18 Benign Gynecologic Lesions

Vulva, Vagina, Cervix, Uterus, Oviduct, Ovary, Ultrasound Imaging of Pelvic Structures

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KEY POINTS

- The most common large cyst of the vulva is a cystic dilation of an obstructed Bartholin duct, with a lifetime risk estimated to be 2%. These cysts occur most often during the third decade. Inflamed cysts may be treated with oral antibiotics or incision and drainage.
- The vulva contains 1% of the skin surface of the body, but 5% to 10% of all malignant melanomas in women arise from this region. Melanoma is the second most common malignancy arising in the vulva and accounts for 2% to 3% of all of the melanomas occurring in women.
- Ideally all vulvar nevi should be excised and examined histologically. Special emphasis should be directed toward the flat junctional nevus and the dysplastic nevus because they have the greatest potential for malignant transformation. The dysplastic nevus is characterized by being more than 5 mm in diameter, with irregular borders and patches of variegated pigment.
- The management of nonobstetric vulvar hematomas is usually conservative unless the hematoma is greater than 10 cm in diameter or rapidly increasing.
- In adult women, 50% of cases of chronic vulvovaginal pruritus are due to allergic and irritant contact dermatitis. The most common causes of vulvar contact dermatitis are cosmetic and local therapeutic agents. Initial treatment of severe lesions is removal of all irritants or potential allergens and application of topical steroids until the skin returns to normal.
- Women usually develop psoriasis during their teenage years, with approximately 3% of adult women being affected. Approximately 20% of these have involvement of the vulvar skin. The margins of psoriasis are better defined than the common skin conditions in the differential diagnosis, including candidiasis, seborrheic dermatitis, and eczema.
- Psoriasis does not involve the vagina, only the vulva.
- Lichen sclerosus does not involve the vagina, whereas lichen planus may involve the vagina.
- Vulvar pain (vulvodynia) is one of the most common gynecologic problems, reported by up to 16% of women in the general population; 30% of women will have spontaneous relief of their symptoms without any treatment.
- Classically the symptoms associated with the urethral diverticulum are extremely chronic in nature and do not resolve with multiple courses of oral antibiotic therapy.
- Cervical stenosis may occur after loop electrocautery excision procedures (LEEPs). The volume of tissue removed and repeated excisional procedures have been reported to increase the risk for cervical stenosis.
- Endocervical polyps are smooth, soft, red, fragile masses found most commonly in multiparous women in their 40s and 50s. After the endocervical polyp is removed, endometrial sampling should be performed to diagnose a coexisting endometrial hyperplasia or carcinoma.
- Endometrial polyps are noted in approximately 10% of women when the uterus is examined at autopsy. Approximately one in four women with abnormal bleeding will have an endometrial polyp.
- Leiomyomas are the most common benign neoplasms of the uterus. The lifetime prevalence of leiomyomas is greater than 80% among African American women and approaches 70% among white women.
- Cytogenetically, leiomyomas are chromosomally normal and arise from a single cell (they are clonal). All the cells are derived from one progenitor myocyte.
- Abnormal bleeding is experienced by a third of women with myomas, the most common pattern being intermenstrual spotting. Women with myomas and abnormal bleeding should be thoroughly evaluated for concurrent causes of bleeding.
- Adenomyosis is often asymptomatic. If multiple serial sections of the uterus are obtained, the incidence may exceed 60% in women aged 40 to 50 years.
- Adenomyosis rarely causes uterine enlargement greater than a size that corresponds to 14 weeks' gestation unless there is concomitant uterine pathologic change.
- The initial management of a suspected follicular cyst is conservative observation. The majority of follicular cysts disappear spontaneously by either reabsorption of the cyst fluid or silent rupture within 4 to 8 weeks of the initial diagnosis.
- The practice of aspirating cysts laparoscopically should be limited to cysts that are completely simple and associated with normal CA-125 levels. The intraoperative spillage of malignant cystic tumors should be avoided if possible, although the true risk that spillage poses is unknown.
- The differential diagnosis of a woman with acute pain and a suspected ruptured corpus luteum cyst includes ectopic pregnancy, a ruptured endometrioma, and adnexal torsion.
- The treatment of unruptured corpus luteum cysts is conservative. However, if the cyst persists or intraperitoneal bleeding occurs, necessitating operation, the treatment is cystectomy.
- Drainage or fenestration is effective for follicular cysts and poorly effective for cystadenomas. They will tend to recur. When cysts are drained, it is essential to remember that the cytologic examination of cyst fluid has poor predictive value and poor sensitivity in differentiating benign from malignant cysts.
- Theca lutein cysts arise from either prolonged or excessive stimulation of the ovaries by endogenous or exogenous gonadotropins or increased ovarian sensitivity to gonadotropins. The condition of ovarian enlargement secondary to the development of multiple luteinized follicular cysts is termed *hyperreactio luteinalis*. Approximately 50% of molar pregnancies and 10% of choriocarcinomas have associated bilateral theca lutein cysts.

Continued

KEY POINTS—cont'd

- Benign ovarian teratomas vary from a few millimeters to 25 cm, may be single or multiple, and are bilateral 10% to 15% of the time. Dermoids are believed to arise during fetal life from a single germ cell. They are 46,XX in karyotype.
- Operative treatment of benign cystic teratomas is via cystectomy with preservation of as much normal ovarian tissue as possible.
- Fifty percent of patients with an ovarian fibroma will have ascites if the tumor is greater than 6 cm. The incidence of associated ascites is directly proportional to the size of the tumor.
- Transitional cell tumors (Brenner tumors) are small, smooth, solid, fibroepithelial tumors of the ovary. They usually occur in women between the ages of 40 and 60 and are predominantly unilateral.
- Adnexal torsion occurs most commonly in the reproductive years, with the average age of patients being in the mid-20s. Pregnancy predisposes to adnexal torsion.
- Ovarian tumors are discovered in 50% to 60% of women with adnexal torsion.
- Abnormal color Doppler flow is highly predictive of torsion of the ovary. However, approximately 50% of women with surgically confirmed adnexal torsion will have a normal Doppler flow study.
- Conservative surgery, either through the laparoscope or via laparotomy, entails gentle untwisting of the pedicle, possibly cystectomy, and stabilization of the ovary with sutures. Detorsion and fixation of the ovary is a safe procedure that reduces the risk of recurrence.
- The risk of pulmonary embolus with adnexal torsion is approximately 0.2%. The risk is similar regardless of whether the condition is managed by conservative surgery with untwisting or adnexal removal without untwisting.

INTRODUCTION

This chapter reviews benign gynecologic lesions; however, the symptoms and differential diagnoses of these lesions have definite similarity with those of malignant disease. As in many areas of medicine, gynecologic problems do not fall into definitive categories, and those that include malignant disease often overlap with those that include benign disease. When the diagnosis from the history, physical examination, and laboratory tests is clear, management is usually self-evident. When a specific diagnosis is unclear, tissue biopsy may be appropriate. Thus the clinical approach to patient complaints or findings must be broad and not so focused as to prematurely exclude dangerous pathologic conditions within the differential diagnosis.

The discussions in this chapter are arranged anatomically, beginning with the vulva and subsequently covering the vagina, cervix, uterus, oviducts, and ovaries. This chapter does not attempt to be encyclopedic; rather, lesions have been selected based on their clinical importance and prevalence. Therefore extremely rare lesions have been omitted. Because several nonneoplastic abnormalities and lesions present in ways similar to those of benign tumors, this chapter also discusses entities that are not specifically abnormal growths. Clinical problems such as torsion of the ovary, lacerations of the vagina, and hematomas of the vulva are examples of common conditions included in this chapter. Gynecologic infections and associated changes are discussed in Chapter 23.

The successful clinician uses both deductive and inductive reasoning in making a diagnosis. To master both these techniques, one must be adept at history taking and physical examination and be able to form a complete list of possible causes that may be related to the patient's complaint. An understanding of the problems discussed in this chapter will be helpful in that endeavor.

VULVA

Urethral Caruncle and Urethral Prolapse

Urethral caruncle and urethral prolapse are conditions that primarily affect postmenopausal women and premenarchal girls. They are thought to occur as a result of decreased estrogen. A urethral caruncle is a small, fleshy mass that occurs at the posterior portion of the urethral meatus. The tissue of the caruncle is soft, smooth, friable, and bright red and initially appears as an eversion of the urethra (Fig. 18.1). Urethral caruncles are generally small, single, and sessile, but they may be pedunculated and grow to be 1 to 2 cm in diameter. Urethral caruncles are believed to arise from an ectropion of the posterior urethral wall associated with retraction and atrophy of the postmenopausal vagina. The growth of the caruncle is secondary to chronic irritation or infection.

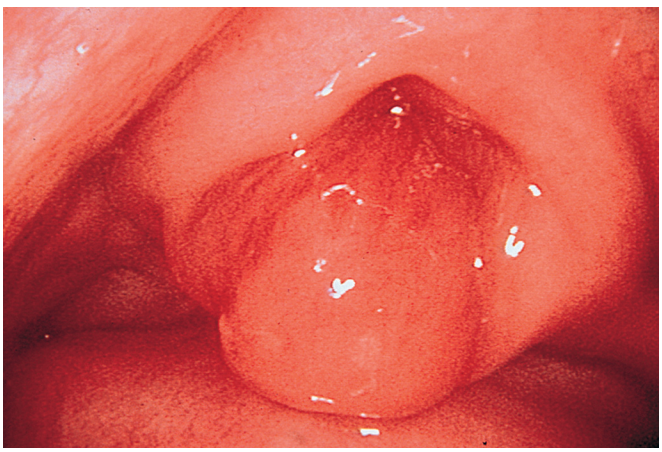

Fig. 18.1 Photo of urethral caruncle at the base of the meatus. (From Cundiff GW, Bent AE. *Endoscopic Diagnosis of the Female Lower Urinary Tract.* London: WB Saunders; 1999.)

