of the tumor should be attempted for successful therapy. Some patients have survived for many years after incomplete resection of the tumor. A review of 14 cases of this rare uterine tumor from the file of the Armed Forces Institute of Pathology has been reported by Norris and Parmley. In this series, two of three patients with incomplete resection had a recurrence; the recurrent tumor was excised surgically, and the patients were alive and free of disease 5 and 11 years after operation. The authors concluded that this tumor behaves clinically like a benign neoplasm, although its wormlike extensions may involve uterine, vaginal, ovarian, and iliac veins. The uterine veins in the broad ligaments are the most common sites of extension. The mitotic index is quite low, with the most active lesions showing only one mitosis per 15 high-power fields. The material from the Armed Forces Institute of Pathology provides histologic evidence consistent with both theories of origin of intravenous leiomyomatosis, namely, that it may be the result of unusual vascular invasion from a leiomyoma or may arise de novo from the wall of veins within the myometrium.

Extension of benign leiomyomatosis up the vena cava and into the right atrium has been reported in several cases, with a fatal outcome in some. Before 1994, approximately 27 cases of intravenous leiomyomatosis extending to the heart were reported. Several recent cases requiring open heart surgery to remove the intracardiac tumor thrombosis have been successful and without recurrence. All reported cases occurred in women. Tierney and colleagues reported that substantial quantities of cytoplasmic estradiol and progesterone receptors were found in the right atrial tumor removed from a patient with intravenous leiomyomatosis. Their patient was treated with the antiestrogen tamoxifen because of residual tumor in the vena cava that could be estrogen dependent. lrey and Norris have presented evidence that female reproductive steroids can produce intimal proliferation of veins in predisposed persons. Interestingly, of the 30 patients with leiomyomata and leiomyosarcomas of the vena cava reviewed by Wray and Dawkins, 80% were female. Both intravenous leiomyomatosis and benign metastasizing leiomyoma have been reported to metastasize to the lung. As suggested by Banner and coworkers, by Horstmann and associates, and by Evans and colleagues, oophorectomy may be indicated in patients with these conditions, again because of the possibility that these tumors may be estrogen dependent or that estrogens may have the ability to stimulate their development, whether in a uterine or extrauterine location and whether they appear to be endothelial or mesenchymal in origin.

The possibility of metastases from a histologically benign uterine leiomyoma has been discussed by Idelson and Davids and by Clark and Weed. When such a case occurs, it is usually settled by finding a sarcomatous component in the leiomyoma or by finding evidence of intravenous leiomyomatosis. However, multiple cases have now been reported in which a benign uterine leiomyoma metastasized. Idelson and Davids' case showed metastases to the aortic lymph nodes. The patient reported by Cramer and associates had metastatic tumor to

the omentum, ovary, periaortic lymph node, and lung. In each location, the histology and estrogen receptor content of the tumor resembled those of a benign leiomyoma. The recommended treatment consists of surgical removal with castration and little or no estrogen replacement.

Leiomyomatosis peritonealis disseminata is sometimes confused with intravenous leiomyomatosis. However, only subperitoneal surfaces of the uterus and other pelvic and abdominal viscera are involved with leiomyomatosis peritonealis disseminata, and invasion of the lumen of blood vessels does not occur. Only about 15 cases have been reported, according to Pearce. All occurred in patients in the reproductive years who often had large uterine leiomyomata and were usually pregnant or taking oral contraceptives. The condition is likely to be confused with a disseminated intraabdominal malignancy, but it is entirely benign histologically and clinically. Parmley and colleagues have demonstrated the histologic similarities between this peritoneal lesion and the decidual change of the mesothelium in the pelvis, and they propose that the condition represents a benign reparative process in which fibroblasts replace soft peritoneal decidua. They suggest that this fibrotic reaction occurs during pregnancy and especially in the postpartum period, resulting in nodules with a pseudoleiomyomatous pattern. Similar findings have been noted in patients with endometriosis treated with prolonged Enovid therapy. These findings indicate that prolonged and continuous stimulation of subperitoneal decidua by either endogenous or exogenous estrogen and progesterone is important in the pathogenesis of this condition. Parmley and coworkers suggest that the condition is more appropriately called *disseminated fibrosing deciduosis.* Goldberg and associates, on the other

hand, on the basis of electron microscopy studies, believe that the tumors arise from smooth muscles of small blood vessels. This has been confirmed by Ceccacci and colleagues. It has been possible to show a continuum from fibroblastic cells through myofibroblasts to leiomyocytes. Although the cell of origin of this tumor is still controversial, the tumor is benign, and the acceptable treatment to date is total abdominal hysterectomy and bilateral salpingo-oophorectomy. If this tumor occurs in the omentum, an omentectomy should also be performed to define more clearly the histologic nature of the lesion.

In attempting to distinguish between benign and malignant disease in a patient with uterine leiomyomata who also has unusual clinical findings, it is appropriate to keep the entities mentioned earlier (intravenous leiomyomatosis, atypical bizarre leiomyoma, benign metastasizing leiomyoma, and disseminated intraperitoneal leiomyomatosis) in mind. Although they all have features similar to those of malignant disease, they are almost always benign and amenable to treatment. One should also remember that benign uterine leiomyomata have been associated with pseudo-Meigs syndrome in a few cases. Meigs reported five cases in 1954. In these cases, the ascites did not reappear after removal of the uterine leiomyomata.

There is a high frequency of endometrial hyperplasia when the uterus contains leiomyomata. Degligdish and Loewenthal reported that cystic glandular hyperplasia is often found in the endometrium at the margin of the leiomyoma. Yamamoto and coworkers have reported high concentrations of estrone and estrone sulfatase activity in the endometrium overlying a myoma. They suggest that the local hyperestrogenism in the endometrium overlying a leiomyoma may assist in the genesis or enlargement of these tumors.

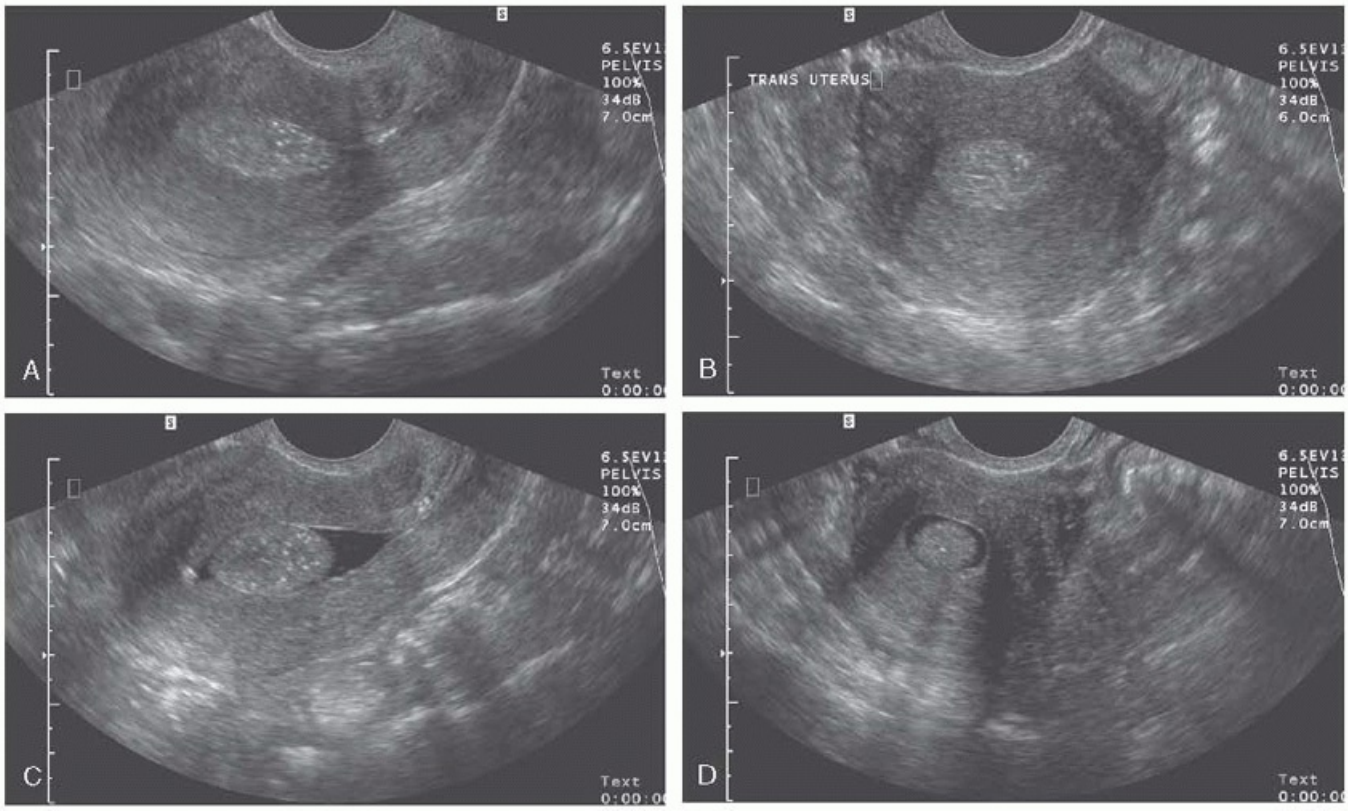

FIGURE 31.9 Sonographic images of a 48-year-old patient with a history of pelvic pain. Both transabdominal and transvaginal images were obtained on cycle day 8. Longitudinal (**A**) and transversely oriented (**B**) transvaginal images reveal a suspicious endometrial cavity, suggesting a thickened lining, endometrial polyp, or a submucosal myoma. **C and D:** Fluid-enhanced sonohysterographic studies clearly demonstrate a mass lesion and not generalized thickening of the endometrial lining. The patient underwent a hysteroscopy and uterine curettage, which revealed a histologically confirmed endometrial polyp. (Images courtesy of Jeff Dicke, MD.)

Gynecologic surgeons are especially concerned about the vascularity of individual leiomyomata and about the blood flow to the uterus in the presence of multiple and sometimes very large leiomyomata. These considerations are pertinent when surgery, especially myomectomy, is contemplated.

According to Vollenhoven and associates, the vascularization of leiomyomata was studied by Vasserman and colleagues, and the findings were presented to the World Congress of Gynecology and Obstetrics in 1988. Using femoral arteriography, selective intraoperative angiography, radiography, and injection of surgical specimens, these investigators showed that leiomyomata have a rich vascular supply, including blood lakes within tumors. They found more than one nutrient vessel per myoma. Venous channels were predominantly peripheral, whereas the arterial supply was both internal and peripheral. Farrer-Brown and coworkers, using radiologic methods, demonstrated that myomata in various locations within the myometrium can cause congestion and dilatation of endometrial venous plexuses by obstructing venous return. These obstructions can result in ectasia of endometrial and myometrial venules (Fig. 31.9). The degree of vascularity of leiomyomata was also studied by Karlsson and Persson. Vascularity varied from many, to few, to no intrinsic vessels demonstrable. Generally, the sum of the width of the uterine arteries increases with the size of the uterus, but the diameter of the two sides sometimes differs markedly. A rich vascularity was found in 22 of 34 uteri with leiomyomata, but with increasing size, there is a tendency to less vascularity. In none of five cases with very large (20 cm or more) leiomyomata uteri was the vascularity rich. The intrinsic vessels were few in two cases and absent in three cases.

CLINICAL FEATURES OF UTERINE LEIOMYOMATA

Asymptomatic Leiomyomata

Most leiomyomata are asymptomatic. Untold numbers of such symptomless leiomyomata are removed surgically by either hysterectomy or myomectomy when they would have been better left undisturbed. The incidence of malignancy in leiomyomata is less than 0.1%, which is lower than the operative mortality rate of hysterectomy in the average hospital; therefore, unless there is some reason to suspect malignant change, the risk of the operation for asymptomatic leiomyomata may exceed the danger of malignancy. A history of rapid growth, however, particularly postmenopausal growth, does indicate removal, even when the tumor produces no symptoms. Signs of rapid enlargement are important in all patients but are even more ominous in older patients. In younger patients, the most common reason for rapid enlargement of a uterus with leiomyomata is pregnancy. If pregnancy can be ruled out, a leiomyosarcoma may be suspected but is rarely found.

Small leiomyomata that are asymptomatic need only to be observed from time to time, with pelvic examinations perhaps every 6 to 12 months and pelvic ultrasonography (US) when indicated. In the beginning, frequent examination may be indicated to determine the growth rate. Such tumors may remain remarkably constant in size for years. If small leiomyomata are discovered late in menstrual life, it is unusual for symptoms to appear or for surgical treatment to be required. Larger tumors can also be watched safely, but if a policy of watchful waiting is adopted, one should be very sure of the nature of the tumors. If there is uncertainty of the uterine or ovarian origin of a tumor, as may well be the case when the tumor fills the whole pelvis or when a pedunculated tumor is felt in the adnexal region (**Fig. 31.10**), special diagnostic procedures may be indicated. Pelvic examination by an experienced gynecologist can usually clear up the uncertainty. In difficult cases, an examination under anesthesia may be necessary. Laparoscopy may be of great value in determining the nature of an adnexal mass. Before invasive techniques are used, however, noninvasive diagnostic evaluation should be performed. These include radiographic studies of the abdomen and pelvis, US, and computed tomography (CT). The characteristic calcification in a leiomyoma may be seen on radiographs. The US and CT features of uterine leiomyomata have been well described. However, mistakes in the interpretation can still be made. Tada and associates reported that 5% of patients given the diagnosis of uterine leiomyomata by CT actually had an ovarian tumor at operation. Therefore, if uncertainty about the diagnosis persists, laparoscopy or laparotomy should still be performed.

FIGURE 31.10 Although this central pelvic mass may feel like a multiple leiomyomatous uterus on bimanual

pelvic examination, it is actually a bilateral ovarian malignancy. Differentiation between these two diagnoses may require special diagnostic procedures.

When large asymptomatic leiomyomata occur in premenopausal women who have had their families or in whom future childbearing is not desired, a recommendation for removal may be made. It is impossible to predict which patients will become symptomatic in the remaining years before menopause. However, such tumors, with additional years to grow, are likely to require surgical removal eventually. Therefore, it is better to remove them when the patient is a good operative candidate of relatively low operative risk and when conservation of normal ovaries with a good blood supply can be easily accomplished. Such tumors should usually be 12 to 14 weeks in gestational size or larger. Depending on a variety of factors, either myomectomy or hysterectomy can be recommended to the patient. GnRH agonists may be useful in women approaching menopause to control symptoms or asymptomatic uterine myoma growth until menopause. The regrowth of tumors after the cessation of treatment limits the usefulness of these agents, however. Nakamura and Yoshimura reported their experience with GnRH agonists in the treatment of uterine leiomyomata in perimenopausal women. One third of patients reached menopause after 16 weeks of treatment, thus avoiding the need for surgery.

Reiter and colleagues studied 93 consecutive patients undergoing hysterectomy for leiomyomata. When the uterus was larger than 12 weeks gestational size, there was no increased incidence of surgical complications compared with women with smaller uteri. On the basis of this small series, the authors concluded that hysterectomy need not be recommended to women with large asymptomatic uterine leiomyomata to avoid a possible increased risk of surgical complications.

There is no uniform size of an asymptomatic leiomyomatous uterus that can be used as an indication for hysterectomy or myomectomy. When size is the only significant indication for surgery in an asymptomatic patient, the location of the tumors is more important than the total uterine mass. When the leiomyomata are located in the cornual area or in the lateral wall of the uterus and obscure the anatomy of the adnexa and broad ligament, the risk of error in the early recognition of an ovarian tumor is greater. In such cases, one must carefully weigh the advantages and disadvantages of the conservative approach to the management of uterine leiomyomata. When adnexal tumors are present, it is critical that the origin of these tumors be confirmed. The diagnostic studies mentioned earlier should be performed to establish clearly that the tumors are of uterine origin before a decision is made to follow up the patient rather than operate. It is unacceptable to wait to see whether an adnexal tumor enlarges before identifying the site of origin of the mass as either uterine or ovarian. Ovarian carcinoma remains the most lethal disease of the female reproductive tract and the most difficult to diagnose early. Every diagnostic and therapeutic effort must be made to avoid errors in the clinical evaluation of pelvic neoplasms (**Fig. 31.10**). In women who are approaching menopause, relatively large uterine leiomyomata can be kept under observation with the knowledge that after menopause, they will not increase in size and may actually regress somewhat. Still, one must be certain

that the entire central pelvic mass is a leiomyomatous uterus. Patient management is largely dependent on knowledge of the exact location and size of leiomyomas. Imaging modalities play an important role in determining patient management, especially when differentiating a benign leiomyoma from other pathologic conditions that may require different therapies.

Uterine size as an indication for surgical intervention in women with leiomyomata has been thoughtfully discussed by Friedman and Haas. These authors point out that many gynecologists advocate surgical removal of leiomyomata when the uterus reaches 12 weeks gestational size or greater, regardless of the presence or absence of significant symptoms. Historical reasons given for surgical intervention include the following:

- The inability to accurately assess the ovaries by examination

- The possible malignancy of the pelvic mass
- The potential for compromise of adjacent organ function if the mass continues to enlarge
- The greater risk of surgical complications if the mass grows to a larger size
- The potential for better fertility if myomectomy is performed when the uterus is smaller
- The possibility of continued growth of uterine leiomyomata if hormone replacement therapy is given after menopause

Friedman and Haas find very little in the literature to support these indications for surgical intervention and believe the availability of modern high-resolution US and magnetic resonance imaging (MRI) allows for expectant management in many patients with large asymptomatic uterine leiomyomata. They prefer to give primary consideration to the presence and severity of myoma-related symptoms in deciding whether surgical intervention is indicated. We believe that such a course of expectant management is appropriate only when there is relative certainty regarding the benign nature of the central pelvic mass and all of its components and when it is possible to get the patient to return for periodic assessment of gynecologic symptoms and findings on pelvic examination. Repeat MRI may also be required occasionally.

If one elects to observe a patient with a relatively large asymptomatic uterine leiomyoma, it is a good rule to obtain an excretory urogram or renal ultrasound. Everett and Sturgis showed many years ago that ureteral compression at the pelvic brim may occur so that hydroureter and hydronephrosis develop (**Fig. 31.11**). It is usually the symmetrically enlarged uterus with intramural leiomyomata that extends near or above the umbilicus and rests on the pelvic brim that compresses the ureters, in the same way as a symmetrically enlarged gravid uterus. The process is usually slow and painless even when moderate to severe hydronephrosis has occurred. Pyelographic evidence of kidney damage may be the determining factor in a decision to operate on a patient with an entirely asymptomatic leiomyoma. The irregularly and asymmetrically enlarged uterus with subserous tumors usually does not produce pressure on the ureters.

After menopause, asymptomatic leiomyomata generally should be left undisturbed. Again, the gynecologist must be absolutely certain that an ovarian neoplasm can be ruled out. In the postmenopausal years, shrinkage of myomata and the myometrium occurs. However, the myometrial shrinkage may be disproportionately greater than the myoma shrinkage. Therefore, a myoma in an intramural location before menopause may become a submucous myoma after menopause and then become symptomatic for the first time, usually with postmenopausal bleeding.

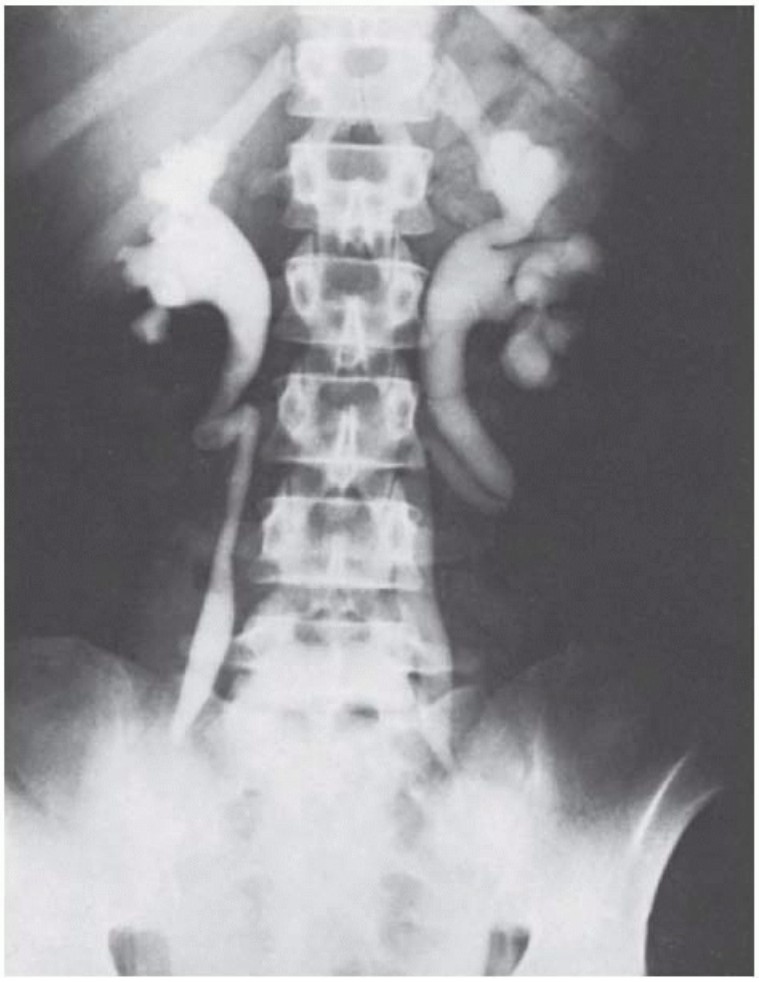

FIGURE 31.11 Bilateral ureteral obstruction and dilatation from pressure of large leiomyomata.

In menopausal women, the appearance of even the slightest trace of vaginal bleeding should make one suspect cervical or endometrial malignancy or the possibility of sarcomatous change in the leiomyoma (**Figs. 31.12** and **31.13**). Careful pelvic examination, Papanicolaou smear, and evaluation of the cervix by colposcopy or biopsy, pelvic US, fractional curettage, and perhaps hysteroscopy should be done. If the bleeding remains unexplained and the presence of atrophic vaginitis or the use of exogenous estrogens has been excluded, the leiomyomatous uterus should be removed because of the risk of sarcomatous change.