Histologically the caruncle is composed of transitional and stratified squamous epithelium with a loose connective tissue, and often the submucosal layer contains relatively large dilated veins. Caruncles are often subdivided by their histologic appearance into papillomatous, granulomatous, and angiomatous varieties.

They are often secondarily infected, producing ulceration and bleeding. The symptoms associated with urethral caruncles are variable. Many women are asymptomatic, whereas others experience dysuria, frequency, and urgency. Sometimes the caruncle produces point tenderness after contact with undergarments or during intercourse. Ulcerative lesions usually produce spotting on contact more commonly than hematuria. The diagnosis of a urethral caruncle is established by biopsy under local anesthesia because it can appear similar to a neoplasm.

Initial therapy is oral or topical estrogen and avoidance of irritation. If the caruncle does not regress or is symptomatic, it

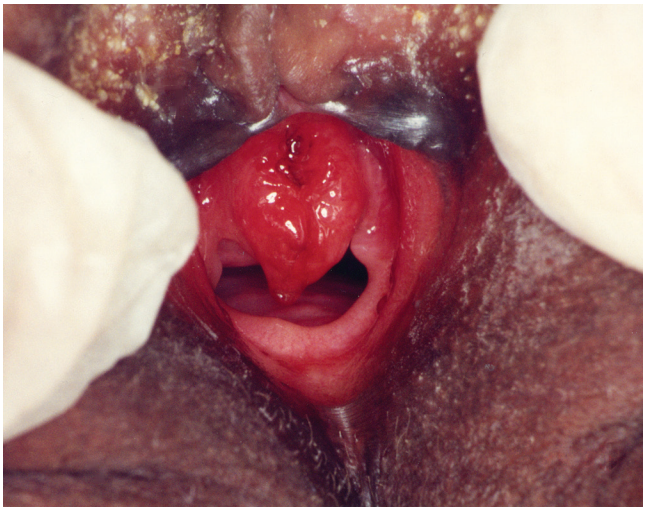

Fig. 18.2 Urethral prolapse found incidentally in a 5-year-old girl on a colposcopic examination for suspected abuse with an edematous red collar of tissue surrounding the urethral meatus. (From Hudson MJ, Swenson AD, Kaplan R, et al. Medical conditions with genital/anal findings that can be confused with sexual abuse. In: Jenny C, ed. *Child Abuse and Neglect: Diagnosis, Treatment and Evidence.* St. Louis: Elsevier; 2011.)

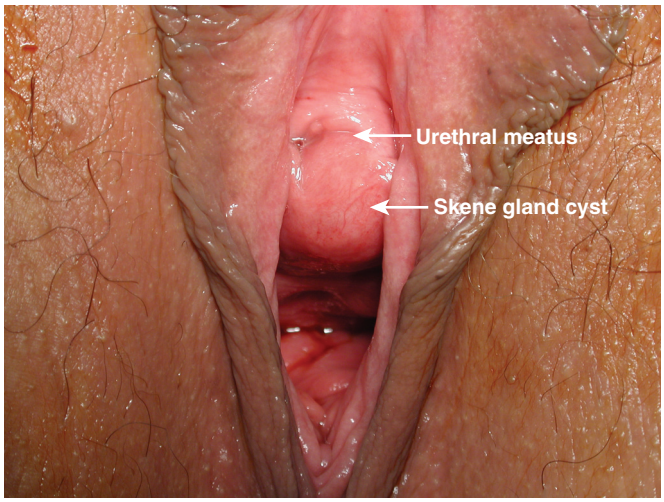

Fig. 18.3 Skene gland cyst. (From Shah SR, Nitti VW. Benign vaginal wall masses and paraurethral lesions. In: Nitti VW, ed. *Vaginal Surgery for the Urologist.* Philadelphia: Elsevier; 2012.)

may be destroyed by cryosurgery, laser therapy, fulguration, or operative excision. After operative destruction, a Foley catheter is usually left in place for 48 to 72 hours to prevent urinary retention. Follow-up is necessary to ensure that the patient does not develop urethral stenosis. It is not uncommon for the caruncle to recur. Small, asymptomatic urethral caruncles do not need treatment.

Urethral prolapse is predominantly a disease of the premenarcheal girl, although it can occur in postmenopausal women (Fig. 18.2). Patients may have dysuria; however, most are asymptomatic. The annular rosette of friable, edematous, prolapsed mucosa does not have the bright red color of a caruncle and is easily distinguished from a caruncle because it is circumferential (Tunitsky, 2012). It may be ulcerated with necrosis or grossly edematous. Therapy for a prolapsed urethra is hot sitz baths and antibiotics to reduce inflammation and infection. Topical estrogen cream is sometimes an effective treatment. In rare cases it may be necessary to excise the redundant mucosa.

The differential diagnosis of urethral caruncles includes primary carcinoma of the urethra and prolapse of the urethral mucosa. Malignant lesions are usually hard and irregular in shape and typically are within the urethra itself (Tunitsky, 2012). Urethral carcinoma is primarily a disease in elderly women. The symptoms of a urethral carcinoma include bleeding, urinary frequency, and dysuria. The majority of urethral carcinomas are of squamous cell origin. Most of these rare carcinomas arise from the distal urethra.

The differential diagnosis of a periurethral mass also includes urethral diverticulum, leiomyoma, vaginal wall inclusion cyst, Skene gland cyst or abscess, and, less commonly, Gartner duct cyst and ectopic ureterocele (Tunitsky, 2012). These are discussed later in this chapter in the Vagina section.

Cysts

The most common large cyst of the vulva is a cystic dilation of an obstructed Bartholin duct. Bartholin glands open into the vulvar vestibule at about the 5 and 7 o'clock position, distal to the hymenal ring. Bartholin duct cysts and abscesses are fairly common, with a lifetime risk estimated to be 2% (Edwards, 2011). They occur most often during the third decade. Noninflamed cysts contain sterile, clear, mucinous fluid. They do not require treatment unless large enough to cause discomfort. Inflamed cysts may be treated with oral antibiotics or incision and drainage. Lesions in the Bartholin gland can occur as carcinomas, a rare tumor that accounts for 2% to 7% of vulvar carcinomas.

Occasionally the ducts of mucous glands of the vestibule become occluded. The resulting small cysts (usually 0.5 to 2 cm) may be clear, yellow, or blue. Similar small mucous cysts occur in the periurethral region. Wolffian duct cysts or mesonephric cysts are rare, but when they do occur, they are found near the clitoris and lateral to the hymeneal ring. These cysts have thin walls and contain clear serous fluid.

Skene duct cysts are rare, usually small, located on the anterior wall of the vagina along the distal urethra, and may present with symptoms of discomfort or be found on routine examination. These cysts arise secondary to infection and scarring of the small ducts (Fig. 18.3). The differential diagnosis includes urethral diverticula; however, clinically, physical compression of the cyst, unlike compression of a urethral diverticula, should not produce fluid from the urethral meatus. Imaging studies such as magnetic resonance imaging (MRI) and ultrasound may also assist in establishing the diagnosis. Asymptomatic cysts in premenopausal women may be managed conservatively. Treatment is excision with careful dissection to avoid urethral injury.

The most common small vulvar cysts are epidermal (or epidermoid) cysts, which are firm, smooth-surfaced, white, yellow, slightly pink, or skin-colored papules or nodules averaging 0.5 to 2 cm in size (Edwards, 2011). They are most commonly located on the hair-bearing areas. One or several lesions may be present, usually nontender and slow growing. They are firm to shotty in consistency, and their contents are usually under pressure. When noninflamed, they are asymptomatic and no treatment is necessary. If confirmation is needed, incision reveals white, caseous material, like thick cheese. Vulvar epidermal cysts do not have sebaceous cells or sebaceous material identified on microscopic examination but have keratin produced by keratinocytes in the lining of the cyst wall (Edwards, 2011). With rupture or leakage of a cyst, inflammation can occur, necessitating treatment with heat applied locally and possibly incision and drainage. Cysts that become recurrently infected or produce pain should be excised when the acute inflammation has subsided. The typical epidermoid cyst

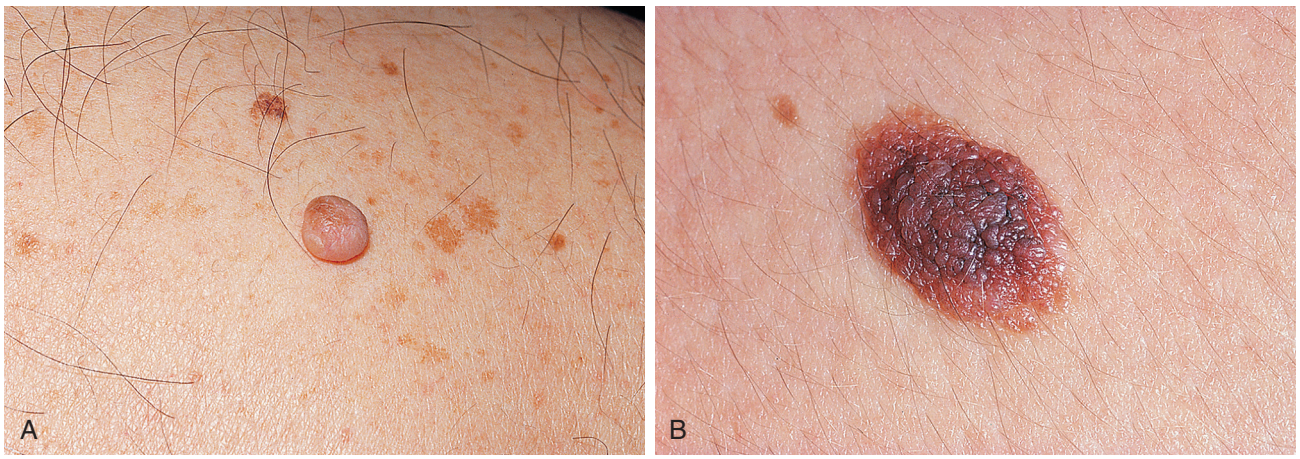

Fig. 18.4 Vulvar nevi. **A,** Dome-shaped intradermal nevus. **B,** Compound nevus with irregular pigmentation. (From Fisher BK, Margesson LJ. *Genital Skin Disorders: Diagnosis and Treatment.* St. Louis: Mosby; 1998.)

develops from embryonic remnants of an anatomically malformed pilosebaceous unit.