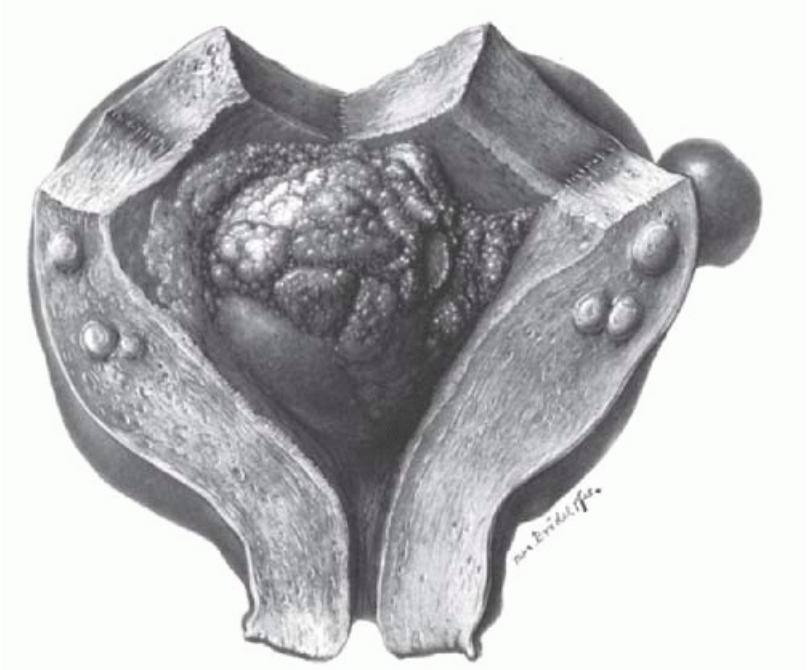

FIGURE 31.12 Adenocarcinoma of the endometrium is present in a symmetrically enlarged leiomyomatous uterus.

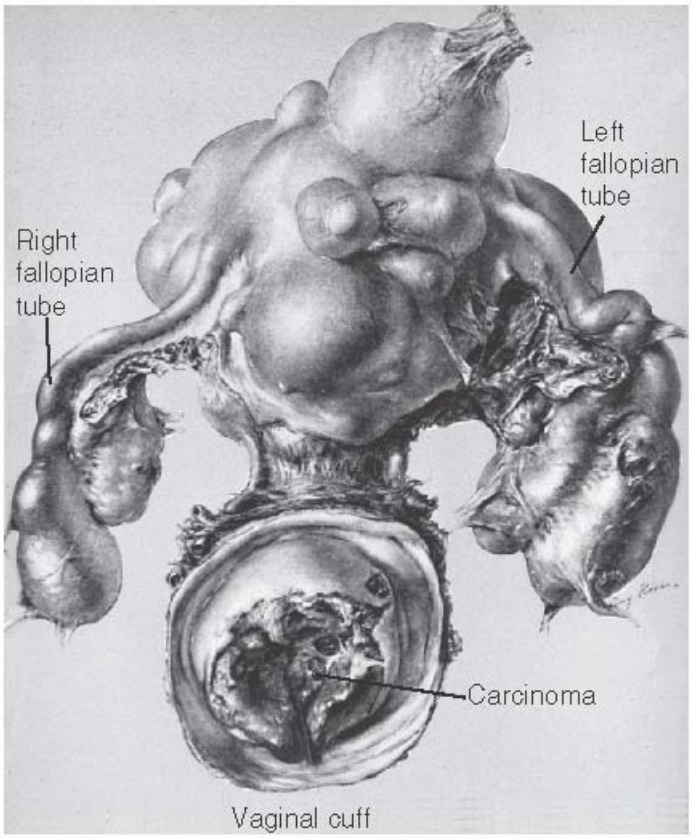

FIGURE 31.13 This specimen shows multiple uterine leiomyomata but also shows chronic pelvic inflammatory disease and cervical carcinoma. Patients with uterine leiomyomata may have abnormal bleeding, but a coexisting cervical carcinoma may also cause bleeding.

Transabdominal and endovaginal US are the standard imaging modalities for the detection of leiomyomas. Pelvic US by transvaginal and transabdominal techniques is most useful because of good patient tolerance, relatively low cost, availability, and accuracy when performed by well-trained and experienced ultrasonographers (**Fig. 31.14**). Ultrasonography is the most cost-effective screening mechanism for uterine masses suggestive of myomata. Sonographic criteria for diagnosis have been well described. Generally, abdominal US is unable to detect myomas less than 2 cm in diameter. Transvaginal probes have allowed for improved visualization of both the uterus and adnexa. With higher frequencies, sensitivity in the detection of small myomas has substantially increased. In a series evaluated by Fedele and colleagues using endovaginal ultrasound before hysterectomy, submucous leiomyomas were identified with a sensitivity of 100%. Difficulties may arise, however, if myomas are small or pedunculated, patients are obese, or the uterus is retroverted.

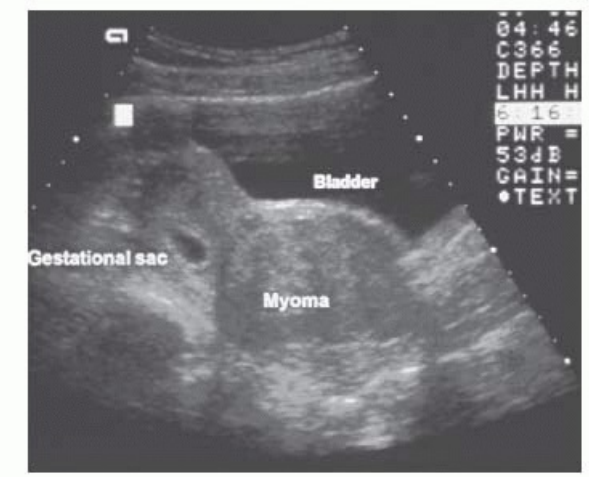

FIGURE 31.14 An US study shows a cervical myoma and a very early intrauterine pregnancy.

Transvaginal fluid-enhanced vaginal probe sonography (sonohysterography) is a useful technique to assess myomata that distort the endometrial cavity. This technique has little to no complications and is generally well tolerated with only mild cramping described by patients. The limitation of detection of leiomyomas with this modality is 0.5 cm diameter. In a study by Hoetzinger, the majority of intrauterine myomata (14 of 16, or 88%) were detected by sonohysterography. Ultrasound transducing catheters have been suggested as a potential tool to supplement abdominal and endovaginal sonography. Threedimensional data display has recently undergone development and application in sonography; however, the role in evaluation and management of leiomyoma remains unclear (**Fig. 31.9**).

There is no technique that reliably identifies a leiomyosarcoma. Plain abdominal or pelvic radiographs and hysterosalpingography are older, standard techniques that are still useful in assessing uterine size, calcification in myomata, intrauterine filling defects caused by submucous myomata, and tubal patency. These techniques, combined with US, are the most useful for assessing patients with a central pelvic mass thought to be a leiomyomatous uterus. CA-125 levels may be elevated in women with uterine leiomyomata, but the levels are generally lower than those in patients with ovarian cancer.

Symptomatic Leiomyomata

Less than 50% of patients with uterine leiomyomata have symptoms. Symptoms may be single or multiple and depend on the location, size, and number of tumors present. A clinical and pathologic study of 298 patients with uterine leiomyomata by Persaud and Arjoon revealed no significant relation between the presenting symptoms and the presence of degenerative changes in the tumors. Some form of degeneration was demonstrated in 65% of the specimens, with hyaline degeneration accounting for 63% of all types of degeneration. Hyaline degeneration produces no characteristic symptoms. Symptoms, especially pain and fever, may be present in some patients with red degeneration of a leiomyoma during pregnancy, with torsion and infarction of a subserous pedunculated leiomyoma, or with an infected leiomyoma. A discussion of the signs and symptoms caused by uterine leiomyomata follows.

Abnormal Bleeding

It is surprising but not unusual that even patients with large uterine leiomyomata may have a history of normal menstruation. Such patients should be questioned carefully about recent slight increases in the amount, duration, and frequency of menstruation. Some patients with a history of normal menstruation are found to have iron deficiency anemia from a gradual increase in menstrual blood loss that even the patient has not recognized. If a case of uterine leiomyomata is to be followed, the patient should be asked to monitor her menstrual blood loss carefully and should be given instructions to keep a menstrual calendar and monthly record of the number of

pads or tampons used each day. A more objective measurement of the amount of menstrual blood loss using the method of Hallberg and Nilsson may be helpful in doubtful cases. Iron depletion may not be evident by laboratory determination unless one checks serum ferritin levels. In the early months of increased menstrual blood loss, the hemoglobin and hematocrit values are normal. Heavy menstruation does not cause anemia until iron stores are first depleted.

Abnormal bleeding occurs in about one third of patients with symptomatic uterine leiomyomata and commonly indicates that treatment is necessary. The menstrual flow is usually heavy (menorrhagia) but can also occur for prolonged periods

of time at irregular intervals (metrorrhagia). It may also be both heavy and prolonged (menometrorrhagia). Abnormal bleeding may be associated with submucous, intramural, and subserous tumors, but there is a distinct clinical impression that bleeding is more common and more severe in the presence of submucous tumors. The submucous leiomyoma bleeds freely at menstruation and may also bleed between periods as a result of passive congestion, necrosis, and ulceration of the endometrial surface over the tumor and ulceration of the contralateral uterine surface. If the submucous myoma is pedunculated, there is usually a constant, thin, blood-tinged discharge in addition to the menorrhagia. An intramural tumor that is just beginning to encroach on the uterine cavity can also be responsible for menorrhagia. Intramural leiomyomata near the serosal surface and pedunculated subserous tumors can also be associated with abnormal bleeding. When bleeding occurs with such tumors, however, one should search for some other lesions to account for it. The mere presence of leiomyomata in a woman who has abnormal uterine bleeding is not proof that the leiomyomata are causing the bleeding. This fact is important, particularly when there is intermenstrual bleeding. When a patient with leiomyomata has intermenstrual bleeding, it is a rule in our practice to examine and study the cervix carefully with special diagnostic procedures and to sample and evaluate the uterine cavity before we proceed with treatment of the leiomyomata. If an endometrial or cervical malignancy is detected, the treatment of the leiomyomata may need to be altered.

There are several mechanisms by which leiomyomata can cause abnormal bleeding, although a single specific mechanism may not be apparent in a particular patient. According to Sehgal and Haskins, the surface area of the endometrial cavity in a normal uterus is 15 cm^2. The surface area of the endometrial cavity in the presence of leiomyomata may exceed 200 cm^2. These authors demonstrated a correlation between the severity of the bleeding and the area of endometrial surface. In addition to an increased surface area from which to bleed, the endometrium may demonstrate local hyperestrogenism in areas immediately adjacent to submucous tumors, and endometrial hyperplasia and endometrial polyps are commonly found. Degligdish and Loewenthal noted a broad spectrum of histologic abnormalities in the endometrium associated with leiomyomata, ranging from atrophy to hyperplasia. Thinning and ulceration of the endometrial surface may be present over large submucous tumors; smaller ones may show slight thinning without ulceration. The presence of leiomyomata may interfere with myometrial contractility as well as contractility of the spiral arterioles in the basalis portion of the endometrium. Miller and Ludovici suggested that anovulation and dysfunctional uterine bleeding are more common in the presence of uterine leiomyomata.

Sampson in 1913 was the first to study the blood supply of uterine leiomyomata and its effect on uterine bleeding. More recent studies have been performed by Faulkner and by Farrer-Brown and associates. The most prominent and important change is the presence of endometrial venule ectasia. Tumors that are strategically located in the myometrium may cause obstruction and proximal congestion of veins in the myometrium and endometrium. Thrombosis and sloughing of these large dilated venous channels within the endometrium produce heavy bleeding (**Fig. 31.15**).

Makarainen and Ylikorkala have presented evidence that further supports the concept that prostanoids play a

role in primary menorrhagia. They found that the production of 6-keto-prostaglandin F1 alpha (6-keto-$PGF_{1\alpha}$), a metabolite of prostacyclin (PGI_2), and thromboxane B_2 (TXB_2), a metabolite of thromboxane A_2 (TXA_2), was normal in menorrhagic endometrium. However, the balance between TXA_2 and PGI_2 shifted to a relative TXA_2 deficiency and was negatively related to blood loss in patients with menorrhagia. Although ibuprofen decreased the blood loss in patients with primary menorrhagia, it failed to reduce myoma-associated menorrhagia. The authors suggest that uterine factors other than prostanoids are more important in causing menorrhagia associated with uterine leiomyomata.

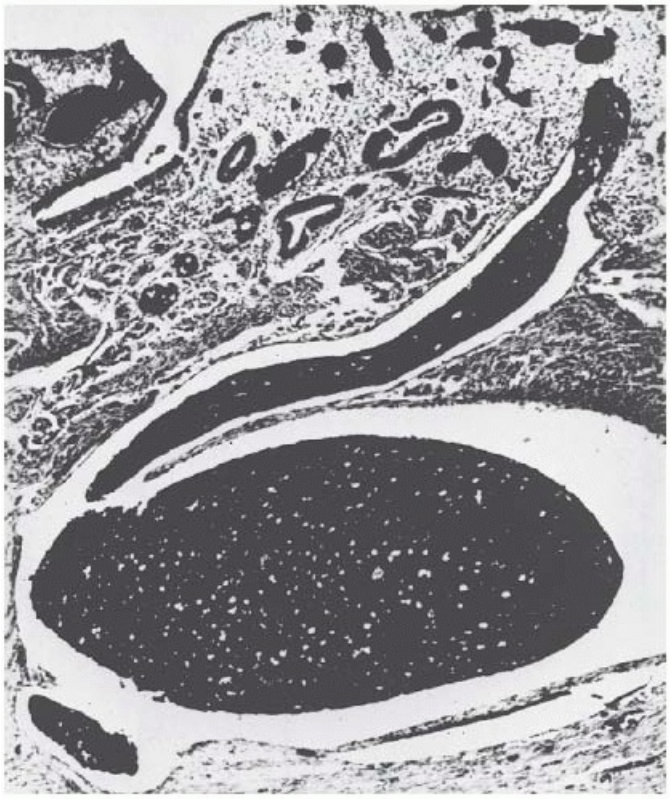

FIGURE 31.15 Dilated endometrial venous space communicating with a grossly enlarged vessel in the inner myometrium of a uterus with submucous leiomyomata. (Reprinted from Farrer-Brown G, Beilby JO, Tarbit MH. Venous changes in the endometrium of myomatous uteri. *Obstet Gynecol* 1971;83:743, with permission. Copyright 1971, The American College of Obstetricians and Gynecologists.)

In most cases, when bleeding occurs postmenopausally and leiomyomata are discovered on bimanual examination, the bleeding is due to some other factors, such as cervical or endometrial abnormalities, atrophic vaginitis, or exogenous estrogen, and the leiomyomata are purely incidental. Occasionally, however, the postmenopausal leiomyoma can be responsible for the bleeding. As stated earlier, leiomyomata that do not bleed during the menstrual life of the patient have been found to migrate to a submucous position in later years. This occurs because after menopause, the myometrium atrophies and the uterine wall becomes thinner. Leiomyomata also shrink somewhat, but not as much as the surrounding myometrium. Thus, a leiomyoma that was intramural before menopause may work itself into a submucous position after menopause, become ulcerated, and bleed. Postmenopausal growth of uterine leiomyomata may indicate malignant change, especially if associated with postmenopausal bleeding. We have rarely observed postmenopausal growth in a leiomyoma without finding malignancy in the tumor; whenever there is enlargement of the leiomyoma after menopause, one should seriously consider the possibility of sarcomatous change and remove the leiomyoma.

Patients with heavy menstruation and uterine leiomyomata should be evaluated for the presence of submucous myomata. Even patients without palpable evidence of uterine leiomyomata or uterine enlargement who have

should be evaluated for the presence of submucous myomata. When endometrial curettage is performed, irregularity of the uterine cavity may suggest the presence of a submucous myoma. However, a submucous myoma may not be detected with the curette. An accurate diagnosis is more likely to be made by hysterosalpingography, conventional transvaginal or transabdominal US, sonohysterography, MRI, or hysteroscopy. Cincinelli and colleagues reported their experience with transabdominal sonohysterography, a technique that involves transabdominal ultrasonographic scanning while 30 mL of sterile isotonic saline is slowly injected into the uterine cavity. According to these investigators, this technique provided the most accurate evaluation of the size of submucous myomata, intracavitary and intramural growth, and location within the uterine cavity, with sensitivity, specificity, and predictive values of 100%.

Pressure

Evidence of pressure on nearby pelvic viscera may be an indication for treatment. The urinary bladder suffers most often from such pressure, giving rise to urgency and frequency of urination and sometimes even urinary incontinence (**Fig. 31.16**). Although this symptom is common with large leiomyomata, one frequently finds the pelvis filled with leiomyomata when there is no urinary frequency. Occasionally, acute retention of urine or overflow incontinence results from a leiomyoma and necessitates surgical intervention. These effects can occur as a result of rapid interior growth of the leiomyoma with compression of the urethra and bladder neck against the pubic bone. More often, a tumor the size of a 3-month pregnancy may become incarcerated in the cul-de-sac, wedging the cervix forward against the urethra and obstructing the flow of urine through the urethra. A large pedunculated submucous tumor may fill and distend the vagina and press the urethra against the symphysis, causing urinary retention.

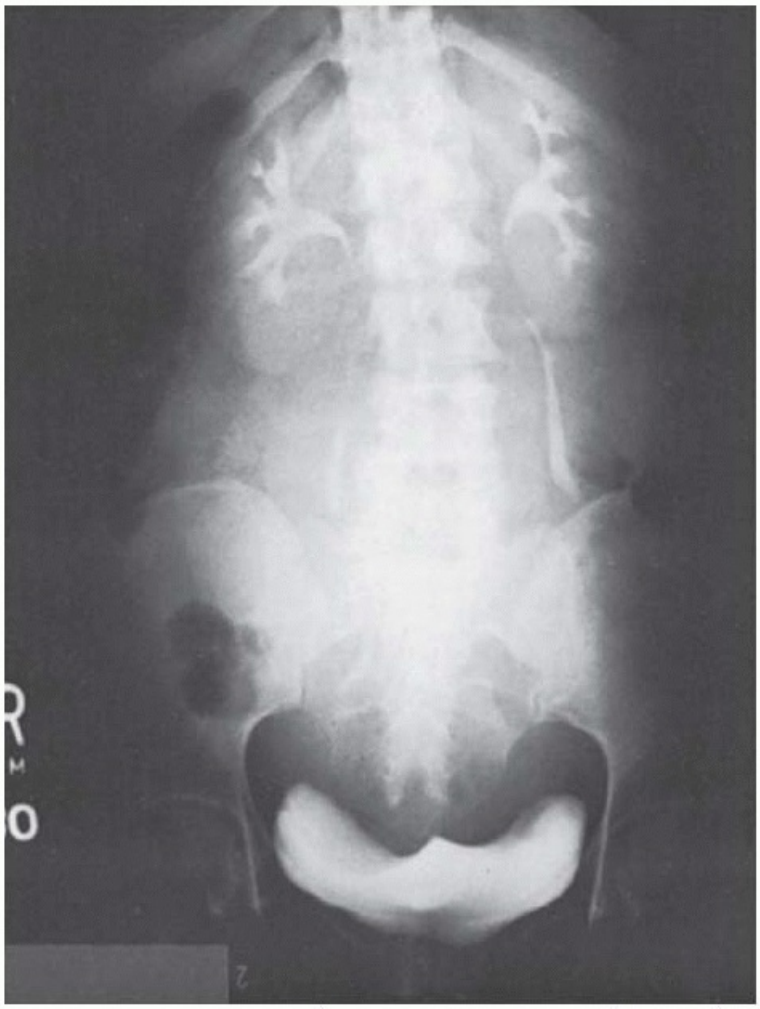

FIGURE 31.16 Cystogram and intravenous pyelogram showing distortion of the bladder by pressure from a leiomyoma.

As pointed out by Mattingly, one can expect to encounter women who have uterine leiomyomata of significant size and in addition have protrusion of the bladder base and posterior urethra through a widened levator muscle hiatus and a weakened urogenital diaphragm. Both conditions are relatively common. In addition to the usual symptoms produced by the leiomyomata, socially disabling stress urinary incontinence may be present. When the anterior wall of the uterus is greatly distorted by the presence of these tumors, pressure against the bladder can cause urinary frequency. If anatomic pressure equalization incontinence is also present, it may be aggravated by the increased intravesical pressure caused by the leiomyomata. However, the presence of anatomic stress urinary incontinence has no etiologic relation to the uterine enlargement caused by the leiomyomata.

Silent ureteral obstruction from pressure against the pelvic brim is an uncommon complication of uterine enlargement caused by multiple large leiomyomata. Such an asymptomatic anatomic change occurs more often with a symmetrically enlarged leiomyomatous uterus that becomes large enough to fill the pelvis and compress the ureter against the pelvic sidewalls (**Fig. 31.11**). Although an infrequent complication, the obstruction can occur in either ureter, depending on the location of the uterine tumors. If there has been no infection or parenchymal damage to the kidney, this anatomic alteration is completely reversible with removal of the uterus and relief of the pressure against the ureter. However, if urinary tract obstruction from leiomyomata has been neglected, uremia may result. Removal of the tumor and relief of obstruction are necessary to restore kidney function. Chronic bladder neck obstruction from uterine leiomyomata can be so severe as to cause a remarkable increase in the thickness of the bladder wall and enlargement of the bladder resembling that seen in men with urethral obstruction from prostatic enlargement. Indeed, in these neglected cases, the bladder may fill the entire lower abdominal wall so that an incision above the umbilicus is required to enter the peritoneal cavity to remove the tumor without injury to the bladder.

The bowel is less apt to show symptoms from pressure than is the bladder, but constipation can be caused and aggravated by pressure of leiomyomata against the rectum. The small intestines can become entwined with subserous pedunculated tumors, causing intermittent intestinal obstruction.

Pain

Abdominal and pelvic pain or discomfort, a feeling of heaviness in the pelvis, and dyspareunia are present in about one third of patients with symptomatic uterine leiomyomata and may be an appropriate reason for intervention. There are several causes of pain with leiomyomata. However, the usual hyaline or cystic degeneration of these tumors does not produce symptoms. In rare instances, pedunculated subserous leiomyomata twist and give rise to a clinical picture of acute abdominal pain, much like that seen with a torsed ovarian tumor. These pedunculated tumors twist more often during pregnancy and after menopause. Acute carneous or red degeneration of a leiomyoma can occur at any period of reproductive life, although pain from this form of degeneration is more common during pregnancy. Dysmenorrhea, acquired in the fourth or fifth decade, may be the outstanding symptom of the growth of leiomyomata. A common symptom complex resulting from leiomyomata at this time of life is menstrual pain coupled with increased menstrual flow. Diffuse adenomyosis can also

cause these symptoms, and the differentiation of this condition from a symmetrically enlarged intramural leiomyoma may be extremely difficult and may require MRI. The differentiation may be academic when surgery is planned; however, in cases when UAE is considered, this distinction is important because it may be less effective in cases of adenomyosis.