An "inclusion cyst" may arise when bits of epithelium are implanted in the skin during surgery or trauma sufficient to break the skin surface. These may be seen at the site of an episiotomy or obstetric laceration. Large epidermal cysts may be confused with fibromas, lipomas, and hidradenomas.

Nevus

A nevus, commonly referred to as a *mole*, is a localized nest or cluster of melanocytes. These undifferentiated cells arise from the embryonic neural crest and are present from birth. Many nevi are not recognized until they become pigmented at the time of puberty. Vulvar nevi are one of the most common benign neoplasms in women. As with nevi in other parts of the body, they exhibit a wide range in depth of color, from blue to dark brown to black, and some may be amelanotic. The diameter of most common nevi ranges from a 3 to 10 mm. Grossly a benign nevus may be flat, elevated, or pedunculated. The borders are sharp, the color even, and the shape is symmetric. Dysplastic nevi are commonly 6 to 20 mm with one or more atypical features such as speckling of color, diffuse margination, additional red, white, or blue hues, and asymmetry. Other pigmented lesions in the differential diagnosis include hemangiomas, endometriosis, malignant melanoma, vulvar intraepithelial neoplasia, and seborrheic keratosis.

Vulvar nevi are generally asymptomatic. Most women do not closely inspect their vulvar skin; however, during examination, the use of a mirror held by the patient may facilitate teaching self-vulvar exam. Histologically the lesions are subdivided into three major groups: junctional (a symmetric macule), compound, and intradermal nevi (both papules) (Fig. 18.4).

Melanoma is the second most common malignancy arising in the vulva and accounts for 2% to 3% of all of the melanomas occurring in women, even though the vulva contains approximately 1% of the skin surface area of the body. The incidence of vulvar melanoma is stable or slightly decreasing. It is more common in older, white women, with a mean age at diagnosis of 68 years (Sugiyama, 2007). It is estimated that 50% of malignant melanomas arise from a preexisting nevus. Family history of melanoma is one of the strongest risk factors for the disease.

Ideally, all vulvar nevi should be excised and examined histologically. Special emphasis should be directed toward the flat junctional nevus and the dysplastic nevus because they have the greatest potential for malignant transformation (Fig. 18.5). The lifetime risk of a woman developing melanoma from a congenital junctional nevus that measures greater than 2 cm in diameter is estimated to be approximately 10%. The lifetime risk of a melanoma forming in women with dysplastic nevi is 15 times that of the general population.

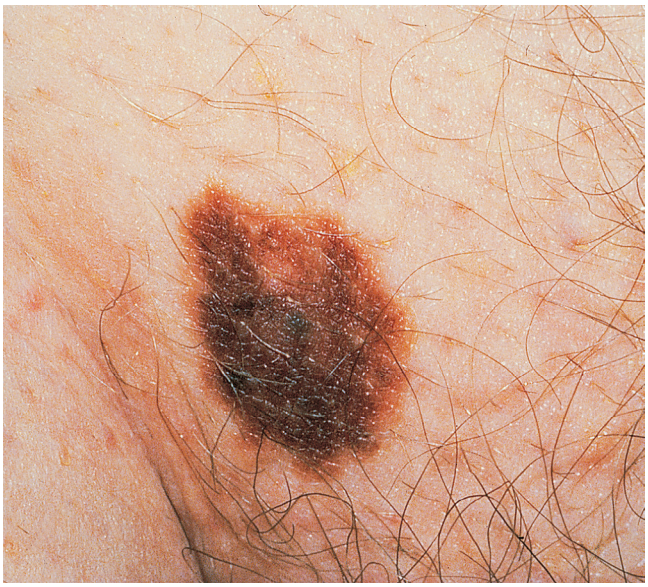

Fig. 18.5 Suprapubic dysplastic nevus with an irregular shape, reddish hue to the edges, and indistinct margins. (From Fisher BK, Margesson LJ. *Genital Skin Disorders: Diagnosis and Treatment.* St. Louis: Mosby; 1998.)

Removal may be accomplished with local anesthesia or coincidentally with obstetric delivery or gynecologic surgery. Proper excisional biopsy should be three-dimensional and adequate in width and depth. Approximately 5 to 10 mm of normal skin surrounding the nevus should be included, and the biopsy specimen should include the underlying dermis as well.

Some patients are reluctant to have a "normal" appearing nevus removed. Nevi that are raised or contain hair rarely undergo malignant change. However, if they are often irritated or bleed spontaneously, they should be removed. Recent changes in growth or color, ulceration, bleeding, pain, or the development of satellite lesions mandate biopsy. The characteristic clinical features of an early malignant melanoma may be remembered by

thinking *ABCD: asymmetry*, *border* irregularity, *color* variegation, and a *diameter* usually greater than 6 mm.

Hemangioma

Hemangiomas are rare malformations of blood vessels rather than true neoplasms. Vulvar hemangiomas often are discovered initially during childhood. They are usually single, 1 to 2 cm in diameter, flat, and soft, and they range in color from brown to red or purple. Histologically the multiple channels of hemangiomas are predominantly thin-walled capillaries arranged randomly and separated by thin connective tissue septa. These tumors change in size with compression and are not encapsulated. Most hemangiomas are asymptomatic; occasionally they may become ulcerated and bleed.

There are at least five different types of vulvar hemangiomas. The strawberry and cavernous hemangiomas are congenital defects discovered in young children. The strawberry hemangioma is usually bright red to dark red, is elevated, and rarely increases in size after age 2. Approximately 60% of vulvar hemangiomas discovered during the first years of life spontaneously regress in size by the time the child goes to school. Cavernous hemangiomas are usually purple and vary in size, with the larger lesions extending deeply into the subcutaneous tissue. These hemangiomas initially appear during the first few months of life and may increase in size until age 2. Similar to strawberry hemangiomas, spontaneous resolution generally occurs before age 6. Senile or cherry angiomas are common small lesions that arise on the labia majora, usually in postmenopausal women. They are most often less than 3 mm in diameter, multiple, and red-brown to dark blue. Angiokeratomas are approximately twice the size of cherry angiomas, are purple or dark red, and occur in women between the ages of 30 and 50. They are noted for their rapid growth and tendency to bleed during strenuous exercise. In the differential diagnosis of an angiokeratoma is Kaposi sarcoma and angiosarcoma. Pyogenic granulomas are an overgrowth of inflamed granulation tissue that grow under the hormonal influence of pregnancy, with similarities to lesions in the oral cavity. Pyogenic granulomas are usually small, slightly pedunculated nodules approximately 1 cm in diameter, appearing "pinched in" at the base. They may be mistaken clinically for malignant melanomas, basal cell carcinomas, vulvar condylomas, or nevi. Treatment of pyogenic granulomas involves wide and deep excision to prevent recurrence.

The diagnosis is usually established by gross inspection of the vascular lesion. Asymptomatic hemangiomas and hemangiomas in children rarely require therapy. In adults, initial treatment of large symptomatic hemangiomas that are bleeding or infected may require subtotal resection. When the differential diagnosis is questionable, excisional biopsy should be performed. A hemangioma that is associated with troublesome bleeding may be destroyed by cryosurgery, sclerotherapy, or with the use of lasers. Cryosurgical treatment usually involves a single freeze/thaw cycle repeated three times at monthly intervals. Obviously, if the histologic diagnosis is questionable, any bleeding vulvar mass should be treated by excisional biopsy so that the definitive pathologic diagnosis can be established. Surgical removal of a large, cavernous hemangioma may be technically difficult. Lymphangiomas of the vulva do exist but are extremely rare.

Another rare malformation is the vulvar venous malformation. These lesions may become symptomatic at any age and are relatively prone to thrombosis. Venous malformations are different from vulvar varicosities, which are exacerbated with pregnancy and tend to regress postpartum. There are reports of the successful use of sclerotherapy for the treatment of the malformations.

Fibroma

Fibromas are the most common benign solid tumors of the vulva. They are more common than lipomas, the other common benign tumors of mesenchymal origin. Fibromas occur in all age groups and most commonly are found in the labia majora (Fig. 18.6). However, they actually arise from deeper connective tissue. Thus they should be considered as dermatofibromas. They grow slowly and vary from a few centimeters to one gigantic vulvar fibroma reported to weigh more than 250 pounds. Most are between 1 and 10 cm in diameter. The smaller fibromas are discovered as subcutaneous nodules. As they increase in size and weight, they become pedunculated. Smaller fibromas are firm; however, larger tumors often become cystic after undergoing myxomatous degeneration. Sometimes the vulvar skin over a fibroma is compromised by pressure and ulcerates.

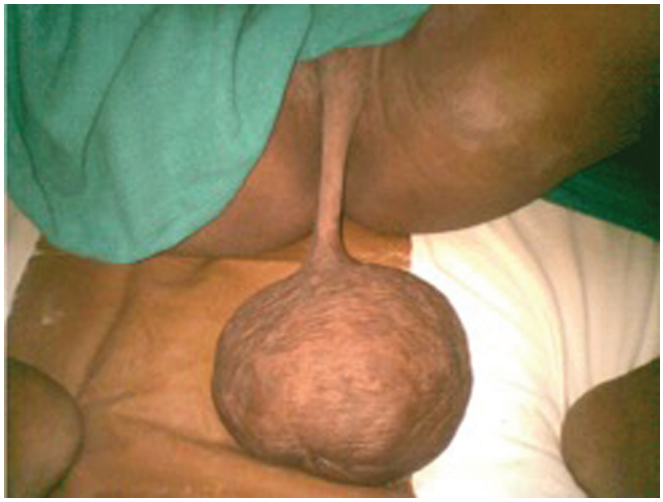

Fig. 18.6 Clinical photograph of a patient showing a pedunculated fibroma from the labia majora. (From Najam R, Chowdhury HH, Awasthi S. A large fibroma polyp of labia majora—a case report. *J Clin Case Rep.* 2013;3:297.)

Fibromas have a smooth surface and a distinct contour. On cut surface the tissue is gray-white. Fat or muscle cells microscopically may be associated with the interlacing fibroblasts. Fibromas have a low-grade potential for becoming malignant. Smaller fibromas are asymptomatic; larger ones may produce chronic pressure symptoms or acute pain when they degenerate. Treatment is operative removal if the fibromas are symptomatic or continue to grow. Occasionally they are removed for cosmetic reasons.

Lipoma

Lipomas are the second most common type of benign vulvar mesenchymal tumor. A common hamartoma of fat, lipomas of the vulva are similar to lipomas of other parts of the body. In the vulva, they are most commonly located periclitorally or within the labia majora (Edwards, 2011). When discovered they are softer and usually larger than fibromas (Fig. 18.7). The majority of lipomas in the vulvar region are smaller than 3 cm. The largest vulvar lipoma reported in the literature weighed 44 pounds. They are slow growing, and their malignant potential is extremely low.

When a lipoma is cut, the substance is soft, yellow, and lobulated. Histologically, lipomas are usually more homogeneous than fibromas. Prominent areas of connective tissue occasionally are associated with the mature adipose cells of a true lipoma. Unless extremely large, lipomas do not produce symptoms. Computed tomography and MRI may be used to evaluate tumor extensions and anatomic connections with surrounding structures. MRI has been reported to facilitate the differentiation of vulvar lipomas from vulvar liposarcomas (Jayi, 2014). Excision is

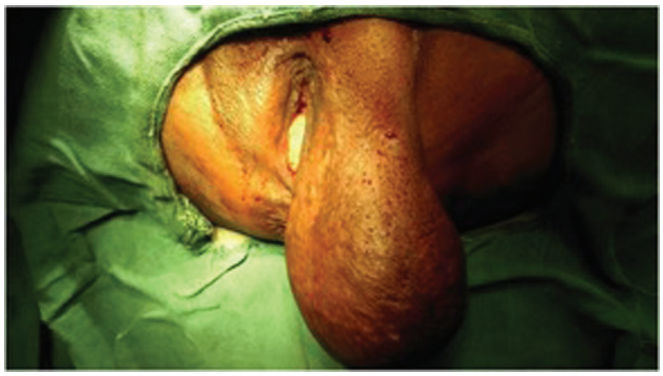

Fig. 18.7 Vulvar lipoma arising from the left labia majora. (From Hasija S, Khoiwal S, Bilwal B. Vulvar lipoma—a rare case report. *Am J Med Case Rep.* 2015;3(12):413-414.)

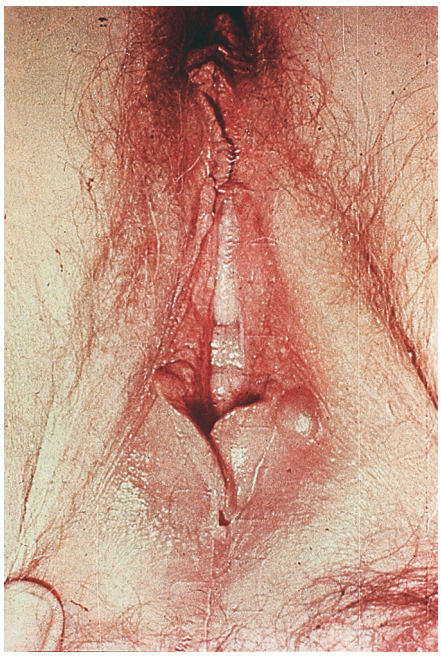

Fig. 18.8 Hidradenoma. (From Shea CH, Stevens A, Dalziel KL, et al. The vulva: cysts, neoplasms, and related lesions. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

usually performed to establish the diagnosis, although smaller tumors may be followed conservatively.

Hidradenoma (Mammary-Like Gland Adenoma)

The hidradenoma is a rare, small, benign vulvar tumor thought to be derived from mammary-like glands located in the anogenital area of women (Fig. 18.8). In a review of 46 cases, the tumors occurred only in postpubertal women aged 30 to 90 (Scurry, 2009). Clinically, hidradenoma are small, smooth-surfaced, medium soft to firm nodules found most commonly on the labia majora or labia minora. They appear cystic and are usually asymptomatic; however, some patients report itching, bleeding, and mild pain. Hidradenomas may be cystic or solid, and approximately 50% are less than 1 cm in diameter. These tumors have well-defined capsules and arise deep in the dermis. Histologically, because of its hyperplastic, adenomatous pattern, a hidradenoma may be mistaken at first glance for an adenocarcinoma. On close inspection,

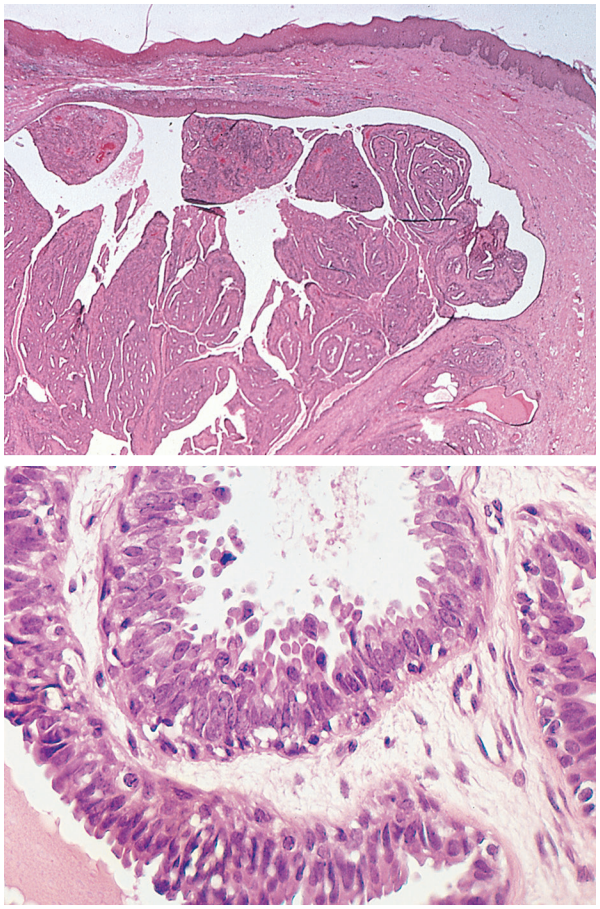

Fig. 18.9 Histologic views: low- and high-power micrographs of hidradenoma. (From Clement PB, Young RH. *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders; 2000.)

however, although there is glandular hyperplasia with numerous tubular ducts, there is a paucity of mitotic figures and a lack of significant cellular and nuclear pleomorphism (Fig. 18.9). Excisional biopsy is the treatment of choice.

Syringoma

The syringoma is a benign skin adnexal neoplasm thought to be of eccrine origin. It is common on the face and eyelids but unusual on the vulva. In the vulvar area these small, asymptomatic papules (usually less than 5 mm in diameter) are located on the labia majora. The papules are skin colored or yellow and may coalesce to form cords of firm tissue. They may be hormonally active because pregnancy may aggravate associated pruritus and progesterone receptors have been detected in this neoplasm (Heller, 2012). This tumor is usually treated by excisional biopsy, cryosurgery, or laser therapy. The most common differential diagnosis is Fox-Fordyce disease, a condition of multiple retention cysts of apocrine glands accompanied by inflammation of the skin. The latter disease often produces intense pruritus, whereas syringoma is generally asymptomatic. Fox-Fordyce disease improves with pregnancy and oral contraceptive use and remits after menopause. It is treated with topical steroids, topical tretinoin cream, and oral isotretinoin.

Endometriosis

Endometriosis of the vulva is uncommon. Only 1 in 500 women with endometriosis present with vulvar lesions. The firm, small

nodule or nodules may be cystic or solid and vary from a few millimeters to several centimeters in diameter. The subcutaneous lesions are blue, red, or purple, depending on their size, activity, and closeness to the surface of the skin. The gross and microscopic pathologic picture of vulvar endometriosis is similar to endometriosis of the pelvis (see Chapter 19). Vulvar adenosis may appear similar to endometriosis. The former condition occurs after laser therapy of condylomata acuminata.