Patients who have uterine leiomyomata and pain may have concomitant pelvic disease such as ovarian pathology, pelvic inflammatory disease, tubal pregnancy, endometriosis, or urinary tract or intestinal pathology, including appendicitis. One must be careful to rule out other pathologies that may be obscured by uterine leiomyomata.

Abdominal Distortion

Distortion of the normal abdominal wall contour because of large tumors may justify their removal. Tumors of such size often give rise to other symptoms also, so there is ample reason for surgical interference. However, when no other symptoms are present, one may recommend removal of the tumors if the abdominal distortion is of such a magnitude as to be embarrassing to the patient.

Rapid Growth

Evidence of rapid growth of uterine leiomyomata, as observed by the same examiner over time or as confirmed by US, is an indication for surgical intervention. Such rapid growth in a premenopausal patient is only rarely due to sarcoma. Parker and others reviewed the medical records of 1,332 women admitted for surgical management of uterine leiomyoma. They found no correlation between rapid growth and the presence of uterine sarcoma. It may be due to pregnancy or to the use of oral contraceptives containing large amounts of estrogens. In the latter case, these drugs should be discontinued and an alternative method of contraception prescribed. In the postmenopausal patient, however, growth of a uterine leiomyoma is highly suggestive of a malignancy. The malignancy may be a sarcomatous change in the leiomyoma itself, a sarcoma or carcinoma in the endometrium causing uterine enlargement, or an ovarian neoplasm whose estrogen secretion is stimulating enlargement of the leiomyoma or whose growth may be mistaken for rapid enlargement of uterine leiomyomata. Although malignancy is not invariably found, the chances in its favor are so great that one must proceed on the assumption that it exists and should perform dilatation and curettage followed by removal of the enlarged uterus.

Rapid growth of a leiomyomatous uterus is difficult to define in exact terms. Buttram and Reiter have arbitrarily defined it as a gain of 6 weeks or more in gestational size within a year or less. Although this definition could apply in premenopausal women, it might be disastrous to wait for this amount of growth in a postmenopausal woman. It is important to have a definite method of documenting uterine size at periodic intervals. Repeated sounding of the uterine cavity may be of some benefit, although leiomyomatous growth is not always accompanied by concomitant enlargement of the uterine cavity. It is important to document the size of specific leiomyomata or the total uterine size in terms of centimeters or grams of uterine weight rather than in terms of gestational size of the uterus, although the latter method has become quite popular. Changes in a patient's weight can make evaluation of growth more difficult. Ultrasonography is a much more objective way of establishing the size of a uterine leiomyoma in the beginning and, when indicated, of evaluating its rate of growth. There is a need for more information about the natural growth patterns of myomata before and after menopause.

Although leiomyomata can increase dramatically in size during pregnancy, usually there is no appreciable growth. Winer-Muram and coworkers studied 89 pregnant women with uterine leiomyomata documented by US examination. In 83 of the patients, there was no demonstrable increase in the size of the leiomyomata. In 6 patients, there was an increase in size of up to 4 cm. Those myomata that increase in size during pregnancy will decrease in size a few weeks after the pregnancy is over.

Spontaneous Abortion and Other Pregnancy-Related Problems

Fibroid size and location affect the type and degree of patient symptoms and may also have reproductive consequences including pregnancy loss and infertility. The extent of uterine fibroids' effect on pregnancy rates and outcomes remains controversial.

Various mechanisms have been proposed to explain the occurrence of spontaneous abortion from uteri with leiomyomata. These include disturbances in uterine blood flow, alterations in blood supply to the endometrium, uterine irritability, rapid growth or degeneration of leiomyomata during pregnancy, difficulty in enlargement of the uterine cavity to accommodate for the growth of the fetus and placenta, and interference with proper implantation and placental growth by poorly developed endometrium or by subjacent leiomyomata. Implantation in a thin, poorly vascularized endometrium over a submucous leiomyoma is doomed to failure, because proper growth and development of the embryo and placenta are impossible (**Fig. 31.17**). Matsunaga and Shiota found a twofold increase in the number of malformed embryos recovered from patients with uterine leiomyomata having artificial termination of pregnancy.

Uterine leiomyomata may also be associated with other obstetrical concerns, including premature delivery, stillbirth, and interstitial pregnancy, as in the case reported by Starks. In a retrospective population-based study by Sheiner and colleagues, obstetrical outcomes appeared to be compromised by uterine leiomyoma. Compared with controls, women with myomata during pregnancy had an increase in intrauterine growth restriction (6.8% vs. 1.9%), placental abruption (2.8% vs. 0.7%), abnormal presentation (16.9% vs. 2.4%), cesarean section rate (57.7% vs. 10.8%), premature rupture of membranes (9.6% vs. 5.5%), and likelihood to receive a blood transfusion (4.2% vs. 1.4%). All of these outcomes were statistically significant ($P < 0.001$). Muram and associates have followed patients with leiomyomata through pregnancy with US. When a leiomyoma was in close proximity to the placental site, an increased incidence of pregnancy-related complications was seen. These were mainly bleeding complications, but pain, premature delivery, and postpartum hemorrhage also occurred. Exacoustos and Rosati reviewed the US scans of 12,708 pregnant patients. Four hundred ninety-two patients had myomata. A statistically significant increased incidence of threatened abortion, threatened preterm delivery, abruptio placentae, and pelvic pain was observed in patients with myomata. Abruptio placentae was particularly evident in women with myoma volumes greater than 200 cm^3, submucosal location, or superimposition of the placenta. The authors suggest that US findings make it possible to identify women at risk for myoma-related complications of pregnancy. Factors responsible for spontaneous abortion in patients without uterine leiomyomata may also be responsible for spontaneous abortion in patients with leiomyomata.

Occasionally, pregnancy causes a remarkable growth of leiomyomata in the same way that the myometrium undergoes hypertrophy in pregnancy. Red or carneous degeneration of

leiomyomata during pregnancy is associated with pain, tenderness over the tumor, low-grade fever, and leukocytosis. Management should be expectant with analgesic medications and bed rest. If premature uterine contractions occur, tocolytics may be given. Pain usually subsides within a few days. Operation is not indicated unless it is necessary to rule out other problems that require surgery for relief, because differentiation from appendicitis, placental abruption, torsed adnexa, and other problems may be difficult. After delivery, leiomyomata involute and generally return to their prepregnancy size by the third postpartum month.

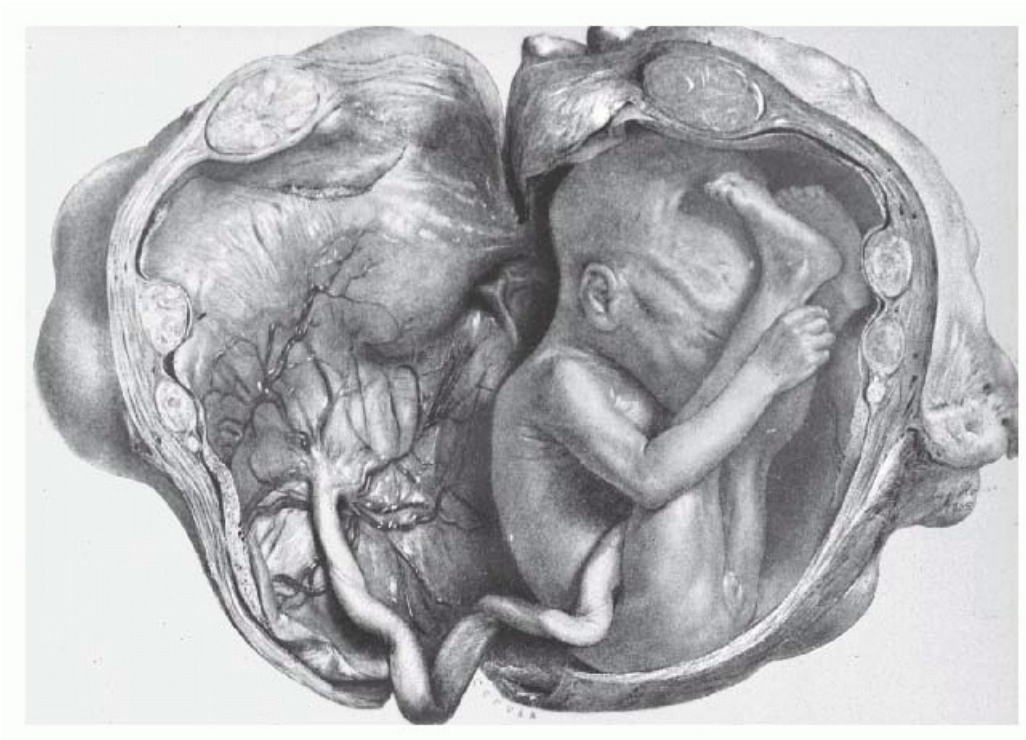

FIGURE 31.17 When the placenta is implanted over a myoma in the uterine wall, the blood supply to the fetus may be tenuous.

Torsion with infarction of subserous pedunculated leiomyomata is more common in pregnancy. A leiomyoma may interfere with labor and delivery by causing an abnormal presentation, by causing dysfunctional labor, or by obstructing the pelvis. A submucous leiomyoma in the lower uterine segment may entrap the placenta, necessitating manual removal. Indeed, furious postpartum hemorrhage can result if a submucous leiomyoma is disturbed at delivery or during exploration of the uterine cavity. Immediate hysterectomy may be necessary to control the bleeding.

Most patients with uterine leiomyomata have no difficulty conceiving and carry their pregnancies to term without complications. The only problem encountered may be a difficulty in estimating gestational age from uterine size because of the presence of leiomyomata.

Infertility

When asymptomatic leiomyomata are discovered in young women, the question of how these tumors relate to sterility and pregnancy usually arises. A number of factors may be responsible for infertility in a patient with uterine leiomyomata. Anovulatory cycles may occur more commonly. There may be interference with sperm transport caused by distortion and an increased surface area within the uterine cavity, impingement of leiomyomata on the endocervical canal or interstitial portion of the fallopian tube, or interference with prostaglandin-induced uterine contractions, which are thought to enhance sperm migration. Endometrial changes (atrophy, ulceration, focal hyperplasia, and polyps), vascular alterations (venous congestion, venule ectasia, impaired blood flow), and enlargement of the uterine cavity may be present. Because uterine leiomyomata occur in later reproductive years, relatively greater difficulty accomplishing conception can be expected in older couples.

The finding of small leiomyomata in sterile women is not an indication for immediate myomectomy. Quite often, an infertile patient with uterine leiomyomata is found to have some other causes of infertility. Tubal inflammatory disease with associated pelvic adhesions is especially common in patients with uterine leiomyomata. Both marital partners should have a complete infertility investigation, and the leiomyomata should initially be disregarded if it is asymptomatic. The ultimate decision regarding disposal of the tumors depends on their size and location.

Usually, small subserous leiomyomata are not considered a factor in infertility. Even if the woman fails to become pregnant, removal of small subserous leiomyomata is not justified. When leiomyomata are intramural or submucous and of significant size, they may well be factors causing the infertility, and a myomectomy may be rewarded with a subsequent pregnancy.

When an unsuspected asymptomatic leiomyomatous uterus of significant size is found in a woman who is planning to become pregnant in the future, great tact is required in describing the problem to the patient. The best surgical and obstetric judgment is needed to make a proper recommendation. Should the patient be discouraged from attempting pregnancy because the risk of complications may be increased? Should a myomectomy be advised before pregnancy is attempted, with the knowledge that postmyomectomy adhesions may cause infertility? Such questions cannot be answered in a stereotypical manner. Each case presents its own problems, and the answers depend on the patient's age, her general physical health, her pelvic findings, and, most important, her own desires. All must be considered before a final recommendation can be made. In general terms, under these circumstances, an attempt to become pregnant will be rewarded with a satisfactory outcome in most cases. If pregnancy does not occur or is not successful, a myomectomy may be advised, but one must keep in mind that all causes of infertility, spontaneous abortion, and other pregnancy-related problems must also be investigated in patients with uterine leiomyomata; uterine leiomyomata represent an infrequent cause of infertility.

Eldar-Geva and colleagues performed a retrospective review of the treatment outcome of 106 assisted reproductive technology cycles in 88 patients with uterine myomata (subserosal,

intramuscular without cavity distortion, and submucosal). Patients underwent controlled ovarian hyperstimulation and advanced reproductive technology. Not surprisingly, pregnancy (30.1%) and implantation (15.7%) rates were significantly lower in women with submucosal myomas; however, both pregnancy (16.4%) and implantation (6.4%) rates were also significantly lower in women with intramural myomas. In some advanced assisted reproductive technology patients, this information may influence the decision for surgical intervention regardless of menstrual pattern. A study by Olive et al. suggests that submucosal myomas that significantly distort or encroach on the uterine cavity may lower implantation and pregnancy rates in infertile women undergoing IVF. Several recent studies evaluated the effect of fibroids on in vitro fertilization cycles; the balance of data from independent studies by Farhi, Ramzy Jun, and Surrey suggests that pregnancy outcomes and implantation rates are adversely affected by submucosal myomas that enter the uterine cavity but not by subserosal or intramural fibroids that are less than 5 to 7 cm in size. Resection of submucosal fibroids clearly within the uterine cavity is likely warranted in patients with dysfunctional uterine bleeding, infertility, or pregnancy loss who desire to optimize future fertility.

A review of information about infertility and uterine leiomyomata was published by Wallach and Vu, by Vercellini and colleagues, and by Verkauf.

Miscellaneous Signs and Symptoms

A variety of other unusual problems may be associated with uterine leiomyomata and may require treatment. Ascites and uterine inversion have already been mentioned. Sudden intraperitoneal hemorrhage can result from rupture of a dilated vein beneath the serosal surface of a subserous leiomyoma. Although leiomyomata are more often associated with iron deficiency anemia from chronic uterine blood loss, occasionally, patients present with polycythemia. Islands of extramedullary erythropoiesis have been found in leiomyomata. Arteriovenous shunts within the tumors have been found and may be etiologically important in polycythemia. If the tumor obstructs the ureters and causes back pressure on the renal parenchyma, erythropoiesis can be stimulated. Weiss and coworkers and other investigators have found marked erythropoietin activity within uterine leiomyomata. The

polycythemia in these cases is cured by hysterectomy.

CHOICE OF TREATMENT FOR UTERINE LEIOMYOMATA

According to statistics from the Centers for Disease Control, 600,000 hysterectomies are performed annually in the United States. Approximately 33% are performed with uterine leiomyomata as the primary indication. Nearly 35,000 myomectomies were reportedly performed annually in 2001, and it is believed that this number is increasing substantially. There are no statistics to indicate the number of hysteroscopic and laparoscopic myomectomies performed each year. Effective medical therapies are available to use as adjuncts to surgical treatment. Additional radiologic procedures may also be desirous in patients who may not be suitable surgical candidates. However, surgery is the preferred method of therapy in many circumstances.

Hysterectomy (abdominal, vaginal, and laparoscopic or robot assisted) is discussed in Chapter 32. In this chapter, surgical techniques that allow conservation of uterine function are discussed, as are medical therapies that can be used as adjuncts to surgical therapy.

Medical Management of Uterine Leiomyomata

Most (70% to 80%) uterine leiomyomata are asymptomatic and are discovered incidentally during a routine pelvic examination. Such patients require an explanation and reassurance and reexamination at periodic intervals. An initial baseline pelvic US examination or MRI study may be indicated for comparison with future examinations and to evaluate the adnexa if the ovaries cannot be felt on pelvic examination. An experienced pelvic examiner can be fairly certain that a central pelvic mass is a leiomyomatous uterus. However, pelvic US examinations and repeat pelvic examinations can add to the certainty of the diagnosis. If the diagnosis remains doubtful, however, visualization of the mass, usually by laparoscopy, may be indicated. Patients with an asymptomatic central pelvic mass should be followed up with periodic pelvic examination only when the mass is benign, usually a leiomyomatous uterus. Otherwise, expectant management is not appropriate.

Effective medical treatment that is likely to result in the permanent cure of uterine leiomyomata is not yet available. Surgical excision by a variety of techniques remains the most effective and widely used method of management for patients with significant symptoms. Medical therapies are available as an adjunct to surgical treatment or as a temporary substitute for definitive surgical treatment. The role of radiologic intervention continues to expand with UAE and recently U.S. Food and Drug Administration (FDA)-approved, MRI-guided, high-frequency focused ultrasonography.

Hormonal therapy for the management of uterine leiomyomata has been the subject of investigation for many years. There is no support for the use of danazol or progestins in view of the disappointing results reported. Antiprogestin therapy with mifepristone (RU-486) for 3 months has been shown by Murphy and colleagues to decrease leiomyoma volume by an average of 49%, with a variation of 0% to 87%. The immunoreactivity of progesterone, but not estrogen, receptors in the myoma and myometrial tissue was decreased significantly by RU-486 treatment, suggesting that regression of these tumors may be attained through a direct antiprogesterone effect. All patients became amenorrheic. Side effects were mild, and bone density was not diminished. An effective dose to cause a clinically significant (50%) decrease in leiomyoma volume appears to be 25 mg daily. Additional experience is needed to further evaluate these promising results. Reinsch and associates have demonstrated that RU-486 and leuprolide acetate are both effective in decreasing blood flow to the uterus. It is suggested that a decrease in uterine artery blood flow may provide a mechanism for a decrease in uterine size.

Gestrinone, a synthetic derivative of ethinyl-nortestosterone with antiestrogen and antiprogesterone properties, has been shown by Coutinho and associates to induce regression of leiomyomata. The treatment lasted 6 months to 1 year. The best results were obtained when the drug was administered intravaginally. Even the regression of large leiomyomata lasted up to a year after treatment. Side effects, though mildly androgenic, were

well tolerated.

Many studies have been performed to investigate the treatment of patients with uterine leiomyomata with GnRH analogs. GnRH analogs bind to GnRH receptors, resulting in a biphasic response: a temporary increase in the levels of gonadotropins and gonadal steroids (agonist phase) is followed by chronic suppression of gonadotropin and gonadal steroid secretion (desensitization phase). In 1 to 3 weeks, a profound hypogonadotropic hypogonadal state begins and exists as long as the treatment lasts, but it is promptly reversed when treatment is discontinued. GnRH agonist treatment results in

"medical oophorectomy" and "medical menopause" and is associated with the usual symptoms of a profound hypogonadal state (e.g., hot flashes, insomnia, mood lability, headaches, vaginal dryness, arthralgias, and myalgias). According to Friedman and associates, these adverse effects of treatment are self-limited and disappear within 3 to 6 months of cessation of GnRH agonist treatment. Dawood and colleagues describe a significant reduction in trabecular bone density after 24 weeks of GnRH agonist treatment that may not be completely reversible when treatment is discontinued. A mean reduction in trabecular bone density of 1% per month occurs in women treated for 6 months. Some of this bone loss may be permanent, but some is reversible.

Friedman and colleagues state that the average reduction in uterine and myoma volume is 40% to 50% after 3 to 6 months of GnRH agonist treatment; this is generally confirmed by others. Most of the response occurs in the first 12 weeks, and it is variable and unpredictable.

According to the analysis by these investigators, 4% of patients had an increase in uterine volume ranging from 0.1% to 25%, 24% had decreases in uterine volume ranging from 0.1% to 25%, 51% had decreases in uterine volume ranging from 25.1% to 50%, and 21% had decreases in uterine volume greater than 50%. No factors were found to predict the degree of uterine shrinkage. There were negative correlations with body weight, pretreatment uterine volume, age, height, and serum estradiol concentration.

It is commonly thought that GnRH analogs affect leiomyomata by reducing vascularity and the individual cell size within the tumor. The biochemical changes in leiomyomata obtained from women treated with the GnRH agonist leuprolide acetate depot for 3 months were studied by Rein and coworkers. The concentrations of amino acids contained in collagen were significantly greater in uterine myomata from treated patients than in myomata from placebo-treated controls. These investigators suggest that the reduction in uterine myoma volume associated with GnRH agonist therapy is due primarily to alterations in the extracellular matrix rather than to a reduction in the number or volume of cells in the myoma. Di Lieto and colleagues evaluated the clinical response; immunohistologic expression of the angiogenetic growth factors βFGF, VEGF, and PDGF; and vascular changes in uterine leiomyomas from women treated with GnRH agonist. They demonstrated that the GnRH agonist therapy caused a reduction in the synthesis of the three considered growth factors in leiomyomatous cells (βFGF, VEGF, and PDGF). The total number of vessels and angiogenetic vessels was also decreased after treatment with leuprolide acetate for 3 months.

Because uterine leiomyomata are hormone-sensitive neoplasms that can be stimulated to grow by estrogen, some clinicians have been reluctant to prescribe oral contraceptive pills in patients with leiomyomata. However, Friedman and Thomas and others have demonstrated conclusively that oral contraceptives containing 30 to 35 mg of ethinyl estradiol do not cause uterine leiomyomata to increase in size. Therefore, low-dose contraceptives can be used to manage menorrhagia in patients with uterine leiomyomata. Friedman and Thomas demonstrated a significant decrease in the mean duration of menstrual flow and a significant increase in hematocrit values in response to low-dose oral contraceptives in patients with uterine leiomyomata.

When myoma-associated menorrhagia is more severe, GnRH agonist and iron treatment may be more effective than oral contraceptives. In about two thirds of patients, GnRH agonist treatment induces amenorrhea. Most of

the remaining patients experience very light, irregular vaginal bleeding or spotting, according to Friedman. A combination of menstrual suppression and iron therapy allows correction of iron deficiency and iron deficiency anemia during a 6-month treatment period. Ovulatory menses resume 3 to 24 weeks after the last depot GnRH agonist injection. Stovall and associates reported that a GnRH agonist plus iron was more effective than iron alone in treating anemia in patients with leiomyomata and in alleviating menorrhagia. With such effective treatment now available, there is rarely a need to use blood transfusions to correct anemia caused by myoma-associated menorrhagia. Only patients with significant symptoms from severe anemia may require transfusion.