Endometriosis of the vulva is usually found at the site of an old, healed obstetric laceration, an episiotomy site, an area of operative removal of a Bartholin duct cyst, or along the canal of Nuck. The pathophysiology of vulvar endometriosis development may be secondary to metaplasia, retrograde lymphatic spread, or potential implantation of endometrial tissue during operation. In one series, 15 cases of vulvar endometriosis were believed to be associated with prophylactic postpartum curettage performed in 2028 deliveries, since there was not a single case in 13,800 deliveries without curettage. In general, symptoms do not appear for many months after implantation.

The most common symptoms of endometriosis of the vulva are pain and introital dyspareunia. The classic history is cyclic discomfort and an enlargement of the mass associated with menstrual periods. Treatment of vulvar endometriosis is by wide excision or laser vaporization depending on the size of the mass. Recurrences are common after inadequate operative removal of the entire involved area, and as a result most would also recommend medical therapy with continuous oral contraceptives, progestins, or gonadotropin-releasing hormone (GnRH) agonists.

Granular Cell Myoblastoma

Granular cell myoblastoma is a rare, slow-growing, solid vulvar tumor originating from neural sheath (Schwann) cells and is sometimes called a *schwannoma*. These tumors are found in connective tissues throughout the body, most commonly in the tongue, and occur in any age group. Approximately 7% of solitary granular cell myoblastomas are found in the subcutaneous tissue of the vulva. Twenty percent of multiple granular cell myoblastomas are located in the vulva. The tumors are usually located in the labia majora but occasionally involve the clitoris.

These tumors are subcutaneous nodules, usually 1 to 5 cm in diameter. They are benign but characteristically infiltrate the surrounding local tissue. The tumors are slow growing, but as they grow, they may cause ulcerations in the skin. The overlying skin often has hyperplastic changes that may look similar to invasive squamous cell carcinoma. Grossly these tumors are not encapsulated, and the cut surface of the tumor is yellow. Histologically, there are irregularly arranged bundles of large, round cells with indistinct borders and pink-staining cytoplasm. Initially the cell of origin was believed to be striated muscle; however, electron microscopic studies have demonstrated that this tumor is from cells of the neural sheath.

The tumor nodules are painless. Treatment involves wide excision to remove the filamentous projections into the surrounding tissue. If the initial excisional biopsy is not sufficiently aggressive, these benign tumors tend to recur. Recurrence occurs in approximately one in five of these vulvar tumors. The appropriate therapy is a second operation with wider margins, as these tumors are not radiosensitive.

Von Recklinghausen Disease

The vulva is sometimes involved with the benign neural sheath tumors of von Recklinghausen disease (generalized neurofibromatosis and café-au-lait spots). The vulvar lesions of this disease are fleshy, brownish red, polypoid tumors. Approximately 18% of women with von Recklinghausen disease have vulvar involvement. Excision is the treatment of choice for symptomatic tumors.

Other Abnormal Tissues Presenting as Vulvar Masses

The differential diagnosis of vulvar masses includes a large array of rare lesions and aberrant tissues, including leiomyomas, squamous papillomas, sebaceous adenomas, dermoids, accessory breast tissue and müllerian or wolffian duct remnants, epidermal inclusion cysts, sebaceous cysts, mucous cysts, and skin diseases such as seborrheic keratosis, condylomata acuminata, and molluscum contagiosum. Some of these diseases are discussed in this chapter, others in Chapter 23.

Hematomas

Hematomas of the vulva are usually secondary to blunt trauma such as a straddle injury from a fall, an automobile accident, or a physical assault. Traumatic injuries producing vulvar hematomas have been reported secondary to a wide range of recreational activities, including bicycle, motorcycle, and go-cart riding; sledding; water skiing; cross-country skiing; and amusement park rides (Fig. 18.10). Spontaneous hematomas are rare and usually occur from rupture of a varicose vein during pregnancy or the postpartum period.

The management of nonobstetric vulvar hematomas is usually conservative unless the hematoma is greater than 10 cm in diameter or is rapidly expanding. The bleeding that produces a vulvar hematoma is usually venous in origin. Therefore it may be controlled by direct pressure. Compression and application of an ice pack to the area are appropriate therapy. If the hematoma continues to expand, operative therapy is indicated in an attempt to identify and ligate the damaged vessel. Often identification of the "key responsible vein" is a futile operative procedure. However, obvious bleeding vessels are ligated, and a pack is placed to promote hemostasis. During the operation, careful inspection and, if needed, endoscopy are performed to rule out injury to the urinary bladder and rectosigmoid.

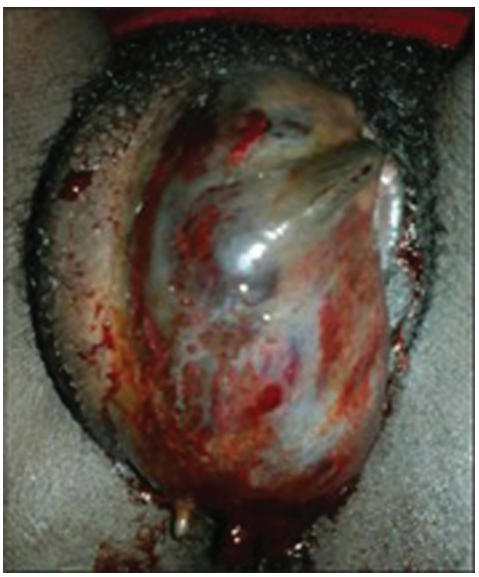

Fig. 18.10 Traumatic hematoma of the left vulva. (From Taingson MC, Adze JA, Bature SB, Durosinlorun AM, Caleb M, Amina A. Haematoma of the labia minora following consensual sexual intercourse. *Sahel Med J.* 2018;21:52-54.)

The majority of small hematomas regress with time; however, a "chronic expanding hematoma" may become particularly problematic. The most familiar clinical example of this type of problem is the chronic subdural hematoma, but a similar situation may accompany vulvar hematomas. The underlying pathophysiology is repetitive episodes of bleeding from capillaries in the granulation tissue of the hematoma, which result in a chronic, slowly expanding vulvar mass. Treatment of a chronic expanding hematoma is drainage and debridement.

DERMATOLOGIC DISEASES

The skin of the vulva is similar to the skin over any surface of the body and is therefore susceptible to any generalized skin disease or involvement by systemic disease. The most common skin diseases involving the vulva include contact dermatitis, neurodermatitis, psoriasis, seborrheic dermatitis, cutaneous candidiasis, and lichen planus. The majority of vulvar skin problems are red, scalelike rashes, and the woman's primary complaint is of pruritus. The diagnosis and treatment of these lesions are often obscured or modified by the environment of the vulva. The combination of moisture and heat of the intertriginous areas may produce irritation, maceration, and a wet, weeping surface. Patients will commonly apply ointments and lotions, which may produce secondary irritation. Therefore it is important that the gynecologist examine the skin of the entire body because the patient may have more classic lesions of the dermatologic disease in another location. The skin of the vulva is susceptible to acute infections produced by *Streptococcus* or *Staphylococcus*, such as folliculitis, furunculitis, impetigo, and a chronic infection, hidradenitis suppurativa.

The nonspecific symptom complex of vulvar pruritus and burning is presented next as an introduction to the discussion of dermatologic diseases of the vulva.

Pruritus

Pruritus is the single most common gynecologic problem; it is a symptom of intense itching with an associated desire to scratch and rub the affected area. Not uncommonly, secondary vulvar pain develops in association or subsequent to pruritus. In some women pruritus becomes an almost unrelenting symptom, with the development of repetitive "itch-scratch" cycles. The itch-scratch cycle is a complex of itching leading to scratching, producing excoriation and then healing. The healing skin itches, leading to further scratching. Pruritus is a nonspecific symptom. The differential diagnosis includes a wide range of vulvar diseases, including skin infections, sexually transmitted diseases, specific dermatosis, vulvar dystrophies, lichen sclerosus, premalignant and malignant disease; contact dermatitis; neurodermatitis; atrophy; diabetes; drug allergies; vitamin deficiencies; pediculosis, scabies; psychological causes; and systemic diseases such as leukemia and uremia.

The management of pruritus involves establishing a diagnosis, treating the offending cause, and improving local hygiene. For successful treatment the itch-scratch cycle must be interrupted before the condition becomes chronic, resulting in lichenification of the skin (lichen simplex chronicus). Lichenification clinically is recognized by palpably thickened skin, exaggerated skin markings, and lichen-type scale. The resulting dry, scaly skin often cracks, forms fissures, and becomes secondarily infected, thus complicating the treatment (see Chapter 30).

Contact Dermatitis

The vulvar skin, especially the intertriginous areas, is a common site of contact dermatitis. The vulvar skin is more reactive to exposure by irritants than other skin areas such as the extremities. Contact dermatitis is usually caused by one of two basic pathophysiologic processes: a primary irritant (nonimmunologic) or a definite allergic (immunologic) origin. A large proportion of adult patients with chronic vulvovaginal pruritis are symptomatic because of contact dermatitis. Substances that are irritants produce immediate symptoms such as a stinging and burning sensation when applied to the vulvar skin. The symptoms and signs secondary to an irritant disappear within 12 hours of discontinuing the offending substance. In contrast, allergic contact dermatitis requires 36 to 48 hours to manifest its symptoms and signs.

Allergic contact dermatitis is a cell-mediated delayed-type (type IV) hypersensitivity reaction. There is development of antigen-specific T cells that may return to the skin at the next contact with the allergen. Often the signs of allergic contact dermatitis persist for several days despite removal of the allergen. Rarely, some women will be allergic to latex or semen. These elicit type 1, immunoglobulin E (IgE)–mediated, immediate reactions. Angioedema and urticarial plaques and papules arise within minutes of contact, and anaphylaxis may result.