Medical therapy may also be used transiently before surgery. By initiating the medication preoperatively, the maximum decrease in myoma volume may play a role in determining the route of surgery. If a hysterectomy is planned, the pharmacologic effect may facilitate a vaginal hysterectomy when the uterus is of borderline size. Vercellini and colleagues performed a multicenter, prospective, randomized, controlled study to assess if this shrinkage may increase the likelihood of a vaginal procedure. One hundred and twenty-seven premenopausal women with uterine volumes of 12 to 16 weeks were enrolled. After examination and disposition for an abdominal or vaginal hysterectomy, patients were randomized for GnRH therapy. Clinical assessment after the treatment course showed that abdominal hysterectomy was no longer indicated in 25 of 53 (47%) patients. No appreciable difference was found between the groups in postoperative complications. These findings are consistent with previously published studies, as well.

GnRH agonist treatment alone should not be given for periods longer than 6 months. A prolonged hypoestrogenic state is undesirable for a number of reasons, the most important being the loss of trabecular bone. If there are circumstances that require that GnRH treatment be extended beyond 6 months, consideration should be given to adding low-dose steroids after 3 months of GnRH therapy. The usual postmenopausal estrogen-progestin replacement regimen can be prescribed without interfering with the reduction in uterine volume anticipated. Loss of trabecular bone may not be as great. By adding estrogen-progestin replacement to GnRH agonist therapy, the adverse effects of a prolonged hypoestrogenic state may be prevented, and treatment with GnRH agonists may be prolonged. Friedman and colleagues treated 51 premenopausal women with large, symptomatic myomata with leuprolide acetate depot for 104 weeks. After the first 12 weeks, 0.75 mg of estropipate plus 0.7 mg of norethindrone was added on days 1 through 14 each month. Menorrhagia and other symptoms of uterine leiomyomata were controlled successfully. Hemoglobin and hematocrit levels increased. Symptoms of hypoestrogenism (hot flashes, vaginal dryness) were decreased significantly. Bone density decreased in the first 12 weeks, but only a small additional decrease occurred between weeks 12 and 52.

The use of GnRH analogs in the medical management of uterine leiomyomata is an emerging issue. How valuable it will be remains to be seen. Additional information and experience will define its use more exactly. For example, it may be possible for patients with symptomatic uterine leiomyomata who are approaching menopause to be managed medically through menopause without having a hysterectomy. It may be possible to improve fertility in some patients with uterine leiomyomata by treatment with GnRH analogs without myomectomy. With additional data, these and other questions can be answered.

Vaginal Myomectomy

In 1845, Atlee performed the first successful vaginal myomectomy on a patient with a submucous pedunculated myoma.

When a submucous myoma becomes pedunculated within the uterine cavity, there is a natural tendency for the uterus to try to expel it through the endocervical canal. Eventually, the cervix dilates. Even very large submucous pedunculated myomata can be delivered gradually through a markedly dilated cervix. Because adequate blood

circulation through a long pedicle is difficult to maintain, the myoma becomes necrotic and infected (**Figs. 31.5** and **31.6**).

Patients report cramping lower abdominal pain; pressure and heaviness in the pelvis; a thin, bloody, foul discharge; difficulty with urination; and other symptoms. Episodes of profuse vaginal hemorrhage can occur. Such large submucous myomata may resemble a fetal head.

After satisfactory preoperative preparation, including broad-spectrum antibiotics and correction of anemia, vaginal myomectomy should be performed in the operating room. Morcellation may be required to remove very large tumors in many small pieces. Usually, there is very little bleeding. One should avoid too much downward traction on the tumor because the uterine fundus may invert. Eventually, the pedicle is identified. It should be clamped and ligated as high as possible within the uterine cavity. The use of a laparoscopic instrumentation, such as the Endoloop, can be advantageous to facilitate safe, secure ligation of the pedicle as high as possible. If ligation of the pedicle is not possible, the clamps can be left in place and safely removed 48 hours later.

Smaller submucous pedunculated myomata can be diagnosed by hysteroscopy, by hysterosalpingography, by sonohysterogram, or at the time of dilation and curettage. They can also be felt on digital exploration through a slightly dilated external cervical os. If the myoma can be grasped with an instrument (ring forceps or Allis clamp), it can be removed by twisting it free of its attachment. A tonsil snare can also be used. Bleeding is usually minimal. If brisk bleeding does occur, a 26-French, 30-mL Foley catheter can be inserted through the cervix and inflated for tamponade. If necessary, the cervix can be sutured around the catheter to hold it in place.

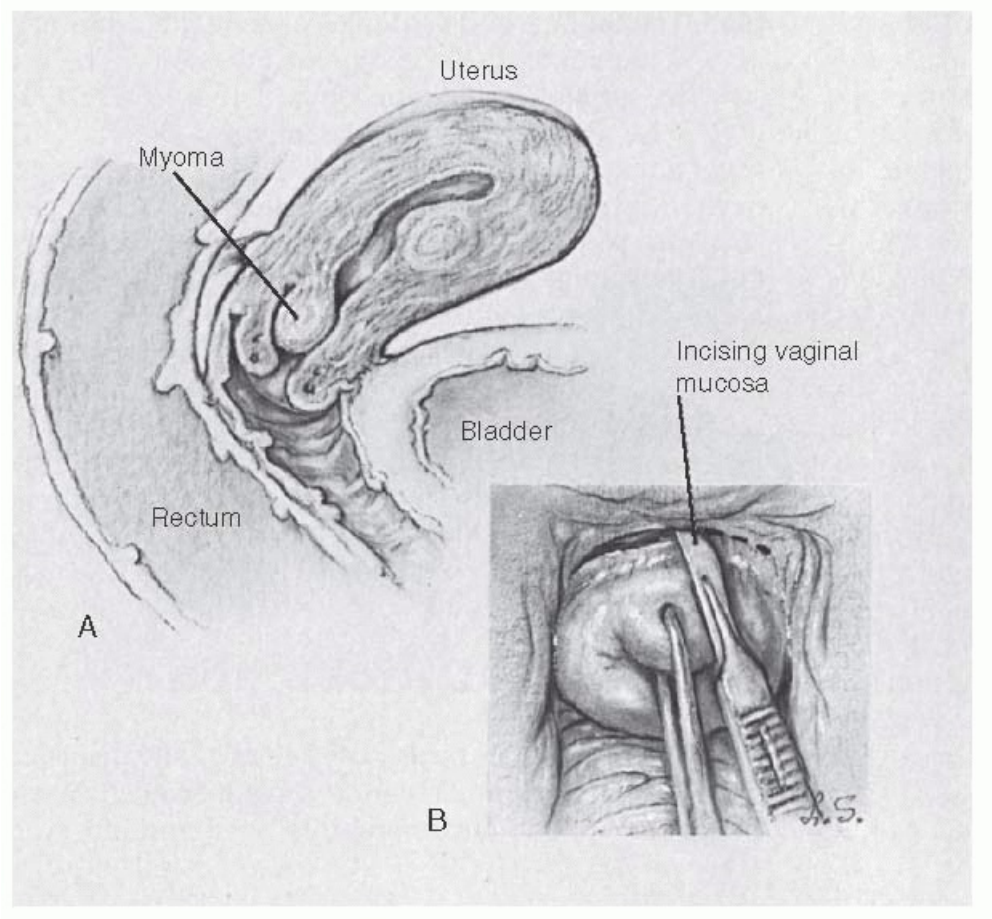

FIGURE 31.18 Transvaginal removal of a pedunculated submucous myoma that presents itself at the external cervical os. **A:** Sagittal view of uterus, demonstrating the location of the myoma originating on the posterior wall of the fundus just above the cervix. **B:** A transverse incision made anteriorly through the vaginal mucosa at the cervicovaginal junction.

To gain access to submucous pedunculated myomata that are higher in the endocervical canal or uterine cavity,

special procedures are required. An attempt at hysteroscopic removal may be successful. Alternatively, the cervix can be dilated with instruments or with *Laminaria japonica,* as described by Goldrath. Dührssen incisions can be made in the cervix. Also, the cervix can be incised by having the surgeon perform a vaginal hysterotomy (**Fig. 31.18A, B**). After the bladder is advanced, the cervix is dilated, and an anterior midline incision is made in the cervix high enough to identify the myoma. The pedicle of the myoma is ligated as high as possible (**Figs. 31.18C, D**). The incision in the cervix is repaired with 2-0 interrupted delayed absorbable sutures. The vaginal mucosa is reapproximated with 3-0 delayed absorbable sutures (**Figs. 31.18E, F**).

A submucous pedunculated myoma may be solitary, and there may not be other myomata in the uterus. In fact, many patients exhibit no evidence of uterine enlargement. After a successful vaginal myomectomy, most patients are asymptomatic and menstruate normally. A few even become pregnant and deliver vaginally without difficulty. Cervical incompetence has been reported. Hysterectomy or myomectomy is required only for those few patients who have multiple leiomyomata and continue to have significant symptoms.

Excellent results of vaginal removal of submucous pedunculated myomata in 151 patients were reported by Goldrath. Ben-Baruch and coworkers also achieved excellent results in 43 of 46 women in whom vaginal myomectomy was attempted. Vaginal myomectomy is recommended as the most appropriate initial treatment for pedunculated submucous myomata.

Vaginal myomectomy is traditionally used for submucosal myomata; however, it has been described for other myomata. Davies and colleagues reported a prospective study regarding the safety and efficacy of excision of intramural and subserosal leiomyoma by a vaginal route. Preoperative criteria included (a) uterine size less than or equal to 16 weeks gestation, (b) good uterine mobility, (c) adequate vaginal access, (d) the presence of intramural or subserosal myomata, and (e) the

absence of adnexal pathology. Essentially, an open abdominal myomectomy technique was performed through an anterior or posterior colpotomy. The uterus was manipulated to bring the myoma into the colpotomy. The management of 35 women was described. The mean number of myomas removed was 2.5 per patient with mean mass of 113.8 g. Three patients (8.6%) required conversion to a laparotomy. Neither mean blood loss nor length of hospital stay was improved. Additionally, four (11.4%) patients developed pelvic hematomas postoperatively. At this time, this procedure does not seem to provide inherent benefits over an open abdominal myomectomy or a laparoscopic approach. With further review, better outcome data may demonstrate the advantages of this technique.

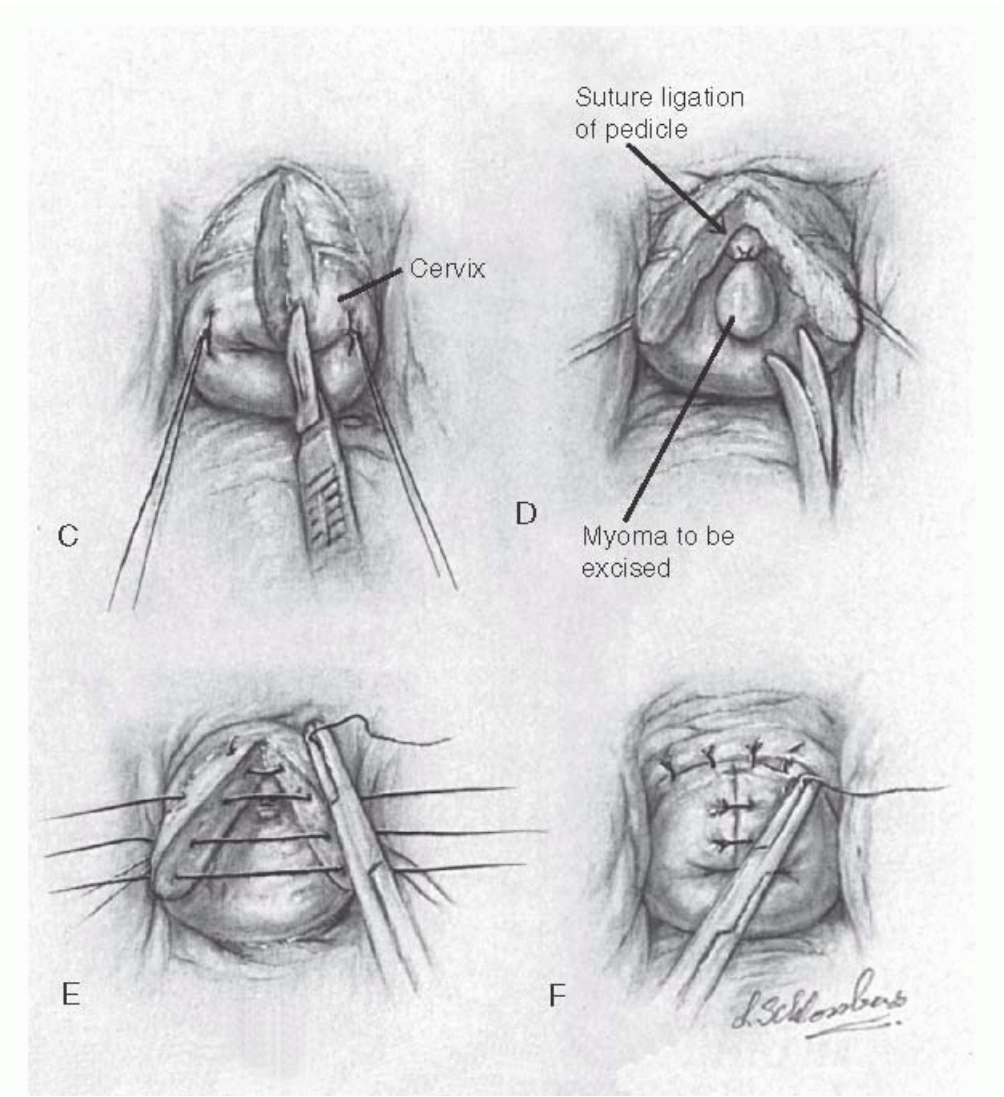

FIGURE 31.18 (*Continued*) **C:** After the bladder is advanced bluntly, the cervix is incised anteriorly in the midline. **D:** The myoma and its pedicle are exposed, and the pedicle is suture ligated for hemostasis. **E:** After the myoma is excised, the cervix is reapproximated with interrupted 2-0 absorbable, nonreactive sutures. **F:** The overlying vaginal mucosa is sutured with interrupted 3-0 absorbable sutures.

The tissue removed at vaginal myomectomy must be submitted for pathologic examination to rule out malignancy.

Hysteroscopic Resection of Submucous Myomata

Hysteroscopic resection of submucous myomata was first reported by Neuwirth and Amin in 1976 and was reported again by Neuwirth in 1978. A urologic resectoscope was used. In 1981, Goldrath and associates used "photocoagulation" of the endometrium with the neodymium-doped:yttrium-aluminum-garnet (Nd:YAG) laser to treat patients with menorrhagia. Many subsequent reports by Derman and associates, Donnez and colleagues, Goldenberg and coworkers, Corson, Indman, Hallez, Baggish and associates, Wamsteker and colleagues, and others have confirmed the advantages of hysteroscopic treatment of menorrhagia in women with and without submucous leiomyomata. The menorrhagia associated with submucous myomata can sometimes be managed with oral contraceptives as long as the bleeding is not too severe. A favorable response can also be expected with GnRH analogs, but the menorrhagia usually reappears when the treatment is discontinued. Friedman has reported three cases of severe menorrhagia with resultant anemia requiring transfusions in women with submucous leiomyomata treated with leuprolide acetate. Both oral contraceptives and GnRH analogs are counterproductive in women who are seeking relief from infertility. The uterine cavity can be curetted several

times, but the benefit of this procedure is temporary at best.

When hysteroscopic resection of submucous myomata is performed, menorrhagia can be controlled in more than 90% of patients. According to Indman, the mean number of pads used during the heaviest day of menses decreased from 17.8 before treatment to 6.8 after treatment in women undergoing myoma resection only and from 21.4 to 1.7 pads per day in women whose treatment also included endometrial ablation. Dysmenorrhea was also reduced significantly. Forty-eight of fifty-one women (94%) with uterine leiomyomata who were seen with menorrhagia were able to avoid major gynecologic surgery for up to 5 years of follow-up. In the report of 156 patients by Derman and associates, 91.3% of patients did not require further surgery after 6 years of follow-up, and 83.9% did not require further surgery after 9 years of follow-up. Further review in recent papers supports Derman's results. Magos and colleagues performed a prospective observational study to identify factors that influence outcomes of hysteroscopic myomectomies by following up patients for almost 8 years. One hundred twenty-two patients enrolled in the study, and results suggest that hysteroscopic myomectomy is successful in treating menstrual symptoms in four of five cases. In addition, statistical analysis demonstrated that outcome is significantly better when the uterus is only slightly enlarged and if the myoma is mainly submucous in nature.

If endometrial ablation is performed with myoma resection, pregnancy is not likely to occur subsequently. Without

simultaneous endometrial ablation, 21 patients became pregnant after myoma resection only, with 18 infants delivered in the series reported by Derman and colleagues. The pregnancy rates among women who wished to conceive varied between 47% and 66% in several reports. These rates are comparable to those reported for abdominal myomectomy.

Donnez and coworkers used a biodegradable GnRH agonist (Zoladex Implant ICI) preoperatively in a series of 60 women with large submucous myomata. Submucous myomectomy by hysteroscopy and Nd:YAG laser was easily performed. In 12 patients, the procedure was accomplished in two stages. Perino and associates used GnRH agonists in 58 women with submucous leiomyomata diagnosed during investigation for infertility or menstrual disorder. There was a significant reduction in operating time, intraoperative bleeding, infusion volume, and failure rate in the treated group compared with the control subjects. Myoma size is reduced and hemoglobin concentration is restored to normal preoperatively. Campo and colleagues collected data on 80 consecutive resectoscopic myomectomies performed on premenopausal women. Fortytwo patients did not receive any preoperative medical therapy, whereas 38 patients received 2 months of intramuscular GnRH analog therapy. Perioperative results were recorded, followed by a 24-month follow-up period when recurrent symptoms, myoma recurrence, and the need for repeat surgery were collected. Surgical time for the pretreated group was significantly longer than that of the untreated patients. Although GnRH analog pretreatment may be beneficial in improving anemia in some patients, Campo and colleagues did not demonstrate any improvement in short- or long-term outcomes.

A hysteroscopic approach is reasonable if the majority of the fibroid is within the cavity or if subtotal hysteroscopic myomectomy is deemed preferable to total abdominal myomectomy. Hysteroscopic resection may be performed using a hysteroscopic morcellator or resectoscope. A resectoscope allows for the use of electrocautery at the time of resection but, as a result, requires electrolyte-poor distending media such as mannitol, sorbitol, or glycine. Morcellating devices resect using a rotating blade rather than electrocautery and allow for use of isotonic distending media such as normal saline or lactated Ringer, which have lower risk for fluid overload and subsequent electrolyte imbalance. The avoidance of electrocautery also has a theoretical benefit of avoiding thermal damage to the myometrium and decreasing the chance of future uterine rupture at time of pregnancy. Both methods incur a risk of procedure abortion secondary to bleeding. Prior to starting the hysteroscopy, injection of vasopressin into the cervical stroma can be used to help decrease myoma bleeding. If bleeding is encountered intraoperatively, conversion from morcellator to electrocautery or use of uterine balloon

for tamponade and uterine compression can be used to help achieve hemostasis.

When submucous myomata extend deeply into the myometrium, it may not be possible to perform a complete resection for obvious technical reasons. However, it should be possible to remove most irregularities in the uterine cavity and to restore the contour of the cavity to almost normal in most cases. According to Wamsteker and colleagues, hysteroscopic resection of submucous myomata with more than 50% intramural extension should be performed only in selected cases. Repeat procedures may be needed in cases of initial incomplete resection.

To avoid the possibility of inadvertent uterine perforation or to allow its prompt diagnosis if it occurs, hysteroscopic resection is usually performed under laparoscopic guidance. However, as reported by Sullivan and coworkers, laparoscopy may be insufficient to evaluate fully the possible sequelae of uterine perforation. Laparotomy may be necessary to assess the pelvic viscera fully. Letterie and Kramer were able to safely substitute intraoperative transabdominal ultrasonographic guidance for laparoscopy. In their opinion, operative hysteroscopy with intraoperative ultrasonographic guidance provides an accurate and precise method to monitor intrauterine surgery, and it can be used to enhance the performance of hysteroscopic myomectomy and endometrial resection. Intraoperative US guidance provided sufficient details of the relation between the hysteroscope and the myoma and uterine walls to gauge the depth of resection and prevent uterine perforation. Lin et al. resected six submucous myomas under ultrasonographic guidance. All cases were completed in under 1 hour without any complications and resulted in improvement in menorrhagia and metrorrhagia. Postoperative hysteroscopy revealed no intrauterine adhesions, and the endometrium at the operative site appeared normal. Wortman and Dagget used ultrasonographic control to remove large submucous myomas and claimed that US may help prevent perforation and obviate laparoscopy.

The success and safety of the procedure depend on the experience and skill of the operator. During hysteroscopic resection, vascular spaces are opened in the endometrium and myometrium. Large volumes of fluid are instilled into the uterine cavity. Fluid balance must be monitored carefully by the surgeon and the anesthesiologist to avoid fluid overload.

All tissue must be submitted for pathologic examination. Among 92 patients undergoing hysteroscopic resection in the series reported by Corson and Brooks, two cases of leiomyosarcoma were diagnosed. Leiomyosarcoma is said to be more common in submucous leiomyomata than in intramural or subserous leiomyomata.

As time passes after hysteroscopic resection of submucous myomata, the possibility of recurrent problems increases because of regrowth of myomata. However, this is no more likely to occur than it is with standard abdominal myomectomy. The experience of many investigators has demonstrated that hysteroscopic management of menorrhagia in patients with submucous leiomyomata is a reasonable alternative to classic surgical hysterectomy or myomectomy. The occasional psychological problems and complications of hysterectomy are avoided. An abdominal incision is avoided, there is less discomfort, the procedure can often be performed in an outpatient setting, and the patient can usually resume normal activity after a very brief recovery period.

Hysteroscopic resection of a small submucous myoma is illustrated in **Figure 31.19**. Details of the indications, technique, complications, and results of hysteroscopic resection are also provided in Chapter 18.

Laparoscopic and Robotic-Assisted Myomectomy

When abdominal myomectomy is indicated, the laparoscopic or robotic-assisted approach can be offered as an alternative to the standard “open” abdominal myomectomy in selected patients. However, this procedure is appropriate in very few patients for several reasons. First, myomectomy is indicated in infertility patients only if there is significant distortion of the uterine wall or endometrial cavity or if there is obstruction or distortion of the

fallopian tubes by myomata. Second, myomectomy is indicated in patients who wish to retain their uterus only if the myomata are significantly symptomatic. In both circumstances, the myomata are likely to be multiple and large, and laparoscopic/robotic-assisted myomectomy should only be considered if the uterine repair is comparable, or superior, to the uterine closure of an abdominal myomectomy.

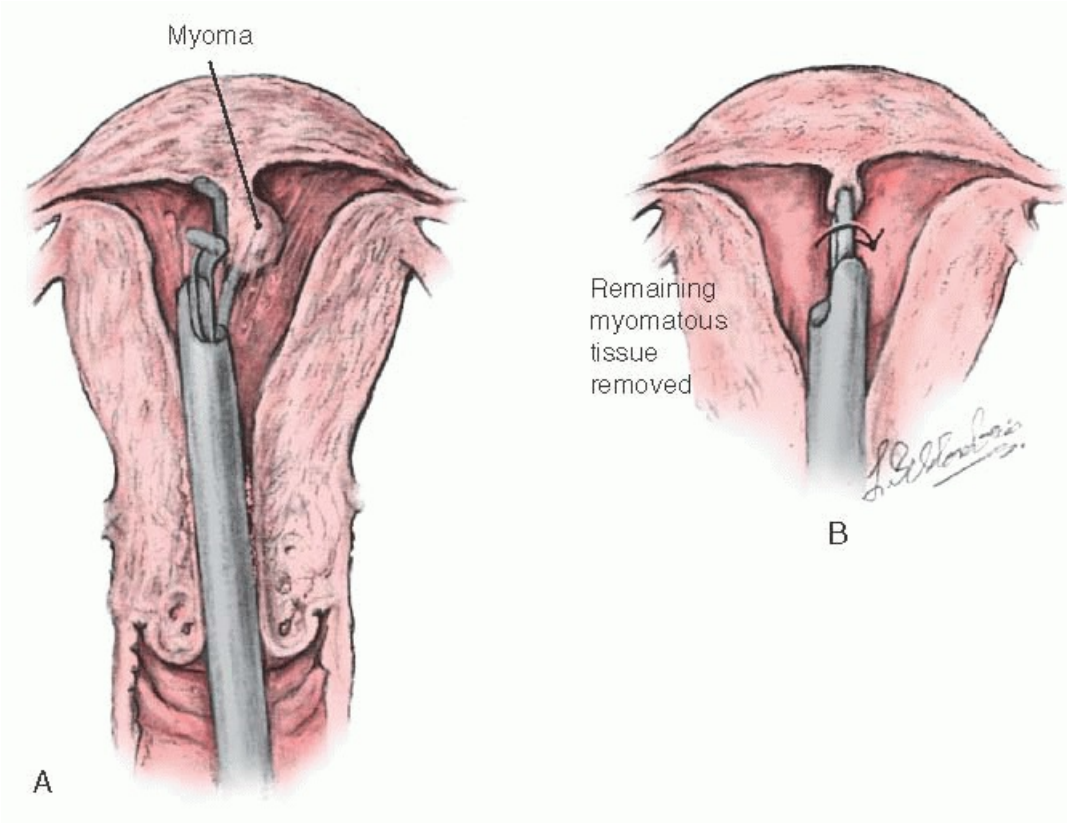

FIGURE 31.19 Hysteroscopic removal of a submucous myoma. **A:** After insertion of the resectoscope, the submucous myoma is removed by progressive shaving. The loop of the resectoscope is placed at the most distant portion of the myoma, and the current is applied as the resectoscope is drawn toward the surgeon. Pressure is exerted by the loop against the myoma with each stroke. **B:** A grasping forceps is used to twist off the remaining tissue once the size has been appreciably reduced.

There are limitations to both laparoscopic and robotic-assisted myomectomies, and these are mostly technical. Myomata in certain locations are difficult to remove. When myomata are large or multiple, or both, operative time and blood loss may be unacceptable. When myomata are embedded deeply in the myometrium, proper repair of the uterine wall may be difficult or impossible, and uterine rupture may occur in a subsequent pregnancy. Retrieval of the resected myomata from the peritoneal cavity can also pose problems. Large myomata must be morcellated into smaller pieces for retrieval. Retrieval through the posterior vaginal fornix or through the abdominal wall requires separate additional incisions, which somewhat defeats the idea of a minimally invasive procedure. Only very skillful laparoscopists or trained robotic surgeons should attempt extensive myomectomy through the laparoscope. According to Mais and colleagues, operation time for myomectomy was significantly longer for laparoscopy than for laparotomy when more than four myomata had to be removed and the largest myoma was greater than 6 cm. Dubuisson and coworkers also reinforce the difficulty of the technique by reporting conversion to laparotomy at a rate of 7.5% (93.7% due to operative difficulties) and a complication rate of 3.8%. These authors echo similar intraoperative concerns: (a) the location of the hysterotomy, (b) the type of hysterotomy, (c) the uterine suture, and (d) removal of the myoma. In addition, they report that one third of patients developed adhesions at the uterine scar.

The robot, which provides additional degrees of freedom as compared to laparoscopy, was first approved by the

U.S. FDA for use in gynecologic surgery in 2005. It improves potential surgical dexterity and allows for 3-dimensional visualization of the tissue. Several technical innovations have been developed to facilitate laparoscopic and robotic-assisted myomectomy. Electrosurgical and laser techniques are used in ingenious ways. Special traction devices, including corkscrews of various sizes, are required. The operator must be able to provide hemostasis using monopolar cutting current and bipolar forceps. The role of the Harmonic scalpel has also expanded for clean dissection and the potential for less blood loss. Aquadissection can be used to establish planes for dissection between myomata and the surrounding myometrium. Special techniques of approximating myometrium with larger curved needles are used with either intracorporeal or extracorporeal suture tying, depending on the surgeon's expertise. Knowledge of available laparoscopic instrumentation is essential to maximize surgical outcome. Autologous blood donation with intraoperative transfusion when necessary reduces the risk of homologous transfusion. Larger myomata can be removed vaginally with morcellation through a posterior colpotomy incision. In cases of myomas of extreme size, Pelosi and colleagues proposed the use of hand-assisted laparoscopy to avoid a laparotomy. This technique allows the insertion of a hand into the abdomen to assist in dissection. This is accomplished through a glove-sized incision at laparoscopy while preserving the pneumoperitoneum. A cylindrical serrated morcellator can also be used to convert smaller myomata to small strips of tissue, which can then be removed abdominally through the trocar sleeve or through a minilaparotomy incision. Retrieval of all bits and pieces of myoma tissue from the peritoneal cavity can be a tedious challenge. Hirai and colleagues from Japan described a microwave coagulator and electromechanical tissue borer to minimize invasion of the myometrium and abdominal wall. The proposed advantage of this technique is that by morcellating the tissue before removal from the uterus, less myometrial trauma is sustained. Horizontal and perpendicular blades at the tip rotate and hollow out the myoma, allowing large myomas to be removed through a small uterine incision. The authors described the use in five patients with four of the five having myomas weighing less than 170 g. The blood loss and operating time were not substantially different than with conventional abdominal procedures. Long-term data regarding myometrial strength over time and pregnancy outcomes are not yet available. More experience with this procedure is necessary to determine its role in myomectomy. A recent review of robotic-assisted technique was published by Quaas and colleagues.

Another technical innovation called myolysis has been described by Goldfarb and is based on earlier experience in Europe. Either Nd:YAG laser or bipolar needles are used laparoscopically to penetrate the myomata at multiple sites at a 90-degree angle to the uterus. In response to treatment,

the myomata ultimately atrophy. The technique is based on the theory that the coagulating effects of lasers or the bipolar needle can necrose myometrial stroma, denature protein, destroy vascularity, and result in substantial shrinkage of myomas when deprived of their blood supply. Goldfarb advises treatment with GnRH agonists before surgery. The ideal candidates for myolysis are perimenopausal women who have symptomatic leiomyomata measuring 3 to 10 cm or uterine size less than 14 weeks gestation. Goldfarb combines myolysis with endometrial ablation in patients with symptomatic myomas with persistent uterine bleeding. The addition of myolysis to endometrial ablation increased the rate of postsurgical amenorrhea from 36.5% to 57%, and second procedures, including hysterectomy, were reduced from 38% to 12.5%. Goldfarb described significant adhesions at follow-up laparoscopy in patients treated with the Nd:YAG laser technique because of excessive serosal injury from multiple punctures. A circumferential technique was later developed to destroy vasculature instead of the myomatous tissue. The devascularized myoma becomes cyanotic, loses viability, and fibroses. Phillips reported on women who underwent elective diagnostic laparoscopy to evaluate adhesions associated with previously performed myolysis. Mean adhesion score was only 1.15 ± 0.6 on a scale of 10.

Zreik and colleagues at Yale University modified the myolysis procedure to include cryotechnology to "freeze" uterine leiomyomas. The technique, *cryomyolysis,* was described in a prospective pilot study of 14 patients. All patients were pretreated with GnRH agonist therapy for 3 months. Thirteen of the fourteen endoscopic

procedures were performed by laparoscopy and the remaining one by hysteroscopic visualization. Cryoprobe placement was verified, and freezing was performed at an internal probe temperature of −180°C until the ice ball encompassed the entire fibroid or reached maximum size. A thaw cycle was then performed, followed by one more freeze-thaw cycle. A hollow track remained within the frozen myoma after removal of the cryoprobe. MRI studies were used to assess uterine and myoma size. The uterus enlarged by 22% after discontinuation of the GnRH therapy. Myoma volume decreased by 6% over 4 months postoperatively, with some patients having a decrease of more than 50%. Four of six women who underwent second-look office laparoscopy had adhesion formation at freezing sites. The authors attributed risk and severity of adhesion formation to the number of punctures with the cryoprobe. The role of this therapy in conservative treatment of uterine myomata remains to be defined.

Hysteroscopic myomectomy and endometrial resection can be performed simultaneously if submucous myomata are present. In more than 300 myolysis procedures, the author reported minimal morbidity with a 30% to 50% reduction in myoma size beyond the reduction achieved with GnRH agonist treatment. No regrowth occurred after several years of follow-up, even after estrogen replacement therapy. Bipolar coagulation myolysis may be less likely to cause damage to the uterine serosa and less likely to cause adhesion formation postoperatively. According to Goldfarb, “As a same-day procedure, myoma coagulation appears to be an extremely safe alternative to hysterectomy, allowing the patient to avoid major surgery and its subsequent recovery time, while providing an alternative solution for patients with symptomatic leiomyomas.”

Nezhat and coworkers used a combination of laparoscopy and minilaparotomy to perform myomectomy in 57 women with uteri at 8 to 26 weeks in gestational size. In this laparoscopically assisted myomectomy procedure, the myomata were removed and the uterus repaired through the minilaparotomy incision. It was technically less difficult than laparoscopic myomectomy and allowed better closure of the uterine defects. This technique may be preferable in the case of large myomas in that it is easier to achieve conventional multilayer suturing and easier to extract myomas.

A recent retrospective review by Pitter et al. included 872 women who underwent robotic-assisted myomectomy and evaluated pregnancy outcomes among 127 of the women who conceived (92 of whom delivered) postoperatively. They found rates of miscarriage, preterm delivery, and uterine rupture to be comparable to those reported for laparoscopic myomectomy. A similar but smaller study by Göçmen including 38 patients noted comparable operative time, hospital stay, and estimated blood loss between patients undergoing laparoscopic and robot-assisted myomectomy. Moreover, several independent studies by Ranisavljevic, Mansour, and Nash suggest that robotic-assisted myomectomy appears to have similar advantages as laparoscopic myomectomy when compared to abdominal myomectomy. Behera, however, contends that, currently, robotic-assisted cases are less cost-efficient than laparoscopic or abdominal cases. This cost discrepancy may improve over time.

A significant disadvantage of myomectomy is the risk of postoperative pelvic adhesions. The adhesions may adversely affect fertility, give rise to pain, and increase the risk of ectopic pregnancy or even intestinal obstruction. Several studies have demonstrated that the risk of postoperative adhesions decreases when a laparoscopic approach is used in lieu of an open abdominal approach. Literature review demonstrates that the average rate of postoperative adhesions after laparoscopic myomectomy is 41% versus more than 90% after a myomectomy via laparotomy. Dubuisson and colleagues assessed adhesion formation after laparoscopic myomectomy in a prospective manner. Forty-five patients underwent a second look after laparoscopic myomectomy. Seventy-two sites were evaluated. The overall rate of postoperative adhesions was 35.6% per patient. The rate of adhesions per myomectomy site was 16.7%. The rate of adhesions on the adnexa was 24.4%. Associations with the occurrence of adnexal adhesions included an additional surgical procedure carried out at the same time, the existence of adhesions before the operation, and posterior location of the myoma. Several factors may increase the risk of postoperative adhesion formation after a laparoscopic myomectomy.

Recognition of these factors may be helpful in limiting adhesion formation.

The use of uterine suture appears to increase the risk of uterine adhesions. In some studies, the frequency doubled after suturing. The suture induces local tissue ischemia with inflammatory changes, which slow the healing process and induce the formation of adhesions. Contradictory data have been published regarding adhesion formation and the use of bipolar coagulation during a laparoscopic procedure.

The location of the myoma also affects adhesion formation. Adhesions are more likely to form when the myomectomy site is located on the posterior uterine wall. During laparoscopy, a uterine incision must be made over each individual myoma. With laparotomy, a single anterior uterine incision may be used for polymyomectomy, even when posterior myomas are present.

The prior existence of pelvic adhesions significantly increases the risk of postoperative adnexal adhesions but has not been shown to affect adhesions at the myomectomy site.

Two prospective, randomized controlled studies have evaluated the efficacy of adhesion barriers during laparoscopic myomectomy, and both found intervention to be beneficial. Mais and colleagues evaluated the efficacy of oxidized regenerated cellulose, Interceed, on adhesion formation in a prospective

randomized study of 50 women after laparoscopic myomectomy. Interceed was placed over all incisions and suture material with a 1 cm margin, and the barrier was then moistened with saline. During the second-look laparoscopy, 60% of the Interceed group was free of adhesions, compared with only 12% of patients in the control group. Interceed appeared to substantially reduce, but not prevent, adhesions after laparoscopic myomectomy. Pellicano and collaborators showed that hyaluronic acid gel reduced adhesions after laparoscopic myomectomy in a prospective randomized study of 36 infertile women. During second look, 72% of patients were adhesion free, with hyaluronic acid gel treatment versus an adhesion-free rate of only 22% in the control group.

Multiple published studies (Seracchioli et al., Bulletti et al., Stringer et al., and Campo et al.) suggest that laparoscopic myomectomy may be a viable option for women with leiomyomata and infertility. The best prognosis is for young women with otherwise unexplained infertility and myomas that distort the endometrial cavity. Pregnancy rates and spontaneous abortion rates are comparable to abdominal myomectomy. Data are currently insufficient to determine the appropriate recommendation regarding mode of delivery.

Laparoscopic myomectomy is further discussed in Chapter 17.

Abdominal Myomectomy

The first successful abdominal myomectomy was performed in the United States by the Atlee brothers, Washington and John, in 1844. The first abdominal multiple myomectomy was performed by W. Alexander of Liverpool in 1898. In the early part of the 20th century, the technique of abdominal myomectomy was refined by many notable gynecologic surgeons, including Kelly, Cullen, Mayo, Rubin, Bonney, and others. The procedure did not gain popularity until the middle of the 20th century. The incidence of complications, including hemorrhage, infection, and postoperative intestinal obstruction from adhesions, was considered to be too high. Advances in surgical techniques to control intraoperative bleeding during myomectomy, along with advances in anesthesia, blood transfusion therapy, and GnRH analogs, have made myomectomy a safe alternative to hysterectomy in women with symptomatic leiomyomata. The number of myomectomies performed in the United States is increasing.

Because myomectomy is rarely an emergency, time is available to prepare the patient for surgery. It is important that she be properly informed of the reasons myomectomy has been recommended. She should understand the nature of the procedure so she can know what to expect and what is expected of her. It is especially important that she be informed of the possibility that intraoperative findings may contraindicate myomectomy and require

that hysterectomy be performed instead. For example, myomectomy may not be technically feasible if diffuse leiomyomatosis is found. The technical challenge of removing a large cervical myoma can also preclude myomectomy.

A preoperative hysterosalpingogram may indicate distortion of the fallopian tubes or uterine cavity, findings that are important in planning the technique of myomectomy. An assessment of fallopian tube patency is helpful in predicting fertility. If the tubes are occluded, however, myomectomy is not necessarily contraindicated. According to Seoud and associates, myomectomy does not interfere with in vitro fertilization performance in relation to overall and ongoing pregnancy rates. The patient whose tubes are occluded should understand that fertility may not be established by myomectomy, and assisted reproductive technologies may still be required after myomectomy. Tubal reconstruction procedures are uniformly unrewarding when performed at the same time multiple myomectomy is done. Indeed, tubal reconstruction may not always be necessary to establish tubal patency. In a report by Lev-Toaff and associates, nonfilling of the fallopian tubes was present on the preoperative hysterosalpingogram unilaterally in two patients and bilaterally in another two. In all four patients, tubal patency was shown after myomectomy. In the experience of these authors, hysterosalpingography before myomectomy can assist the gynecologic surgeon in planning the surgical approach by showing the presence, size, and location of submucous leiomyomata and concomitant tubal disease.

Imaging modalities such as transabdominal, transvaginal US and MRI play an important role in the management of patients with leiomyomata, especially those patients who are being prepared for myomectomy. As explained by Mayer and Shipilov, US is the preferred method for screening and initial evaluation of the pelvis. In many cases, it is the only imaging study necessary. There are special cases for which US cannot provide all the diagnostic information required. In a study by Schwartz and colleagues, US results were inconclusive in 20% of cases and did not yield a definitive diagnosis in 59% of cases. MRI was more definitive in all cases (**Fig. 31.20**).

The preoperative diagnosis of submucous leiomyomata by MRI may allow hysteroscopic resection and avoid abdominal myomectomy in some cases. Differentiation between uterine leiomyomata and adnexal pathology is more accurate with MRI and thus avoids the need for laparoscopy or laparotomy in some cases (**Fig. 31.21**). MRI studies can differentiate between uterine leiomyomata, diffuse and localized adenomyosis, and diffuse leiomyomatosis. MRI is the most accurate imaging technique for the detection and localization of leiomyomata (**Fig. 31.22**). Hricak and coworkers were able to identify accurately by MRI all subserosal (9 of 9), all intramural (37), and 10 of 11 submucosal leiomyomata. Leiomyomata as small as 0.3 cm can be detected. Various degrees of cellularity, degeneration, necrosis, and calcification can be identified by MRI, and sarcomatous change can be suspected. MRI provides imaging planes that are not available on transabdominal or transvaginal US, a feature that permits better visualization of the more lateral and posterior areas of the pelvis. MRI is the most accurate method for preoperative localization of leiomyomata and surgical planning for myomectomy. Given the greater costs of MRI, it should be used judiciously. However, as noted by Mayer and Shipilov, the effective cost differential between MRI and US is decreasing.

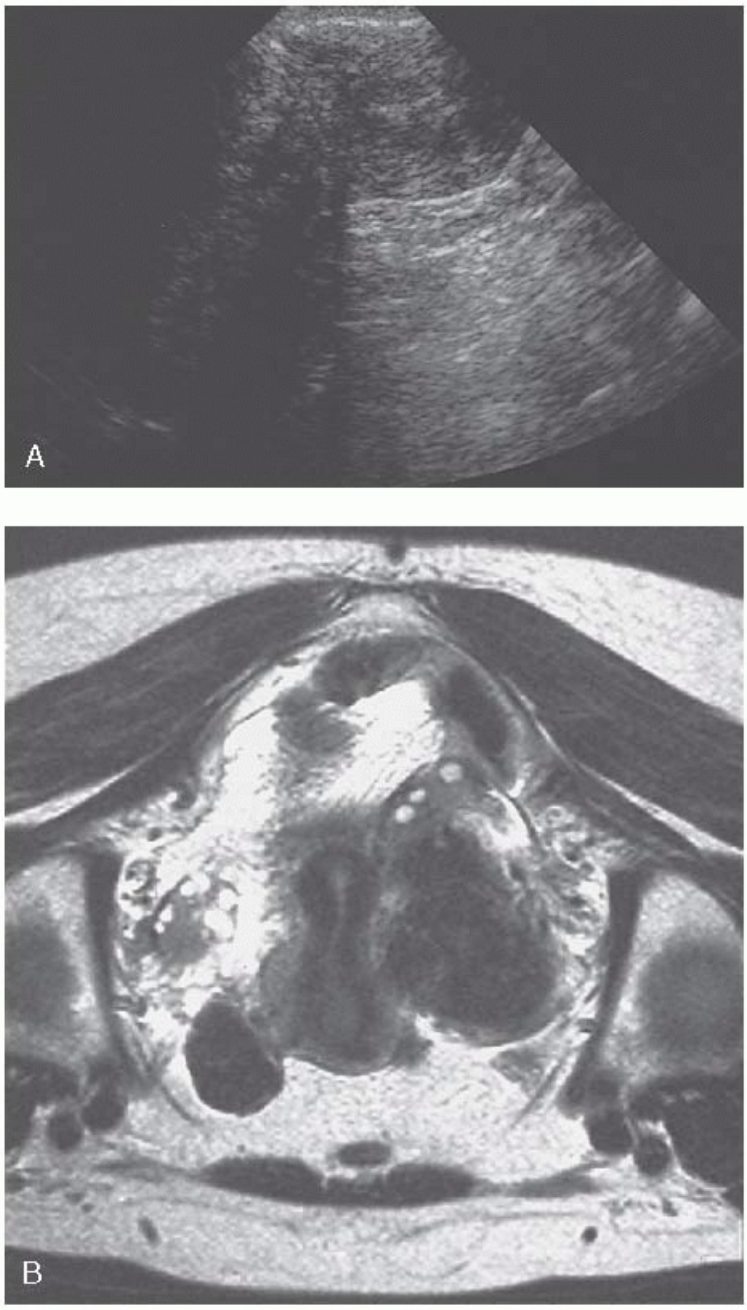

FIGURE 31.20 A: The ultrasound evaluation of this patient with a very large leiomyoma was not helpful in delineating the leiomyoma from the adnexa. **B:** The MRI study demonstrated multiple leiomyomas distinctly separate from the adnexa bilaterally. The ovaries are seen bilaterally with multiple cysts. (Image courtesy of Deborah Baumgarten, MD.)