Excessive cleansing of the vulvar skin and urinary or fecal incontinence may precipitate an irritant dermatitis. The majority of chemicals that produce hypersensitivity of the vulvar skin are cosmetic or therapeutic agents, including vaginal contraceptives, lubricants, sprays, perfumes, douches, fabric dyes, fabric softeners, synthetic fibers, bleaches, soaps, chlorine, dyes in toilet tissues, and local anesthetic creams (Fig. 18.11). External chemicals that trigger the disease process must be avoided. Some of the most severe cases of contact dermatitis involve lesions of the vulvar skin secondary to poison ivy or poison oak. Women with a history of atopy or eczema are more at risk for contact dermatitis and tend to be more sensitive to skin irritations.

Acute contact dermatitis results in a red, edematous, inflamed skin. The skin may become weeping and eczematoid. The most severe skin reactions form vesicles and at any stage may become secondarily infected. The common symptoms of contact dermatitis

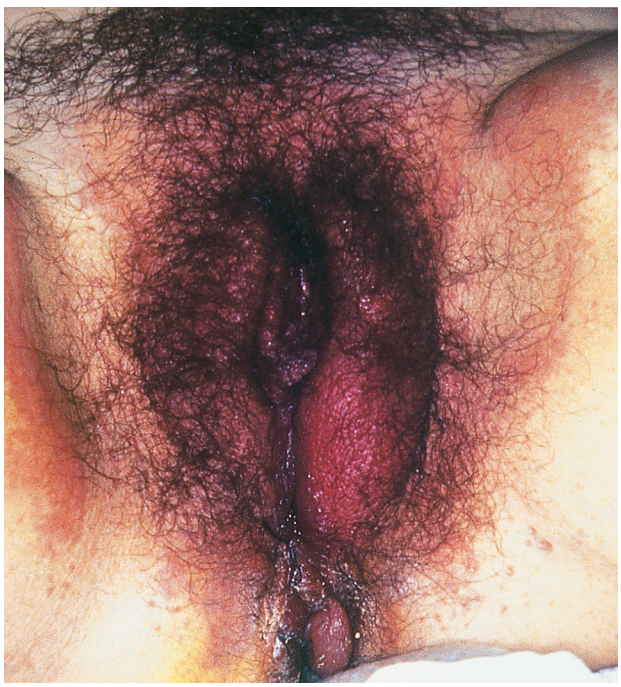

Fig. 18.11 Acute contact dermatitis to chlorhexidine. Edema and erythema are present in areas where the antiseptic chlorhexidine solution was applied. (From Stevens A, Dalziel KL. Vulvar dermatoses. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

include superficial vulvar tenderness, burning, and pruritus. Chronic untreated contact dermatitis can evolve into a syndrome of lichenification, with the skin developing a leathery appearance and texture, known as *lichen simplex chronicus* (Fig. 18.12).

The foundation of treatment of contact dermatitis is withdrawal of the offending substance. Sometimes the distribution of the vulvar erythema helps to delineate the irritant. For example, localized erythema of the introitus often results from vaginal medication, whereas generalized erythema of the vulva is secondary to an allergen in clothing. It is possible to use a vulvar chemical innocuously for many months or years before the topical vulvar "allergy" develops.

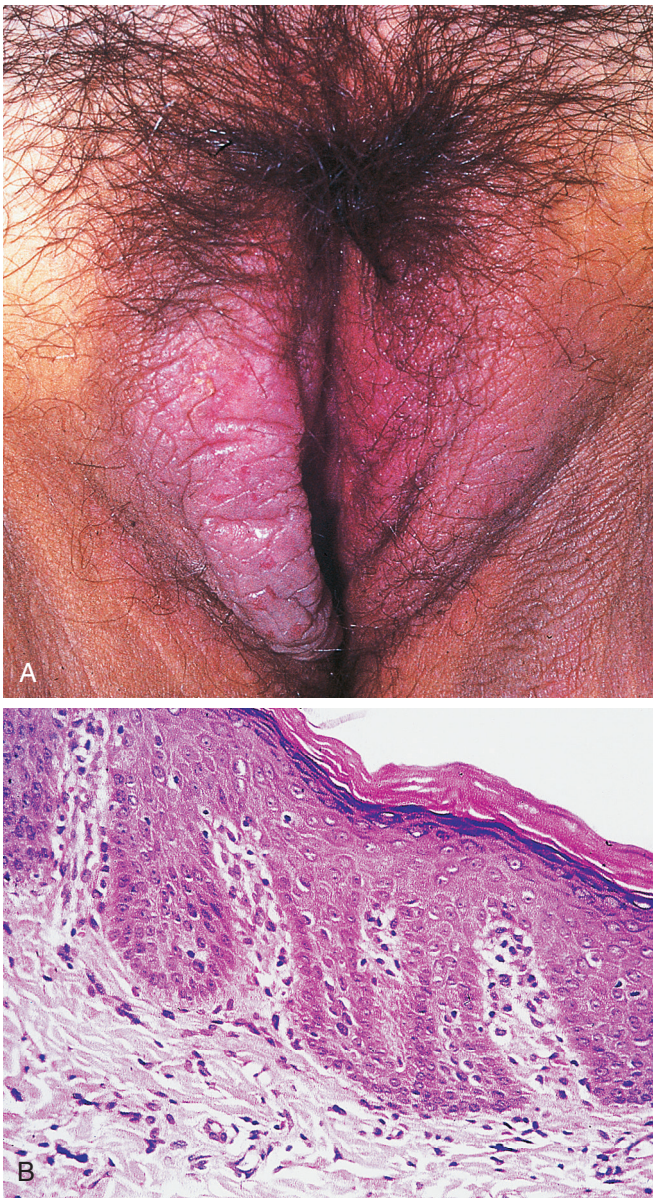

Fig. 18.12 A, Lichen simplex chronicus manifesting of the right labium majus. There is thickening and accentuation of skin markings, with surface excoriation caused by recent scratching. **B,** Lichen simplex chronicus. The epidermis shows thickening of rete ridges, thickening of the granular layer, and overlying hyperkeratosis. (From Stevens A, Dalziel KL. Vulvar dermatoses. In Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

Once the offending substances and all potential allergens have been eliminated, topical steroids can be applied to the vulva until the skin returns to normal. The vulvar skin should be kept clean and dry. Use of a barrier product such as zinc oxide ointment or vitamin A and D ointment may be needed to keep urine and feces away from the skin in patients with incontinence. The pain and burning can be treated with tepid water bath soaks several times a day for the first few days. Use of a lubricating agent such as petroleum jelly or Eucerin cream will reduce the pruritus by rehydrating the skin and should be applied after the soaks. Cotton undergarments that allow the vulvar skin to aerate should be worn, and constrictive, occlusive, or tight-fitting clothing such as pantyhose should be avoided. Use of a nonmedicated cornstarch baby powder may facilitate vulvar dryness. Hydrocortisone (0.5% to 1%) and fluorinated corticosteroids (Valisone, 0.1%, or Synalar, 0.01%) as lotions or creams may be rubbed into the skin two to three times a day for a few days to control symptoms. Synthetic systemic corticosteroids (prednisone, starting with 50 mg/day for 7 to 10 days in a decreasing dose) are sometimes necessary for treatment of poison ivy and poison oak or severe reactions. Antipruritic medications, such as antihistamines, are not of great therapeutic benefit except as soporific agents. Women often experience pruritus after steroid therapy for vulvar dermatitis. This is not necessarily a recurrence but rather represents a type of withdrawal reaction. This rebound pruritus is seen most commonly with prolonged and higher doses of steroids. After examination, the optimal treatment is a step-down to a short course of a low-potency topical steroid such as 1% hydrocortisone. Topical steroids should be continued for a month or more after clinical improvement because microscopic evidence of inflammation remains for a considerable period (Edwards, 2011).

Psoriasis

Psoriasis is a common, generalized skin disease of unknown origin. Generally, women develop psoriasis during their teenage years, with approximately 3% of adult women affected. Approximately 20% of these cases involve vulvar skin. Similar to candidiasis, psoriasis may be the first clinical manifestation of human immunodeficiency virus (HIV) infection. Psoriasis is chronic and relapsing, with an extremely variable and unpredictable course marked by spontaneous remissions and exacerbations. Twenty-five percent of women have a family history of the disease. Genetic susceptibility to develop psoriasis is believed to be multifactorial. Common areas of involvement are the scalp and fingernails. When psoriasis involves the vulvar skin, it produces both anxiety and embarrassment.

Vulvar psoriasis usually affects intertriginous areas and is manifested by red to red-yellow papules. These papules tend to enlarge, becoming well-circumscribed, dull-red plaques (Fig. 18.13). Though the presence of classic silver scales and bleeding on gentle scraping of the plaques may help establish the diagnosis, the scales are less common in the vulva than on other areas of the body.

With psoriasis on the vulvar region, the number of scales is extremely variable and often they are absent. Under the influence of the moisture and heat of the vulva, vulvar psoriasis may resemble candidiasis. Importantly for the diagnosis, psoriasis does not involve the vagina. Sometimes dermatologists treat refractory cases of psoriasis with oral retinoids. The margins of psoriasis are more well defined than the common skin conditions in the differential diagnosis, including candidiasis, seborrheic dermatitis, and eczema. Initial treatment for mild disease is 1% hydrocortisone cream. If the patient has pain secondary to chronic fissures or more moderate disease, a 4-week course of a fluorinated corticosteroid cream should be given. If this treatment is not successful, a dermatologist should be consulted. Several newer antipsoriatic treatments may benefit this condition, especially when it becomes moderate to severe, including vitamin D analogs, topical retinoids,

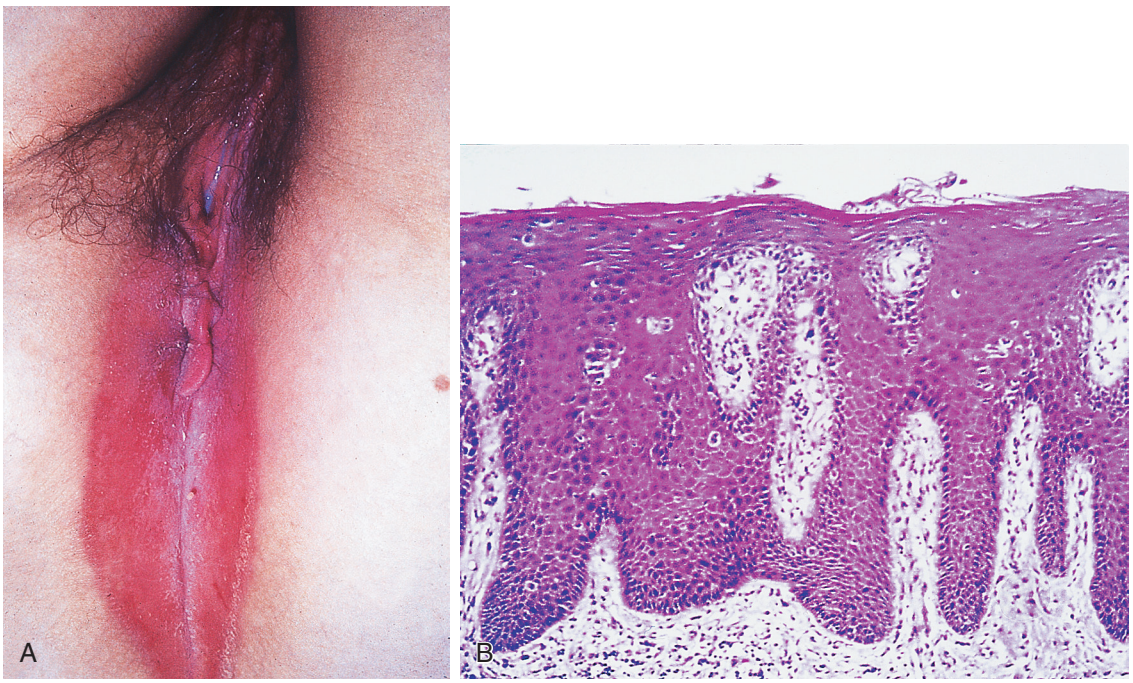

Fig. 18.13 A, Psoriasis of perineum and vulva. Flexural psoriasis often lacks the typical parakeratotic scale of psoriasis on other body sites. Painful erosion of the natal cleft is common. **B,** Psoriasis. There is psoriasiform hyperplasia of rete ridges with papillary dermal edema and telangiectasia. The parakeratotic scale on the skin surface is not prominent in vulvar psoriasis. (From Stevens A, Dalziel KL. Vulvar dermatoses. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

calcineurin inhibitors, salicylic acid, coal tar cyclosporine, and drugs that alter the immune system (biologics). Systemic steroids often produce a rebound flare-up of the disease.

Seborrheic Dermatitis

Seborrheic dermatitis is a common chronic skin disease of unknown origin that classically affects the face, scalp, sternum, and the area behind the ears. Rarely, the mons pubis and vulvar areas may be involved. Vulvar lesions are pale to yellow-red, erythematous, and edematous, and they are covered by a fine, nonadherent scale that is usually oily. Excessive sweating and emotional tension precipitate attacks. Although the cause is unknown, an abnormal reaction in the skin to a commensal yeast, *Pityrosporum ovale*, has been implicated in the pathogenesis. Treatment with topical and oral antifungal agents causes improvement; however, they are not as effective as topical steroids (Edwards, 2011). Approximately 2% to 4% of women have some form of the disease. The pruritus associated with seborrheic dermatitis varies from mild to severe. Treatment is similar to that for contact dermatitis, with hydrocortisone cream being the most effective medication. The differential diagnosis of seborrheic dermatitis includes psoriasis, cutaneous candidiasis, and contact dermatitis. Often it is difficult to differentiate between the cutaneous manifestations of psoriasis and seborrheic dermatitis. Clinically and pragmatically the exact diagnosis is only of academic interest because the treatment is similar.

Lichen Planus

Lichen planus is an uncommon vulvovaginal dermatosis. Women complain of soreness, burning, itching, and dyspareunia. The disease presents most commonly as a hypertrophic, coalesced plaque similar to lichen sclerosis. Lichen sclerosis, though, does not involve the vagina, whereas lichen planus can. Three types of vulvar lichen planus have been described: erosive, classical, and hypertrophic. Erosive lichen planus is the most common and is characterized by erosions around the introitus, clitoris, and labia majora and minora (Fig. 18.14). A lacy white edge is commonly seen. Vaginal involvement is common, and patients may also present with contact bleeding, erythema, and scarring with synechiae. Many patients may also report mouth pain and have gingival lesions that appear erosive and desquamative. The classical type presents with small purple, polygonal papules, with sometimes a reticulate lace pattern. Hyperkeratotic lichen planus presents as single or multiple white, hyperkeratotic papules and plaques. Lichen planus is an inflammatory condition with unknown cause; however, evidence suggests it to be an autoimmune disease of cellular immunity (Edwards, 2011). The autoimmune phenomenon can be triggered by certain drugs, including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and other medications. It may also arise spontaneously. The correct diagnosis is confirmed by a small punch biopsy of the vagina or vulva. Histologic findings (Fig. 18.15) include degeneration of the basal layers, a lymphocytic infiltrate of the dermis, and epidermal acanthosis.

This chronic disease tends to have spontaneous remissions and exacerbations that last for weeks to months. Treatment of local lesions is by use of a potent topical steroid ointment such as clobetasol applied twice daily. Steroid suppositories may be inserted intravaginally at night. If the patient is intensely symptomatic, oral steroids may be necessary. In postmenopausal women, topical or systemic estrogen replacement can also be crucial to avoid additional mucosal thinning. Other treatments for resistant cases include methotrexate, oral retinoids, oral griseofulvin, dapsone, azathioprine, cyclophosphamide, and topical cyclosporine. Surgery may be necessary to separate vaginal adhesions or uncover a buried clitoris. Postoperatively the use of vaginal dilators can prevent scar re-formation. Women with this condition should be monitored at periodic intervals because of an associated increased risk of developing vulvar squamous cell carcinoma.

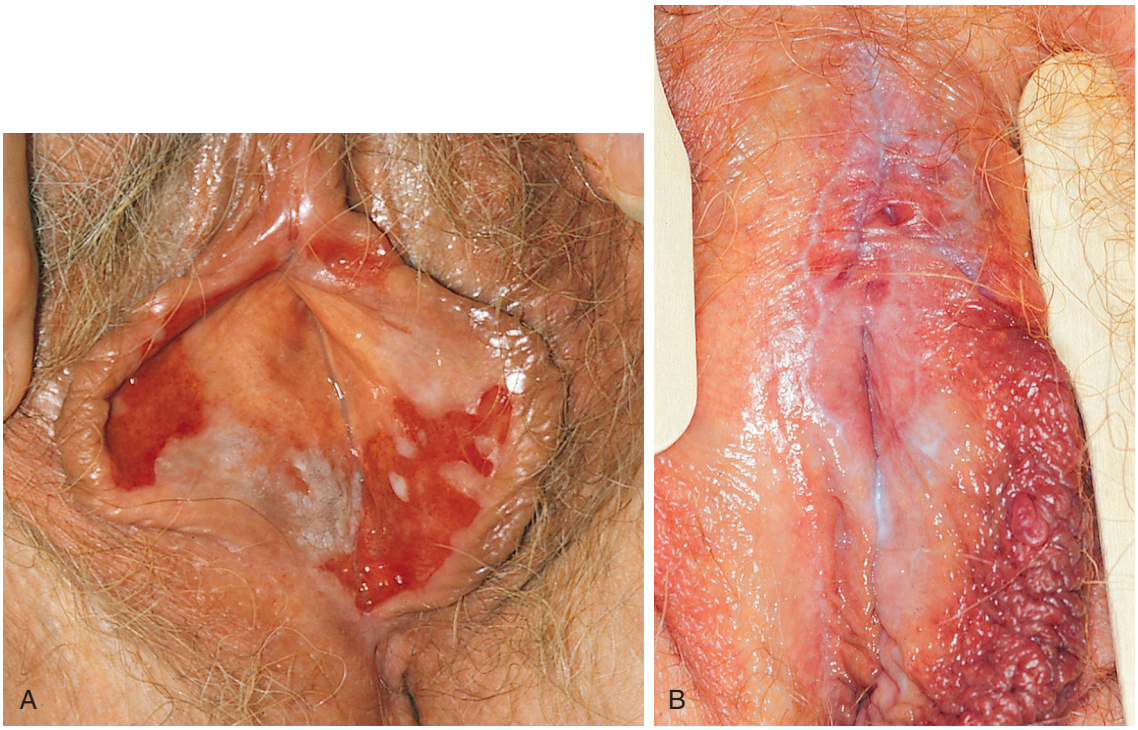

Fig. 18.14 Lichen planus. **A,** Eroded ulcers in the vulva. **B,** Lacy reticulated pattern of lichen planus with periclitoral scarring in a 71-year-old woman who has had oral lichen planus for 10 to 15 years, cutaneous lichen planus of arms and legs for 18 months, and bouts of erosive vaginal lichen planus with scarring and partial vaginal stenosis. (From Fisher BK, Margesson LJ. *Genital Skin Disorders: Diagnosis and Treatment.* St. Louis: Mosby; 1998.)