As discussed by Wiskind and Thompson, one of the most serious risks of surgical bleeding during myomectomy is the risk associated with homologous blood transfusion. The first rule in reducing or eliminating the need for transfusion is to bring the patient to the operating room with the highest possible hemoglobin and hematocrit level. About 30% of myomectomy patients have associated menorrhagia. These small, repeated menstrual hemorrhages deplete the body's iron stores over time and eventually result in iron deficiency anemia of various degrees of severity. Patients scheduled for myomectomy benefit from oral iron supplementation. In a study by Thompson, the liberal use of oral iron therapy preoperatively was shown to decrease the number of blood transfusions on the gynecologic surgical service at the Johns Hopkins Hospital. A blood transfusion is seldom necessary to correct iron deficiency anemia in a gynecologic patient. Blood transfusions should generally be reserved for patients with hypovolemic shock or aregenerative forms of anemia. In most other circumstances, elective surgery should be delayed until the anemia has been corrected by oral iron supplementation.

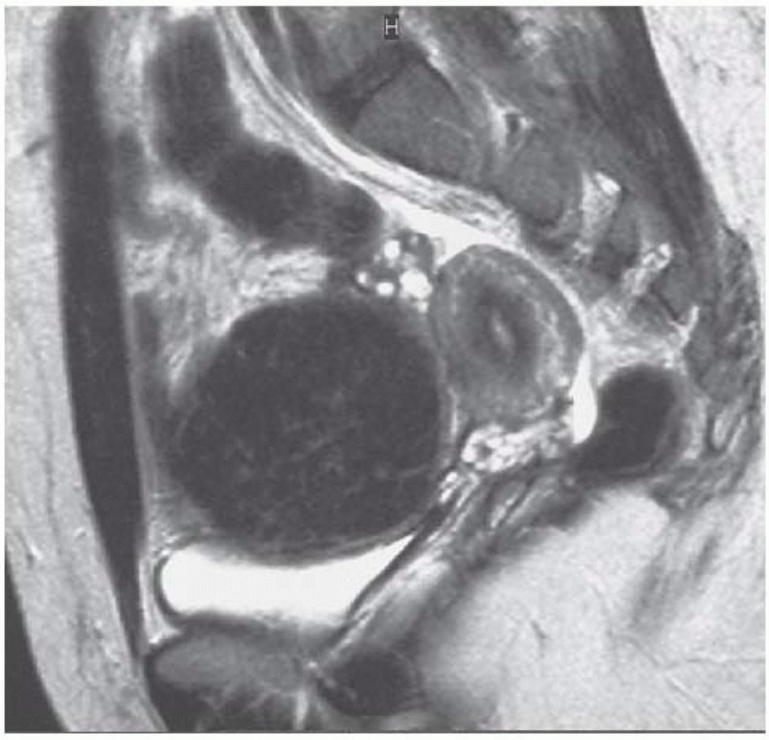

FIGURE 31.21 On MRI, a large anterior, pedunculated leiomyoma is shown as a separate entity from the ovary in this patient. The ovary is displaced superiorly. (Image courtesy of Deborah Baumgarten, MD.)

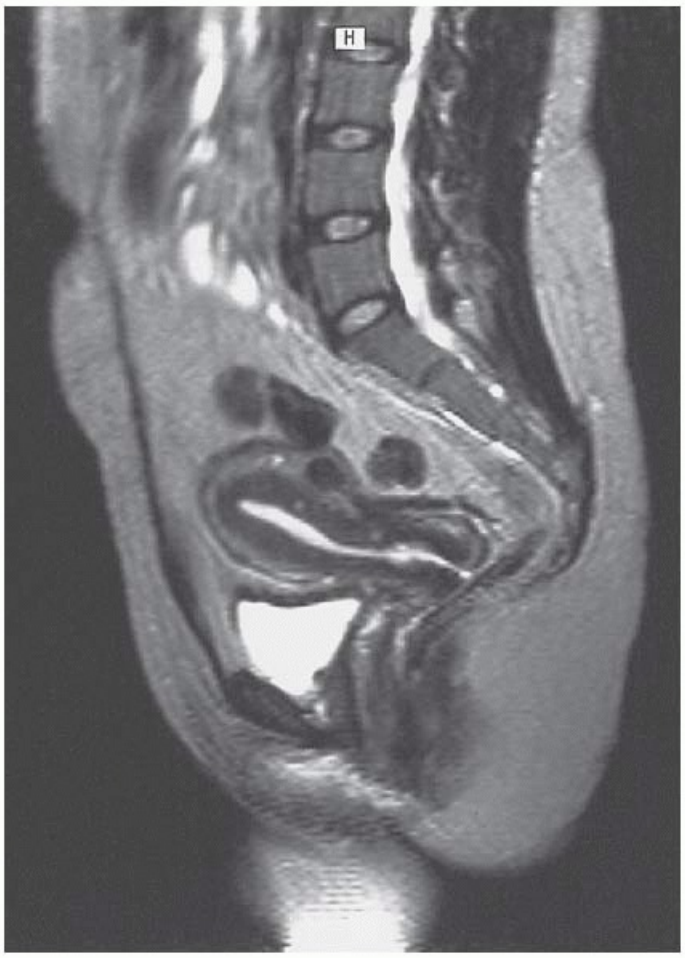

FIGURE 31.22 The location of this small posterior intramural leiomyoma is clearly delineated in this magnetic resonance image. The cervical canal is also easily visible. (Image courtesy of Deborah Baumgarten, MD.)

Occasionally, patients with a myomatous uterus have iron deficiency anemia because of menstrual bleeding that

is too heavy or too continuous to allow a response to oral iron therapy. In this situation, it may be beneficial to induce amenorrhea with hormonal therapy to allow the anemia to be corrected more expeditiously. Amenorrhea can be induced with progestational agents such as norethindrone or medroxyprogesterone acetate, with danazol, or with GnRH agonists. Several studies have demonstrated a significant increase in hemoglobin and hematocrit values in patients with leiomyomata treated preoperatively for 8 to 24 weeks with GnRH analogs compared with matched control groups. Friedman and colleagues also found a significant increase in serum iron and total iron-binding capacity in a study group treated with the GnRH agonist leuprolide acetate. In some patients, oral iron was also given. In an evaluation of 265 patients, GnRH agonists plus iron were more effective than iron alone in treating the anemia of patients with uterine leiomyomata, according to Stovall and coworkers. In a double-blind, placebo-controlled, multicenter study, Friedman and associates reported resolution of menorrhagia in 97% of uterine leiomyomata patients treated with GnRH agonists.

Preoperative treatment with GnRH analogs can actually reduce the operative blood loss during myomectomy, according to studies by Friedman and colleagues, Andreyko and coworkers, Moghissi, and others. In a prospective randomized study of 50 patients undergoing hysterectomy for symptomatic leiomyomata, Stovall and colleagues found a significant decrease in operative blood loss between those patients who

received 2 months of leuprolide acetate treatment preoperatively and matched control subjects. An elegant study by Friedman and associates demonstrated a significant decrease in operative blood loss during myomectomy between patients with pretreatment uterine volumes greater than 600 cm^3 who were treated with depot leuprolide acetate for 12 weeks preoperatively and a matched control group. However, there was no significant difference in blood loss between the two groups when patients with smaller uterine volumes (150 to 600 cm^3) were included in the analysis. It has been suggested that the hypoestrogenic environment caused by GnRH analog therapy reduces the vascular supply to uterine leiomyomata. However, even in patients not treated with GnRH agonists, blood flow has been observed to be lower in myomata and adjacent tissue.

Intraoperative autotransfusion and normovolemic hemodilution are also discussed. These techniques of reducing or avoiding the risk of homologous blood transfusion are discussed in detail by Wiskind and Thompson.

Perioperative antimicrobial prophylaxis is indicated with myomectomy. It is preferable to perform the operation in the follicular phase of the menstrual cycle. This avoids the chance of encountering an unknown or unsuspected pregnancy and reduces the problems encountered when a fresh corpus luteum is inadvertently traumatized.

Surgical Technique: Abdominal Myomectomy

After induction of anesthesia, the patient is placed in Allen universal stirrups, the bladder is emptied, and a careful pelvic examination, including a rectovaginal-abdominal bimanual examination, is performed under anesthesia. Preparation and draping are done to allow access to the vagina and cervix in case it is necessary to place an instrument through the cervix and into the endometrial cavity during the procedure. Cervical dilatation should be done to facilitate postoperative drainage from the endometrial cavity, especially for cases in which the endometrial cavity has been entered during the myomectomy.

Many of the general principles of pelvic surgery are applicable to myomectomy. Perhaps the most important of these is optimum exposure at the operative site. This is accomplished primarily by an adequate incision, but there must also be proper retraction, good lighting, and able assistants. Although a Pfannenstiel incision is considered adequate for myomectomy on a small uterus, we prefer the Maylard incision for larger uteri, even those that exceed a size equivalent to a 12-week pregnancy. A Maylard incision provides excellent exposure throughout the pelvis. Because it is a transverse incision, it is stronger and provides better cosmesis than a vertical midline incision. A Bookwalter retractor optimizes exposure of the operative site. A Pfannenstiel incision can be used for removal of a small, solitary myoma.

The importance of adequate exposure cannot be overemphasized. With proper exposure, operative time can be shortened and surgical bleeding can be more easily identified and controlled. Limited exposure may lengthen operative time, increase the risk of inadvertent injury to other pelvic structures, and force abandonment of a myomectomy in favor of a hysterectomy in especially difficult cases.

After the peritoneal cavity is entered, the abdomen is explored as usual. Adhesions in the pelvis must be carefully released or excised so that the intestines can be placed in the upper abdomen and held there with packs. The operation is performed according to microsurgical techniques and principles. For example, the laparotomy packs that are used to hold the intestines in the upper abdomen are placed in plastic bags to reduce the microscopic trauma to peritoneal surfaces caused by regular laparotomy packs. Lintless laparotomy packs are preferred. Several laparotomy packs in plastic bags can be used to fill the cul-de-sac, thus elevating and stabilizing the uterus for easier access. Visualization of the operative site can be improved by the liberal use of suction to remove blood from the field. Suction should be used instead of sponges because it allows for a more accurate determination of blood loss and is less traumatic to tissues.

The operative field is kept moist and free of clots with a solution of lactated Ringer containing heparin. Very fine instruments and sutures are used when possible, and tissue is handled gently to avoid unnecessary trauma to serosal surfaces. Traumatic instrumentation (e.g., uterine elevators with teeth, Kocher clamps, or any instrument on the uterine serosa) must be avoided. Sutures on serosal surfaces should be of a fine absorbable nonreactive material. Running suture lines are preferable to avoid extra knot volume, which may contribute to adhesion formation. If pelvic adhesions develop after myomectomy, future fertility may be adversely affected. Performing the operation in a way that minimizes adhesion formation greatly improves the possibility of a successful result.

At this point in the operative procedure, one should pause and evaluate the size, location, and number of myomata present. Special note should be made of their proximity to the endocervical canal, uterine vessels, and fallopian tubes. One must decide if myomectomy is still feasible, how the leiomyomata will be removed (and in what sequence), and how the uterus will be reconstructed.

The conservation of uterine function with myomectomy requires control of bleeding from uterine incisions and myoma beds. Contrary to hysterectomy for leiomyomata, conservation of the uterus requires that the blood supply to the uterus through the uterine and ovarian vessels remains intact. Removing multiple myomata embedded deeply in a vascular myometrium can result in considerable blood loss. Proper application of special techniques to limit blood loss can allow multiple myomectomies even in uteri up to 20 weeks pregnancy size if satisfactory reconstruction is possible.

Controlled hypotensive anesthesia has become a useful adjunct to decrease surgical bleeding in selected patients. The main mechanism in the control of operative field bleeding with hypotensive anesthesia is the reduction of venous tone. This can be accomplished by specific vasodilating agents—such as nitroglycerin or sodium nitroprusside, epidural or spinal anesthesia, some inhalation anesthetic agents, and ganglionic blockade—to achieve and maintain a target mean blood pressure of 60 mm Hg. Our experience with this technique has been favorable. Venous bleeding can be further reduced if the patient is placed in a moderate Trendelenburg position. This facilitates venous drainage from the lower extremities and pelvis by gravity and may further reduce the blood pressure at the operative site.

Induced hypotension is contraindicated in patients with cerebrovascular disease, myocardial ischemia, peripheral vascular disease, severe renal or hepatic disease, and hypovolemia. None of these contraindications is seen very often in myomectomy patients. An anesthesiologist experienced with the technique is an essential requirement. The decision to use hypotension should be made jointly by the surgeon and the anesthesiologist. It is essential that the blood pressure be returned to normal before closure of the incision to ensure that adequate surgical hemostasis has been established.

Early proponents of myomectomy focused on methods to temporarily occlude uterine blood flow to control hemorrhage and provide a bloodless operative field. One of the earliest methods was simply to have an assistant grasp the broad ligaments firmly with each hand during myomectomy to impede blood flow through the uterine vessels. In the 1920s, Victor Bonney

introduced a specially designed clamp that was placed around the uterine vessels and the round ligaments. The ovarian vessels were occluded with ring forceps. Using this technique, he was able on one occasion to remove more than 200 myomata from a single uterus. Rubin, in 1938, was the first to use an elastic rubber tourniquet through the broad ligament, encircling the cervix and occluding the uterine vessels during myomectomy. Rubbershod clamps applied to the broad ligaments have also been used to occlude the uterine vessels and control bleeding.

Gynecologic surgeons do not often have the opportunity to use tourniquets to control bleeding; however, a myomectomy is particularly suited to their use. We prefer to use tourniquets fashioned in the manner of a Rumel-type tourniquet, which is used by vascular, thoracic, and trauma surgeons to occlude major vessels. Initially, a small hole is made in an avascular space in the broad ligament on either side of the uterine isthmus just lateral to the uterine vessels. A 5-French pediatric feeding tube is looped around the upper cervix through the holes in the broad ligament, and the two ends of the tube are then threaded through a 4-inch length of 35-French Malecot catheter and held with a clamp. A loop tourniquet can then be placed around each infundibulopelvic ligament through the same holes in the broad ligaments (**Fig. 31.23A**).

As the tourniquets are being placed, controlled hypotension is induced by the anesthesiology staff. Before the tourniquets are tightened, the location of the uterine arterial blood flow is identified with a sterile Doptone. When everything is in readiness and the plan of operation has been selected by the surgical team, the tourniquets are snugged down and tightened progressively until the uterine arterial flow is no longer audible with the Doptone (**Fig. 31.23B**). It is very important that the arterial blood flow be occluded. If the venous flow is occluded while the arterial flow remains intact, blood loss could actually be increased with the tourniquets. The mean blood pressure should be reduced to the target hypotensive level (about 60 mm Hg) before the tourniquets are tightened. The higher the blood pressure, the tighter the tourniquets must be to occlude the uterine circulation.

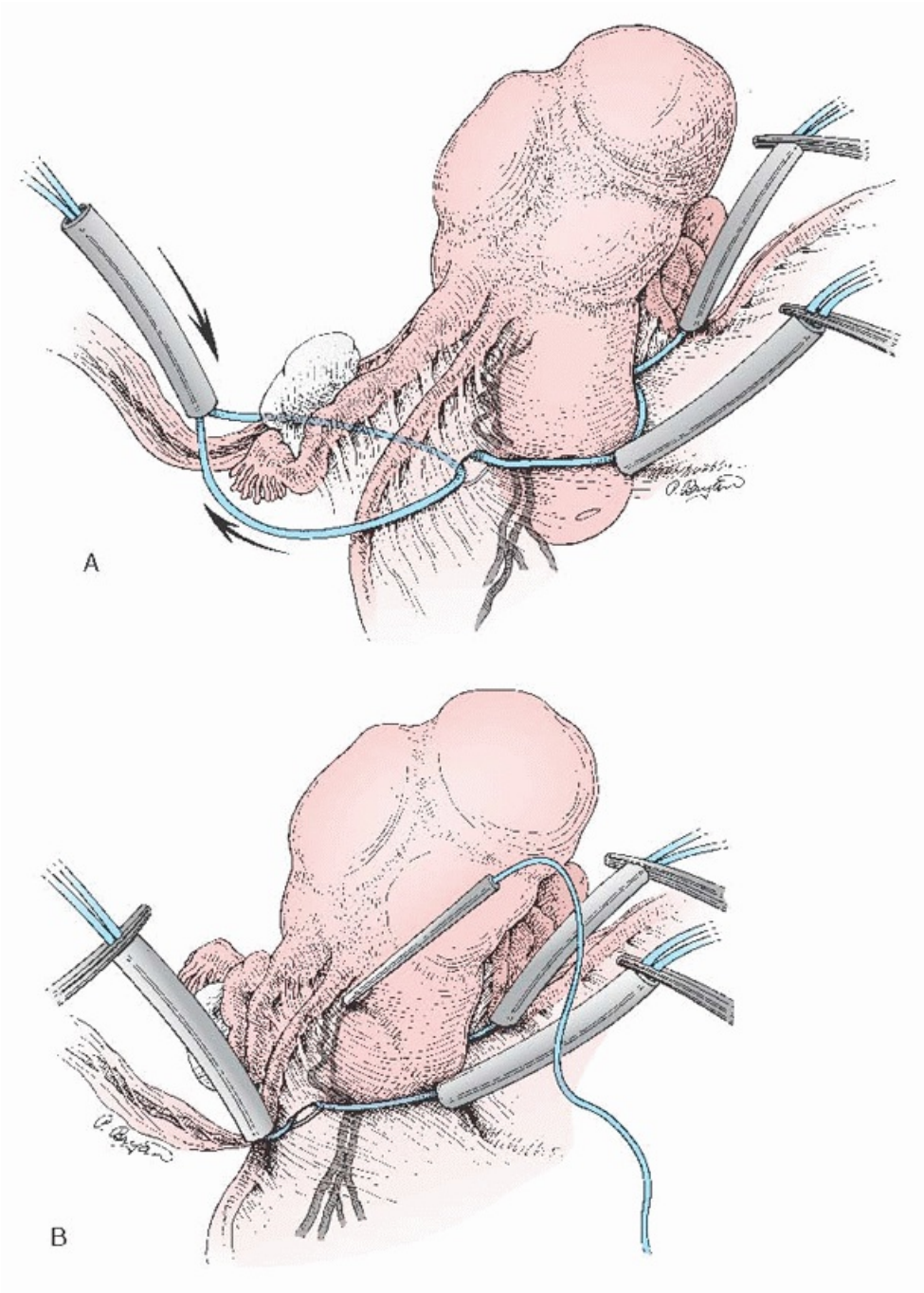

FIGURE 31.23 A: Through a small hole in the broad ligament on each side of the uterus, a Rumel tourniquet is placed around the lower uterus and around each infundibulopelvic ligament. **B:** When the tourniquets are tightened sufficiently, the blood flow to the uterus stops. The absence of arterial pulsations can be determined with the sterile Doptone.

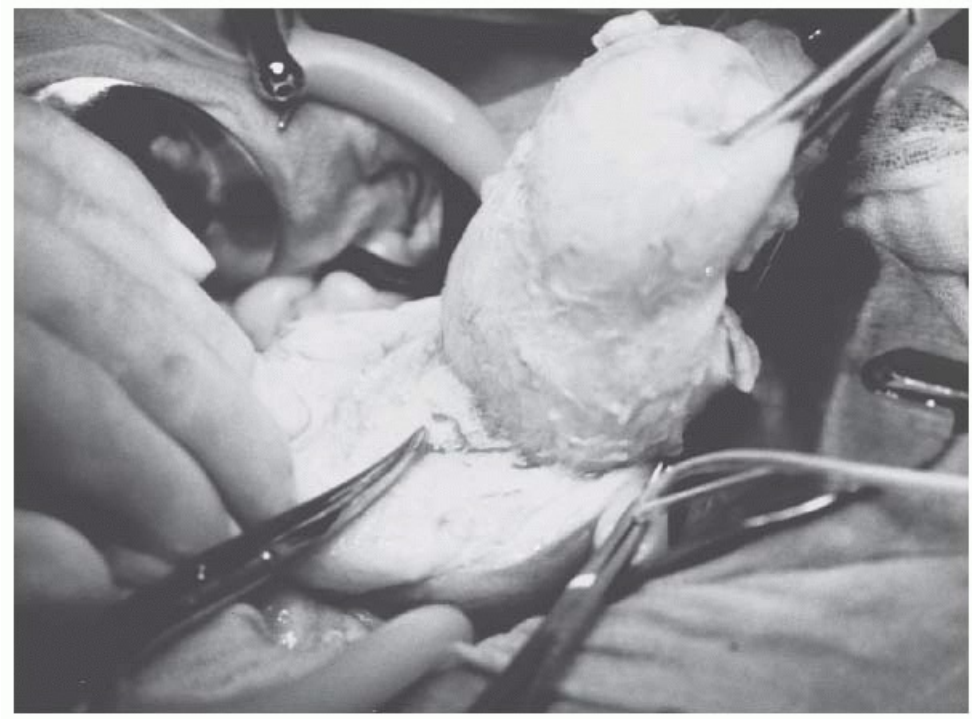

FIGURE 31.24 With tourniquets properly secured, myomectomy can be performed with minimal blood loss.

With the combination of properly applied tourniquets and controlled hypotensive anesthesia, the entire circulation to the uterus can be occluded. The myomectomy can then be performed in a bloodless field, greatly facilitating complete removal of all tumors and a neat reconstruction of the uterus (**Figs. 31.24** and **31.25**). Occasionally, a large cervical or broad ligament myoma prevents placement of the tourniquets. In this situation, the offending tumor should be removed first, the defects repaired when feasible, and the tourniquets applied for the remainder of the multiple myomectomy.

Once the tourniquets are tightened in place, the myomectomy should proceed expeditiously to prevent ischemic damage to the uterus, tubes, and ovaries. The length of time the pelvic structures can be without blood flow before irreversible damage occurs is unknown. We generally do not release the tourniquets until the myomectomy is complete (usually within an hour) and have not experienced any adverse events. Lock also agrees that intermittent release of the tourniquets is unnecessary. However, because the potential for injury does exist, tourniquet time should be monitored and kept to a minimum. The tourniquets should not be tightened until the surgical team is ready to perform the myomectomy. Intermittent release of the tourniquets should be considered if the operating time becomes excessive. We usually release the tourniquets around the ovarian vessels as the uterine serosa is being closed to restore circulation to the tubes and ovaries and to restore some collateral flow to the uterus. After reconstruction of the uterus is complete, the determination of adequate hemostasis in the uterus cannot be made until all the tourniquets are released and the blood pressure has returned to normal. Sometimes, additional sutures are required for hemostasis. Before the abdomen is closed, the small holes in the broad ligament are repaired with figure-of-eight sutures.

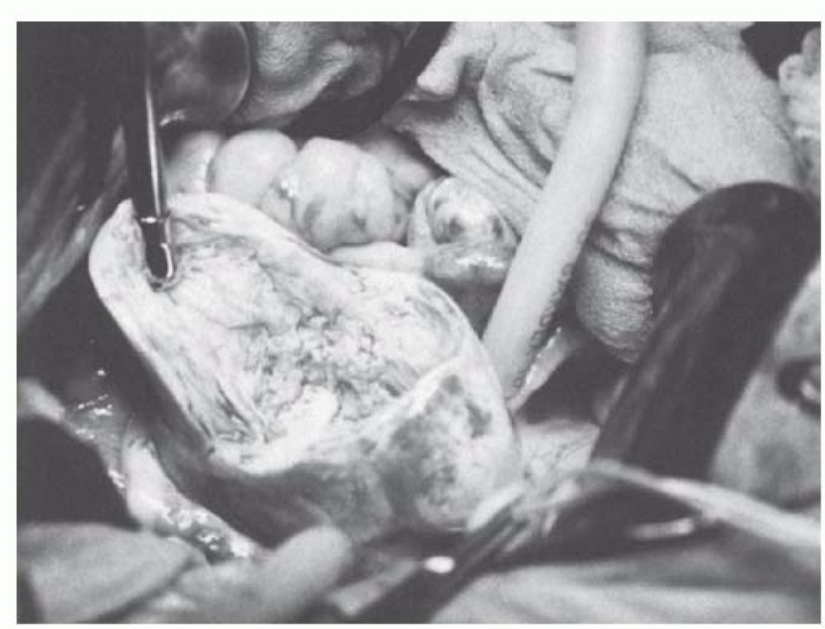

FIGURE 31.25 The use of tourniquets to control bleeding facilitates closure of the myoma bed and uterine incision.

Tourniquets are not necessary for every myomectomy, especially when the tumors are small or pedunculated. However, they are safe and inexpensive to use and can be of great benefit when large or multiple intramural myomata must be removed. A criticism of uterine tourniquets is that they are traumatic to pelvic structures. Our experience, to the contrary, is that soft plastic tubes used as tourniquets are quite atraumatic. No injuries attributable to these tourniquets have occurred in several hundred cases.

An alternative to the use of tourniquets to control bleeding during myomectomy is the local injection of vasoconstrictive agents. Perhaps, the most commonly used agent is vasopressin, a synthetic derivative of the antidiuretic hormone from the posterior lobe of the pituitary gland. In addition to this antidiuretic effect, vasopressin induces smooth muscle contraction of the gastrointestinal tract and the vascular bed. In particular, it has been found to have a potent vasoconstrictor effect on the nonpregnant uterus when injected locally. It has a plasma half-life of 10 to 20 minutes and has been used effectively as a hemostatic agent during myomectomy. Pharmacologic vasoconstriction can be accomplished with vasopressin (antidiuretic hormone), 20 U (Pitressin). Twenty units of vasopressin are diluted in 20 mL of normal saline and injected into the superficial myometrium and serosa overlying the myoma. The effect usually lasts for 30 minutes.

Dillon reported that with the use of vasopressin, 72% of patients requiring myomectomy did not need blood replacement compared with control subjects. Frederick and coworkers noted significantly less blood loss compared with an untreated group. Ginsberg and associates compared vasopressin with mechanical vascular occlusion and found that there were no demonstrable

differences in blood loss, morbidity, or transfusion requirements between the two techniques. A favorable experience with vasopressin has also been reported by Semm and Mettler.

The weight of evidence in current clinical investigation indicates that vasopressin is as effective as mechanical vascular occlusion in controlling blood loss with myomectomy. Nevertheless, careful dissection around myomata and prompt suturing with exertion of direct pressure to bleeding vessels by the operative assistant are necessary to minimize blood loss. Care should be taken to avoid injecting the solution directly into a vascular channel, and no more than 30 mL per patient is recommended because of potential side effects. Vasopressin should not be used in patients with vascular disease, especially disease of the coronary arteries. Inadvertent intravascular

injection can cause anginal pain; larger doses can cause myocardial infarction. Water intoxication can also occur as a result of the antidiuretic effect of vasopressin. This effect is potentiated in patients taking tricyclic antidepressants.

Although late postoperative bleeding does occur with the use of vasopressin, it is not a common complication. Arterial bleeding masked by vasopressin still requires suture ligation. Because of the short half-life of vasopressin, the hemostatic effect is observed only for 20 to 30 minutes and should be over before the incisional closure is started. However, some do claim that vasopressin simply delays bleeding, gives a false sense of security, and is not particularly effective for larger myomata and very extensive myomectomies.

For a variety of reasons, epinephrine as a vasoconstrictive agent is not recommended for use in gynecologic surgery.

Since its introduction into clinical practice in 1972, the CO_2 laser has been touted as a tool that increases surgical precision and decreases bleeding, tissue injury, and adhesion formation. The laser can be used to make a single uterine incision through which multiple myomata are removed. An elliptical incision can also be made around the base of larger myomata to facilitate their removal. Myomata less than 1 cm in diameter can be vaporized directly with the laser, which destroys tissue by vaporizing cellular water. Despite the favorable results reported by Weather, Reyniak and Corenthal, McLaughlin, and Starks, we believe that there is no clear advantage to using the CO_2 laser for abdominal myomectomy, especially considering the added cost to the patient.

Although the methods described earlier to control bleeding during myomectomy are helpful, they cannot substitute for good surgical techniques. Adherence to basic principles is essential for good results. Perhaps the most important of these is careful planning of the uterine incisions. Only a minimal number of incisions should be made. If possible, removal of all leiomyomata should be accomplished through a single incision in the anterior uterine corpus and in the midline, when feasible, to avoid the vascular areas of the uterus and broad ligaments laterally. Even intramural leiomyomata in the posterior uterine wall can be removed through anterior incisions. Incisions in the posterior uterine wall may be necessary, however, if posterior subserous tumors are being removed. If posterior uterine incisions are made, adhesions are more likely to develop and will likely involve the tubes and ovaries as well.

As many tumors as possible should be removed through a single incision. Methods of removing myomata through a single anterior incision have been described by Bonney. The linear or elliptic incision should usually be over the largest myoma. It should be carried through the superficial myometrium directly into the underlying myoma. The myoma is then grasped with a double-tooth tenaculum or a large Lahey thyroid clamp for traction. The plane of cleavage between the myoma and the surrounding myometrium is easily identified. Sometimes in patients who have been treated with GnRH analogs, the plane of cleavage may seem less distinct. Sharp dissection with the scalpel or Metzenbaum scissors, or blunt dissection with the finger or knife handle, is required to enucleate the myoma from its bed. Sometimes, the myoma is larger than expected. It may then be necessary to enlarge the incision or to remove the tumor by morcellation. Other adjacent tumors should be removed through the same incision. Any entry in the endometrial cavity should be noted, and a special attempt should be made to close it with sutures placed in the underlying supporting myometrium. Examples of the step-by-step planning and performance of a multiple myomectomy are illustrated in **Figures 31.26** and **31.27**.

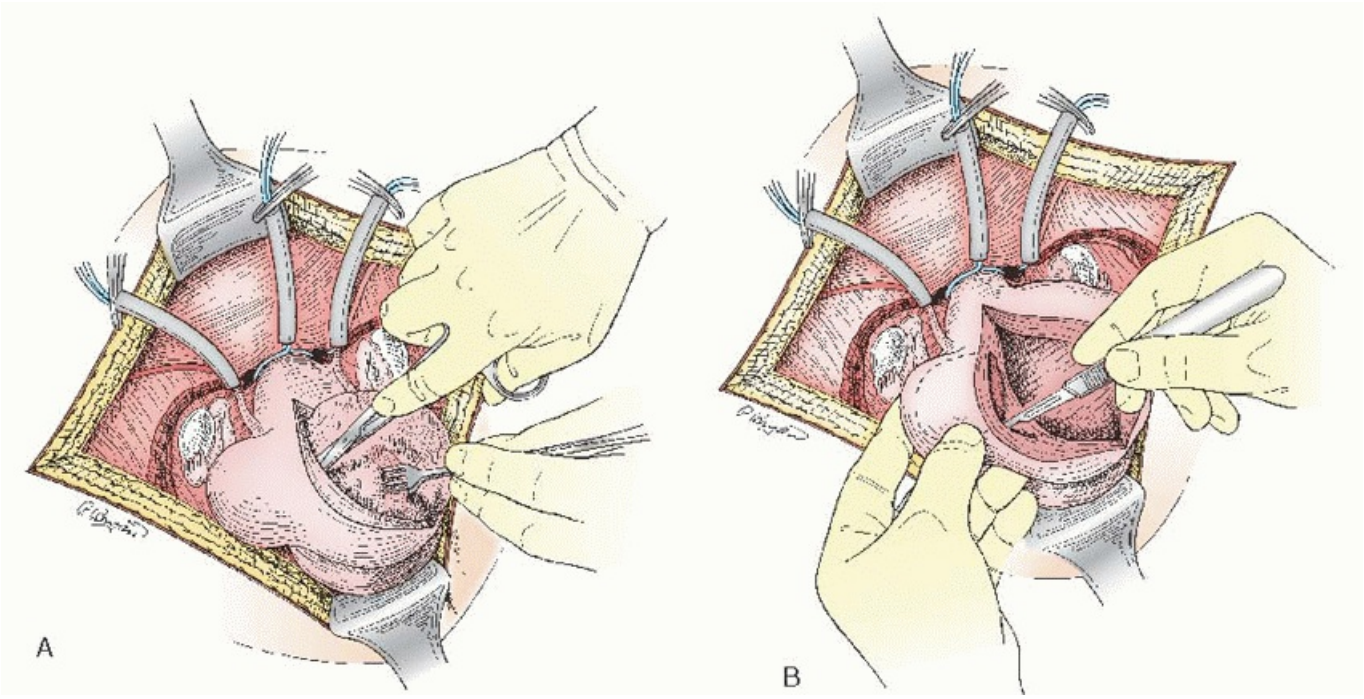

FIGURE 31.26 The sequence of steps in a multiple myomectomy is shown in these illustrations. **A:** Through a transverse Maylard incision, tourniquets are placed to occlude the uterine and ovarian artery flow. Through a single incision in the anterior myometrium, a large anterior myoma is removed first. All other myomas are removed through this incision. **B:** A smaller intramural myoma is removed through the same incision.

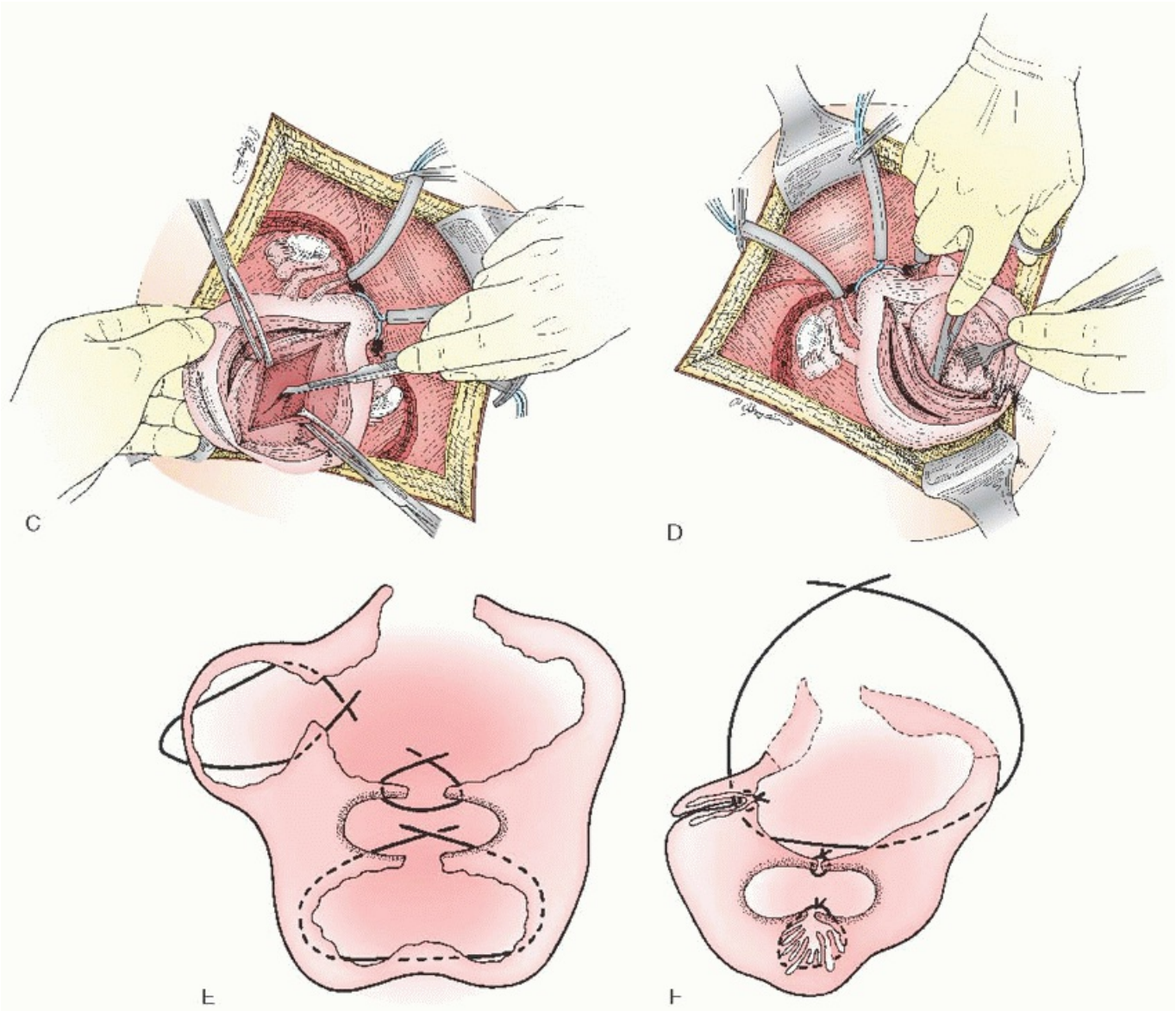

FIGURE 31.26 (*Continued*) **C:** To avoid making a separate incision in the posterior uterine wall, a large posterior myoma is removed through the uterine cavity. After an incision has been made through the anterior endometrium, an incision is made in the posterior endometrium directly over the posterior myoma. **D:** The myoma in the posterior uterine wall is dissected from its bed and removed through the uterine cavity. An incision in the posterior uterine serosa is thus avoided. **E:** Multiple sutures (2-0 delayed absorbable) are used to close the defect in the posterior uterine wall first. Incisions in the uterine cavity are closed. Then, the defects in the anterior uterine wall are closed. **F:** Trimming excess myometrium from the anterior uterine wall allows a better approximation of the myometrium. The edges of the serosa are closed with a continuous “baseball” stitch with 4-0 delayed absorbable sutures.

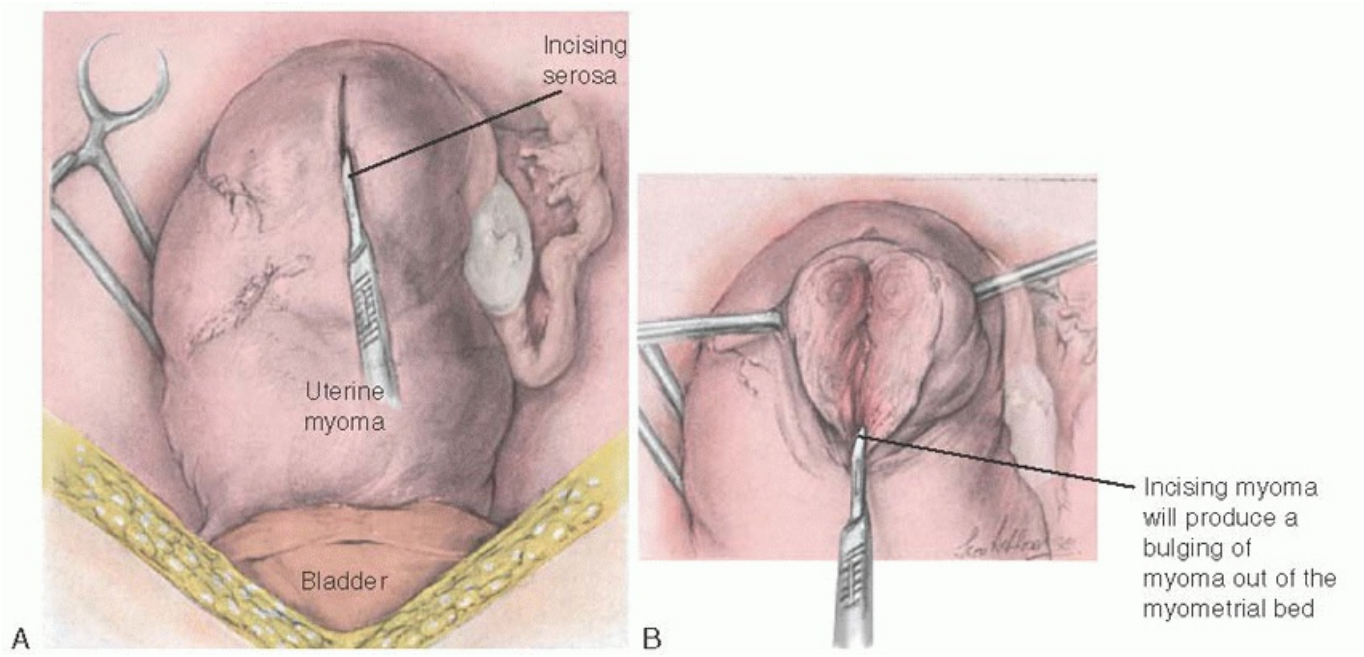

FIGURE 31.27 Techniques of multiple myomectomy. **A:** A vertical incision is made over a myoma on the anterior surface of the fundus as close to the midline as possible. Many myomas can be removed through this single incision. **B:** The incision is extended into the substance of the myoma.

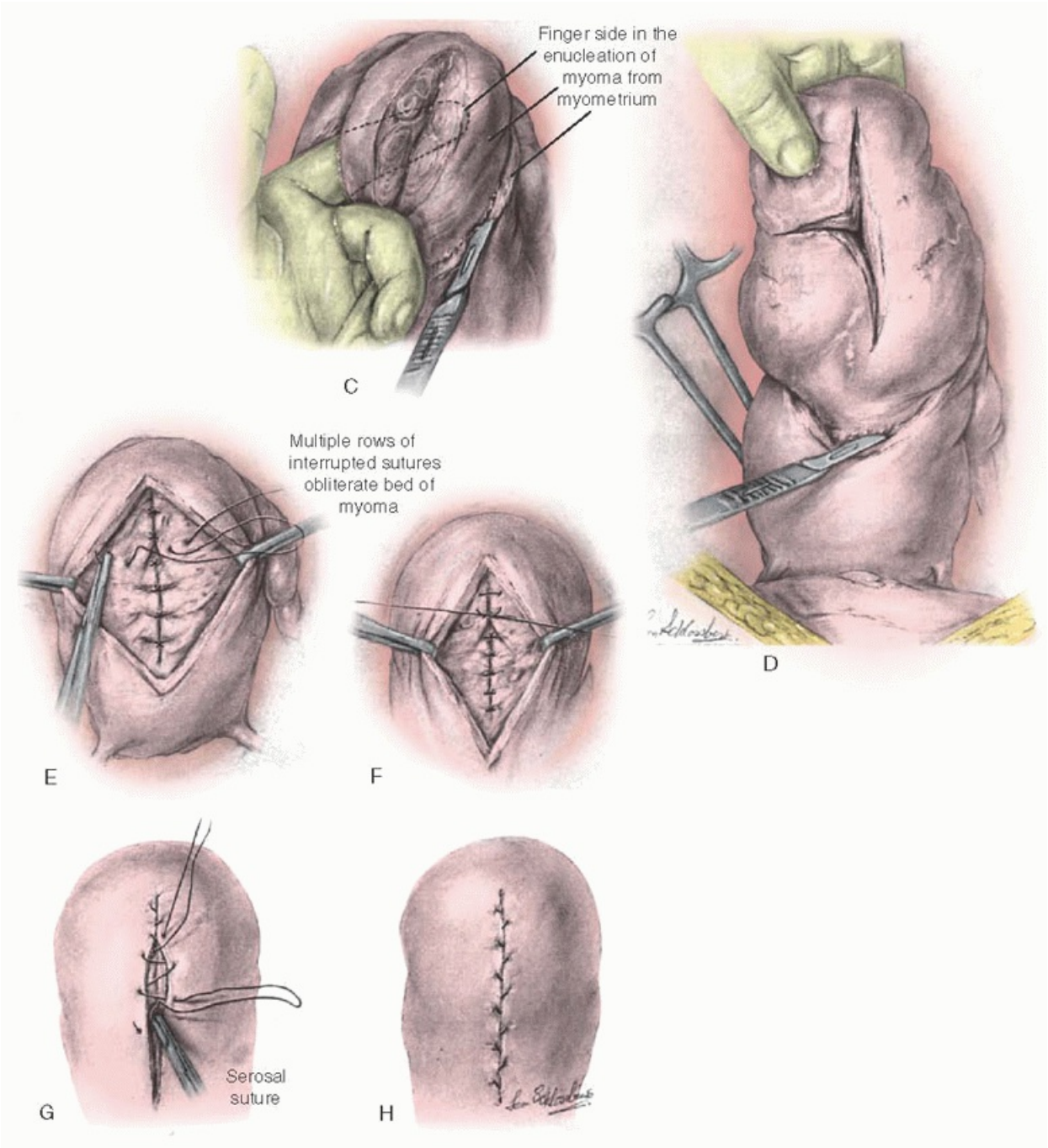

FIGURE 31.27 (*Continued*) **C:** By incising progressively deeper into the myoma, the surgeon can identify and bluntly dissect the plane between myoma capsule and myometrium. **D:** Sharp dissection may be necessary to separate the myoma from its capsule at its base. **E:** After the removal of as many myomas as possible, the remaining cavity is obliterated and hemostasis secured. **F:** Multiple rows of nonreactive interrupted absorbable suture material are used to close the cavity. **G:** When the "dead space" has been obliterated, the serosa is closed with a continuous "baseball" suture of 5-0 or 6-0 nonreactive absorbable material. **H:** This type of closure approximates the serosal edges.

The muscle fibers and blood vessels surrounding a myoma are compressed by its growth. This compression of surrounding tissue forms a pseudocapsule around the myoma. No large blood vessels enter the myoma, and there is no vascular pedicle. If the dissection can be carried out between the myoma and the pseudocapsule, blood loss can be minimized. If blood vessels are cut or left on the surface of the myoma, it usually means that the dissection has been carried out in an improper plane. Dissection in the proper plane may be more difficult if the patient received GnRH analog therapy preoperatively.

Several ingenious techniques for removing leiomyomata and for repairing defects have been described. For

example, Bonney hood can be used to remove a large leiomyoma in the uterine fundus. The myoma is first exposed through an elliptic incision made transversely across the anterior fundus, taking care to avoid the interstitial portion of the fallopian tube on each side (**Fig. 31.28A, B**). After the primary tumor is removed (**Fig. 31.28C**), other leiomyomata can also be removed through the same incision. Excess myometrium can be trimmed away (**Fig. 31.28D**). Interrupted sutures obliterate the dead space, approximate the myometrium, and accomplish satisfactory hemostasis. The sutures are placed in such a way that the posterior flap of myometrium is folded over the anterior uterine wall and sutured in place, thus fashioning Bonney hood (**Fig. 31.28D**).

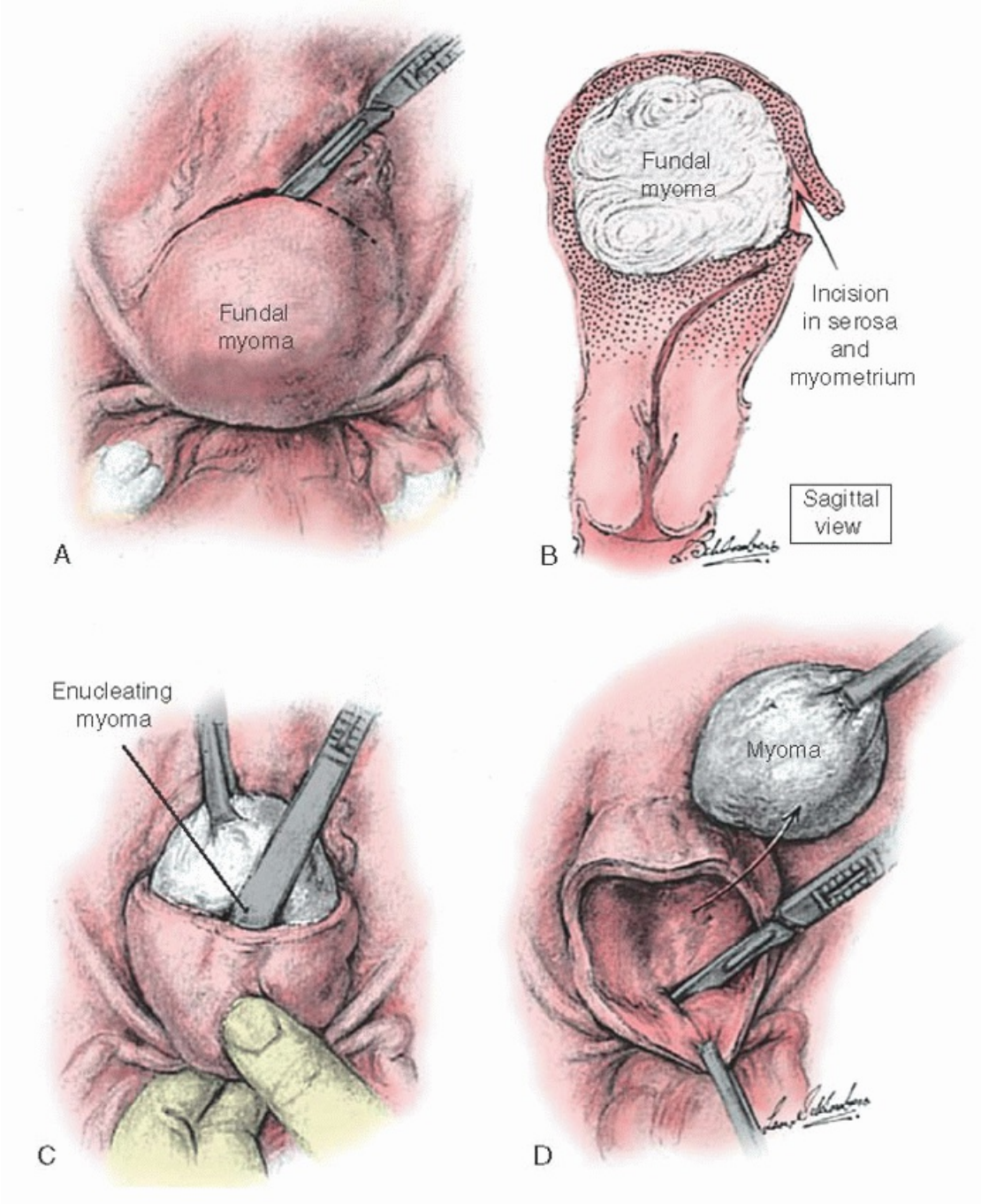

FIGURE 31.28 Technique of myomectomy using an anterior hood incision as described by Bonney. **A:** A transverse incision is made in the anterior fundal wall over the myoma. **B:** Sagittal view of the location of the incision. **C and D:** Using blunt and sharp dissection, the surgeon enucleates the myoma from its bed. Excess hypertrophied myometrium may be trimmed and removed before closure of myometrium and serosa.

Meticulous closure of defects from the enucleated myomata is essential to maintain hemostasis postoperatively, but this should be deferred until all the tumors are removed. Hypertrophy of the normal myometrium is always

present with uterine leiomyomata. Some of this hypertrophied myometrium is considered excess and can be trimmed to facilitate a more normal reconstruction of the uterus. Involution of the myometrial hypertrophy is expected to occur in the first few months after myomectomy. Therefore, only a small amount of normal myometrial tissue should be removed. In reconstructing the uterus, the surgeon should refer to fixed points such as the attachments of the round ligaments and fallopian tubes on each side of the corpus. Symmetric reconstruction is preferred but is not always possible. The myoma beds are usually closed with interrupted figure-of-eight or mattress 2-0 delayed absorbable sutures. Large defects can be closed initially with a purse-string suture to obliterate the dead space. Several layers of sutures may be required. One must be careful to avoid occlusion of the uterine vessels, the endocervical canal, or the interstitial portion of the fallopian tubes. Transfundal or transcervical chromotubation to test fallopian tube patency after uterine reconstruction is complete is not usually possible because of leakage of the dye through the myometrial incisions.

In closing a myomectomy incision, the security of the closure comes from sutures placed in the myometrium. If possible, these sutures and knots must not be exposed. In **Figure 31.26E** and **F**, several techniques of closing myometrial defects are illustrated. The serosal edge of the uterine incision should be carefully approximated with a continuous 5-0 or 4-0 delayed absorbable “baseball” stitch.

The tourniquets are removed, the hypotensive anesthesia is reversed, and the uterus is carefully inspected for evidence of bleeding. Additional sutures are sometimes required. If a uterine suspension is needed, a modified Coffey or modified Gilliam technique along with uterosacral ligament plication is used.

Adhesion prevention can also be achieved by the use of absorbable or nonabsorbable barriers. The absorbable barrier Interceed (oxidized regenerated cellulose) can be placed over the uterine corpus to protect the tubes and ovaries from denuded peritoneal surfaces and uterine incision. Alternatively, a nonabsorbable barrier, Gore-Tex (polytetrafluoroethylene

surgical membrane), can be sutured over the uterine incisions with 7-0 absorbable minimal reactive sutures. The use of Gore-Tex has been associated with a reduction in new adhesion formation. Diamond and the Seprafilm Adhesion Study Group assessed the efficacy of Seprafilm (HAL-F) bioresorbable membrane (sodium hyaluronate and carboxymethylcellulose) in reducing the incidence, severity, extent, and area of uterine adhesions after myomectomy. This prospective, randomized, blinded, multicenter study involved an independent gynecologic surgeon’s review of each patient’s second-look laparoscopy. One hundred twenty-seven women undergoing uterine myomectomy with at least one posterior uterine incision were randomized to treatment with Seprafilm or to no treatment at the completion of the myomectomy. All indices, including incidence, severity, and extent of adhesions, were decreased in the treatment group. This suggests that newer barriers may also have a role in adhesion prevention. Free grafts of peritoneum or omentum should not be used to cover uterine incisions.

In a randomized controlled trial, Imai found fewer adhesions with GnRH analogue pretreatment compared with no treatment after both laparoscopic and abdominal myomectomy. The utility of GnRH analogues in reducing adhesions has also been demonstrated in other clinical and animal studies.

Second-look laparoscopy may be indicated in patients with multiple incisions or in those with posteriorly located incisions adjacent to the adnexa. Early adhesions can be easily lysed, and an additional barrier membrane can be placed. The clinical role of second-look laparoscopy, outside of research, is not well defined, and conflicting studies can be found in the literature regarding the efficacy of this procedure.

A comprehensive review of methods to prevent adhesion formation in gynecologic surgery has been published by Damario and Rock and by diZerega.

Results of Myomectomy

An extensive multiple myomectomy is a major operation with the potential for a higher morbidity than that found with hysterectomy. The major immediate postoperative complications after myomectomy are febrile morbidity and intraperitoneal bleeding.

Postoperative febrile morbidity may be related to extensive tissue trauma or to infection for a variety of reasons. Perioperative antibiotics are routinely given, but antibiotics are not usually continued beyond the day of operation. Any evidence of infection in the recovery period should be treated vigorously and promptly because infection in the operative site may be adhesiogenic and may have devastating effects on future fertility. Unfortunately, subclinical infection in the operative site may not be recognized and therefore may not be treated, but it can also have adverse effects on fertility because of de novo adhesion formation. For these reasons, meticulous and sterile surgical technique during myomectomy must be impeccable.

Intraperitoneal bleeding after myomectomy is usually due to failure to achieve hemostasis of the myometrial vessels during closure of the myoma beds and uterine incisions. Although we do use a heparin solution (5,000 U of heparin per 1,000 mL of lactated Ringer solution) for irrigation during myomectomy, there is no evidence to suggest that this contributes to occult intraperitoneal bleeding.

The diagnosis of intraperitoneal bleeding in the postoperative patient may be difficult. The vital signs can remain stable for several hours before rapidly deteriorating. Peritoneal signs are often subtle and may be masked by incisional pain and analgesic medications. In addition, the peritoneal cavity has an enormous capacity for accommodating occult blood loss. Indeed, as much as 3,000 mL of blood can be shed into the peritoneal cavity with only a 1-cm increase in the abdominal radius.

Therefore, patients must be carefully monitored for the first 24 hours after myomectomy. Vital signs are routinely checked every 15 minutes for the first 2 hours after surgery, then every 30 minutes until stable. Subsequently, they are monitored every 2 to 4 hours for the first 24 hours postoperatively. A hematocrit is usually performed 6 hours after the operation is completed and again on the first postoperative morning. It can also be performed whenever there is a suspicion of intraperitoneal bleeding, anemia, or hypovolemia. Any sign of restlessness, tachycardia, or tachypnea may be an indication of blood loss, especially when associated with hypotension.

When occult postoperative intraperitoneal bleeding is suspected, peritoneal lavage can be a valuable diagnostic tool. If the lavage solution yields a red blood cell count of 100,000/mm^3, intraperitoneal bleeding is likely, and reexploration is indicated without delay. Lavage is unnecessary when the diagnosis of intraperitoneal bleeding is unequivocal and associated with definite hypovolemia. In this situation, immediate return to the operating room for reexploration is indicated.

Postoperative bleeding after myomectomy can be devastating. Intraoperative control of bleeding during an extensive multiple myomectomy often requires that the uterine blood flow be impeded with tourniquets, clamps, or the local injection of vasoconstrictive agents. However, the demonstration of adequate surgical hemostasis in the uterus cannot be made until the uterine circulation has been fully restored. Assiduous attention to this principle intraoperatively prevents postmyomectomy bleeding in almost all cases.

Reports by Smith and Uhlir, Rosenfield, and LaMorte and associates indicate that the morbidity of myomectomy is no greater than the morbidity of hysterectomy. Verkauf reviewed current published reports and found that the operative risk of myomectomy does not exceed that of hysterectomy. One case of disseminated intravascular coagulation, hemolytic anemia, and acute renal failure associated with extensive multiple myomectomy was reported by Sacks and Hoyne.

Myomectomy has an excellent record in reducing heavy menstruation in patients reporting menorrhagia. In more than 80% of patients, menorrhagia is cured or significantly improved. Pelvic pain and discomfort and dysmenorrhea can also be relieved, but the results are not as dramatic because leiomyomata are often

associated with other gynecologic diseases (e.g., endometriosis and pelvic inflammatory disease) that can also cause pelvic pain.

The impact of abdominal myomectomy on infertility is difficult to assess. Other factors besides leiomyomata may be present to a varying degree. The extent to which the uterine cavity or the fallopian tubes are distorted also varies. The percentage of patients in each series who wish to conceive after myomectomy is not the same. There is also considerable variation in the surgical technique and skill of the gynecologic surgeon. Prospective, randomized, controlled studies are lacking. These and other factors make it difficult to assess the impact of abdominal myomectomy on infertility.

There are a number of published reports regarding women who experience recurrent pregnancy wastage or prior infertility with another cause and who undergo myomectomy. According to Verkauf's review, conception occurs in more than half of such women who were not previously pregnant. A comprehensive review of 23 studies by Vercellini and colleagues regarding leiomyomas and reproduction reported an overall conception rate of 57% after myomectomy among prospective studies. Among women with otherwise unexplained infertility,

the conception rate was 61% after myomectomy. The conception rate is approximately 53% to 70% after myomectomy for submucous myomas and 58% to 65% after myomectomy with intramural or subserosal leiomyomas. The conception rate among women older than age 35 may not be as good. Also, the postmyomectomy conception rate may be lower when the uterus is greater than 12 weeks gestational size and when more than four myomata are removed. When abdominal myomectomy includes removal of submucous myomata, Garcia and Tureck report that 53% of patients attempting to establish a pregnancy conceive. Both Li and colleagues and Vercellini and coworkers published retrospective reviews supporting excellent conception and pregnancy rates following abdominal myomectomies. Vercellini's work suggests that certainly age at the time of the procedure is important, as it was one of three independent variables (age, duration of infertility before surgery, and the presence of other infertility factors) associated with postoperative cumulative conception rate.

An ultrasonographic study of uterine remodeling after conservative myomectomy was reported by Beyth and associates. There was a gradual decrease in uterine volume in all patients during the 6 months after myomectomy, with the most remarkable decrease occurring in the first 2 to 3 months. Presumably, this represents an involution of myometrial hypertrophy and postoperative healing of uterine incisions. We recommend that all patients use local methods of contraception (diaphragm, condoms, and spermicidal jelly or foam) for at least 3 months to avoid conception until the myomectomy incisions are healed.

Finally, there is the matter of recurrence of myomata after myomectomy. In Verkauf's review, leiomyomata recurred in 7.5% of patients, and 6.8% required reoperation. Most recurrences appeared more than 3 years after myomectomy, thus allowing sufficient time for conception to occur before recurrence. Friedman and associates investigated a concern that GnRH agonist-induced myoma shrinkage would make some small intramural and submucosal tumors "invisible" at myomectomy, causing early "recurrence" of leiomyomata once gonadal suppression ceased and estrogen production returned. In their study, there was no difference in myoma recurrence between women pretreated with GnRH agonists (67%) and those treated with placebo (56%) 27 to 38 months after myomectomy. Their myoma recurrence rate of 61% is much higher than that previously reported in combined myomectomy series. The authors believe that this discrepancy is most likely due to the use of high-resolution US to diagnose small myomata that would otherwise be missed on bimanual examination. Rosetti and colleagues reported long-term followup of 81 patients randomized to abdominal or laparoscopic myomectomy plus 84 nonrandomized patients and found similar recurrence rates, 23% and 27% respectively, between the laparoscopic and abdominal myomectomy, with most recurrences seen within 24 months of surgery.

Matta and colleagues reported that after GnRH analog treatment, the US outline of some myomata was lost or obscured. Such myomata are probably more difficult to identify and remove with myomectomy and may be more

likely to reappear when GnRH analog treatment is discontinued after myomectomy.

Embolotherapy

With current technology progressing toward less invasive therapies, the minimally invasive procedure of UAE is gaining popularity. This procedure can potentially obviate the need for surgical procedures in patients who suffer from symptomatic leiomyomas.

In the female genital tract, embolotherapy for control of hemorrhage from malignancy was first reported in the late 1970s. In 1980, Pais and colleagues described successful embolization for postpartum hemorrhage. Many more reports followed in the mid-1980s. In the early 1990s, Ravina and coworkers began using embolotherapy as a preoperative maneuver to decrease intraoperative blood loss during surgery for myomas. The protocol generally included embolization about 24 hours before the surgery; however, some occurred a few days or weeks before surgery. Such an improvement in symptoms occurred that many surgeries were canceled altogether. This serendipitous discovery led to the performance of UAE as a primary procedure. UAE for leiomyomas was first performed in the United States by Goodwin and colleagues in 1995. Since then, several large series have been reported, and experience continues to grow.

UAE is appropriate for patients with symptomatic leiomyomata and a preference for treatment other than surgical. Clinical findings, therapeutic goals, and overall medical conditions factor into the decision making. Several concerns have developed in treating patients who may desire future conception. Hypotheses include reduced fertility as a consequence of injury to the uterus or ovaries, placental insufficiency resulting from inadequate blood flow through the uterus, or uterine rupture during pregnancy from UAE-induced myoma necrosis. A limited number of deliveries have been reported after UAE for uterine myomata. Reports of obstetric outcomes following embolization are mixed. Although previous studies have suggested that embolization therapy may increase the risk of miscarriage, postpartum hemorrhage, preterm delivery, and malpresentation compared with laparoscopic myomectomy, a recent retrospective review by McLucas including 28 pregnancies following UAE found no significant difference in preterm delivery or miscarriage as compared to the general population. Nonetheless, desire for future pregnancy remains a contraindication for UAE until more comprehensive long-term outcome data are available.

Interestingly, amenorrhea has been reported in 1% to 2% of patients after UAE; however, some authors have attributed this to the coincidental onset of menopause. Contraindications to this procedure include pregnancy, active pelvic infection, severe contrast medium allergy, arteriovenous malformations, desire for future pregnancy, a strong suspicion of adenomyosis or pedunculated leiomyoma, and undiagnosed pelvic mass. The technique is generally preceded by preprocedural testing, and patients are pretreated with intravenous antibiotics. Many perform preliminary arteriographic mapping of the pelvis. A review by Hutchins and Worthington-Kirsch provides an excellent description of the procedure.

The technical success rate is consistently reported in the 96% to 98% range with experienced teams. Eighty percent to ninety percent of embolized patients have reported improvements in menorrhagia, bulk-related symptoms, or both. Reduction in overall uterine volume peaks at more than 60% by 6 to 9 months after the procedure because of the gradual nature of the process. Individual myomas show average volume reductions of 60% to 65%.

The Fibroid Registry for Outcomes Data was established by the Society of Interventional Radiology and includes 25 core sites and 50 to 60 other participating sites. This clinical registry has enrolled more than 3,300 patients in an effort to obtain rapid and reliable data regarding patient outcomes. Based on 30-day and 1-year data, near 90% of patients responded favorably to UAE. Recurrence of symptoms and repeat procedures occur in about 10% of patients by 3 years. Worthington-Kirsch, a leading member of the steering committee, estimates that by 5 years

postprocedure, as many as 20% of patients will have another procedure. Approximately 1,300 to 1,500 patients continue to provide annual data through self-reported questionnaires, permitting continued long-term follow-up of the UAE procedure.

Forty percent of patients develop a syndrome of fever and malaise in the first 10 to 14 days after UAE. This is also associated with leukocytosis. This entity is well described as postembolization syndrome. It is typically self-limited and resolves in 3 to 5 days and rarely requires treatment except antipyretics. Other complications include those that may be attributed to the angiographic component and target or nontarget organ embolization. Groin infections, groin bleeding or hematoma, contrast-induced renal damage, and vascular damage may be attributed to the angiographic component. Uterine infection or perforation, sexual dysfunction, and myoma sloughing may be attributed to the target organ effects. Reported nontarget organ embolization complications include ovarian sequelae, sciatic nerve effects, and gluteal muscle pain. Current experience confirms a major complication rate of less than 1%.

BEST SURGICAL PRACTICES

- Women with symptomatic or problematic uterine leiomyomata should be considered candidates for surgical or radiologic intervention.
- Management options, including medical, radiologic, and surgical, should be discussed with patients, emphasizing risks and benefits of each option.
- Careful preoperative evaluation for women who undergo surgical treatment of leiomyomata should include radiographic evaluation to determine the extent, location, and size of leiomyomata.
- In patients with infertility, myomectomy—performed by either an abdominal or a laparoscopic approach—should only be performed after complete evaluation of other potential causes of infertility.
- Adhesion barriers are advantageous in reducing adhesions during both abdominal and laparoscopic myomectomies.
- Pregnancy rates and outcomes after laparoscopic myomectomy compare favorably with those after abdominal myomectomy.
- Meticulous repair of the uterine myometrium is essential for patients desiring pregnancy after a myomectomy.
- Hysteroscopic myomectomy is an effective surgical alternative to relieve symptoms associated with submucosal myomas.
- Current information regarding UAE is promising, but patients should be made aware that limited long-term data are available regarding outcomes, especially relating to fertility and pregnancy.

ABDOMINAL MYOMECTOMY CHECKLIST

- Position the patient in Allen stirrups.
- Perform exam under anesthesia, paying careful attention to uterine size and mobility.
- Prep and drape the patient.
- Place Foley.
- Perform cervical dilation, and consider staining the endometrial cavity.
- Make an abdominal incision (consider Maylard for uteri >12-week size), and enter the abdominal cavity.
- Optimize exposure (incision type and size, lighting, packing of intestines, retractors).

- Evaluate number, size, and location of fibroids.
- Minimize blood loss.
  - Make use of delicate surgical technique (avoid traumatic instruments).
  - Consider hypotensive anesthesia.
  - Consider use of a tourniquet.
  - Consider use of dilute Pitressin.
- Make a linear uterine incision over the largest myoma.
  - Dissect along the natural tissue plane, and excise the myoma.
- Meticulously close all uterine defects.
- Confirm hemostasis.
- Close abdominal cavity, fascial, and skin incisions.

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