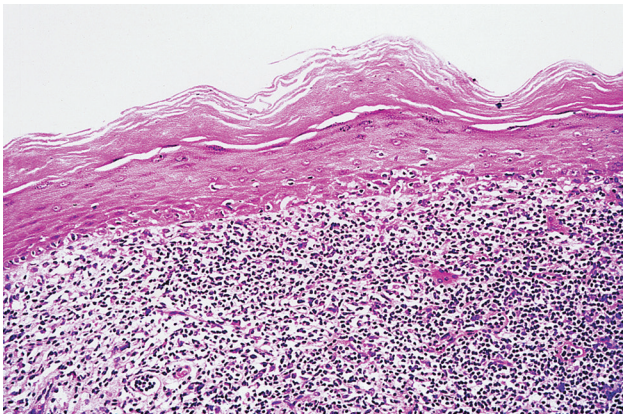

Fig. 18.15 Lichen planus, histologic view. Note hyperkeratosis with extensive basal layer destruction and a dense lichenoid infiltrate at the dermoepidermal junction. (From Stevens A, Dalziel KL. Vulvar dermatoses. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

Behçet Disease

Behçet disease is a rare disorder initially described as a triad of oral aphthous ulcers, genital aphthous ulcers, and uveitis. It is now known to be a multisystem disease with potential development of problems in many organ systems: skin, joints, cardiovascular, central nervous system, and gastrointestinal tract. The prevalence is high in the Mediterranean region, Middle East, and Japan. Turkey has the highest prevalence, with a rate of 100 to 400 in 100,000 individuals (Edwards, 2011). The diagnosis is made after exclusion of herpetic lesions and other ulcerative diseases. The symptoms respond to topical anesthetics. Severe disease may require antineoplastic therapy including methotrexate, steroids, or other medications.

Hidradenitis Suppurativa

Hidradenitis suppurativa is a chronic, unrelenting, refractory infection of skin and subcutaneous tissue that contains apocrine glands. The apocrine glands are found mainly in the axilla and the anogenital region. The disease is rare before puberty; 98% of cases are found in reproductive-age women, and most all disease regresses after menopause. As the infection progresses over time, deep scars and pits are formed (Fig. 18.16). The patient undergoes great emotional distress as this condition is both painful and is associated with a foul-smelling discharge. Theories of the cause of this condition favor an inflammation beginning in the hair follicles (Fig. 18.17). Thus the term sometimes used synonymously is *acne inversa*. The lesions involve the mons pubis, the genitocrural folds, and the buttocks. The differential diagnosis of hidradenitis suppurativa includes simple folliculitis, Crohn disease of the vulva, pilonidal cysts, and granulomatous sexually transmitted diseases. The differentiation from Crohn disease is usually made by history with an absence of gastrointestinal (GI) involvement. The early phase of the disease involves infection of the follicular epithelium, at first appearing as a boil. This is followed by erythema, involvement of multiple follicles, and chronic infections that burrow and form cysts that break open and track through subcutaneous tissue, creating odiferous and painful sinuses and fistula in the vulva. The chronic scarring, fibrosis, and hyperpigmentation with foul-smelling discharge and soiling of underclothes lead to a socially debilitating condition. The diagnosis should be confirmed by biopsy.

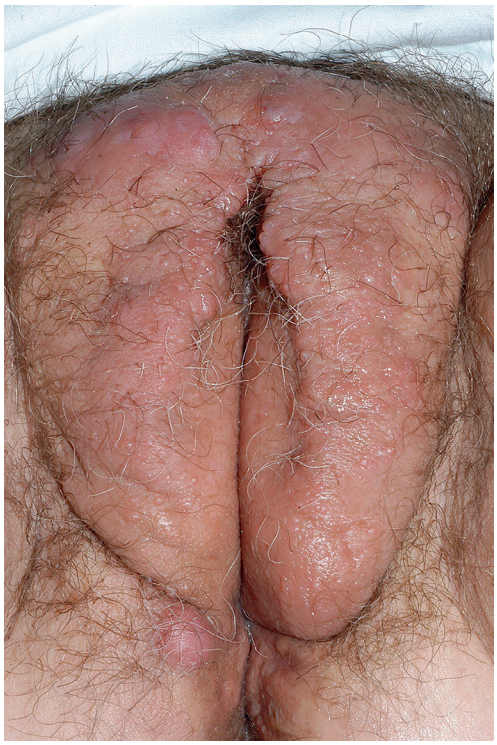

Fig. 18.16 Hidradenitis suppurativa: multiple vulvar abscesses with edema of the mons pubis and labia majora. Notice the "pitting" and "scars" from chronic infection. (From Amankwah Y, Haefner H. Vulvar edema. *Dermatol Clin.* 2010;28(4):765-777.)

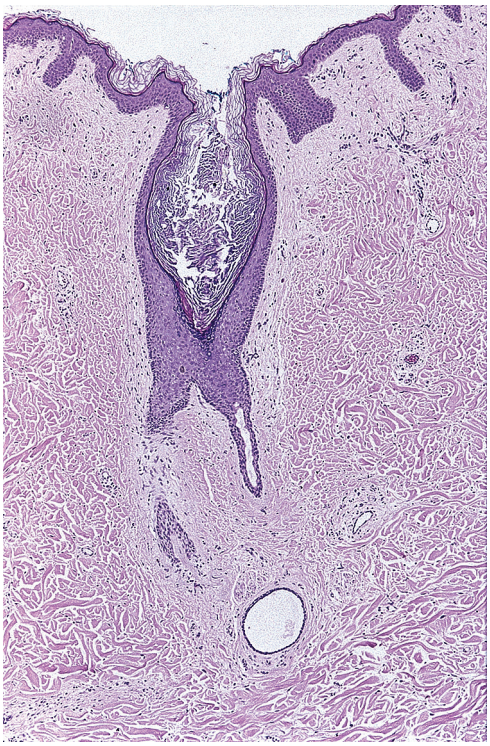

Fig. 18.17 Hydradenitis suppurativa. Biopsy with follicular plugging and connection to dilated apocrine duct. (From Kelly P. Folliculitis and the follicular occlusion tetrad. In Bolognia JL, Jorizzo JL, Rapini RP, eds. *Dermatology.* Edinburgh: Mosby; 2003.)

Early on in the disease process there are small furuncles and folliculitis, for which topical and oral clindamycin is usually effective in the short term, usually requiring a 3-month course of antibiotics. Unfortunately, relapse is common; if treatment with long-term antibiotic therapy and topical steroids is unsuccessful, other medical therapies have included antiandrogens, isotretinoin, and cyclosporine. The treatment of refractory cases is aggressive, wide operative excision of the infected skin.

Edema

Edema of the vulva may be a symptom of either local or generalized disease. Two of the most common causes of edema of the vulva are secondary reactions to inflammation or to lymphatic blockage. Vulvar edema is often recognized before edema in other areas of the female body is noted. The loose connective tissue of the vulva and its dependent position predispose to early development of pitting edema. Systemic causes of vulvar edema include circulatory and renal failure, ascites, and cirrhosis. Vulvar edema also may occur after intraperitoneal fluid is instilled to prevent adhesions or for dialysis. Local causes of vulvar edema include allergy, neurodermatitis, inflammation, trauma, and lymphatic obstruction caused by carcinoma or infection. Infectious diseases that are associated with vulvar edema include necrotizing fasciitis, tuberculosis, syphilis, filariasis, and lymphogranuloma venereum.

Vulvar Pain Syndromes: Vulvar Vestibulitis, Vestibulodynia, and Dysesthetic Vulvodynia

Vulvar pain (vulvodynia) is one of the most common gynecologic problems, reported by up to 16% of women in the general population (Stockdale, 2014). Vulvodynia is a pain disorder that occurs without visible findings, infection, inflammation, neoplasia, or a neurologic disorder. The disease has a wide spectrum of symptomology and response to treatment; therefore causation is most likely multifactorial. The diagnosis is made after excluding other treatable causes. A complete history identifying the onset of pain, other associated symptoms, duration of pain, medical and sexual history, treatments tried, allergies, and triggers for pain should be taken. A physical examination with a cotton swab to identify specific areas of pain should be documented. Large population-based studies have noted that symptoms wax and wane, with many women having spontaneous remission (up to 10% of the time).

The terms *vulvar pain syndrome*, *vulvodynia*, and *vulvar vestibulitis* are often used interchangeably. Vulvar vestibulitis is somewhat of a misnomer because it is not inflammation. Vulvar pain syndrome is further subdivided into two categories: vestibulodynia and dysesthetic vulvodynia. The two conditions have a significant amount of overlap, although with different causes and clinical courses. In general, vestibulodynia is found in younger women, most commonly white, with onset shortly after puberty through the mid-20s. Dysesthetic vulvodynia is most common in peri- and postmenopausal women who have rarely if ever had previous vulvar pain.

The differential diagnosis of vulvar pain includes neurologic diseases, herpes simplex infection, chronic infections, abuse, pain syndromes, neoplasia, contact dermatitis, and psychogenic causes. Chronic pain is considered to be part of the vulvodynia spectrum once the diagnoses of infection, invasive disease, and inflammation have been excluded. Severe chronic pain can be socially debilitating, and these patients have a wide spectrum of associated affective symptomology as well. Women with vulvodynia have greater psychological distress than women who have other vulvar problems. Importantly, these psychological concerns must be addressed as part of the therapeutic management.

Vestibulodynia involves the symptom of allodynia, which is hyperesthesia, a pain that is related to nonpainful stimuli. The

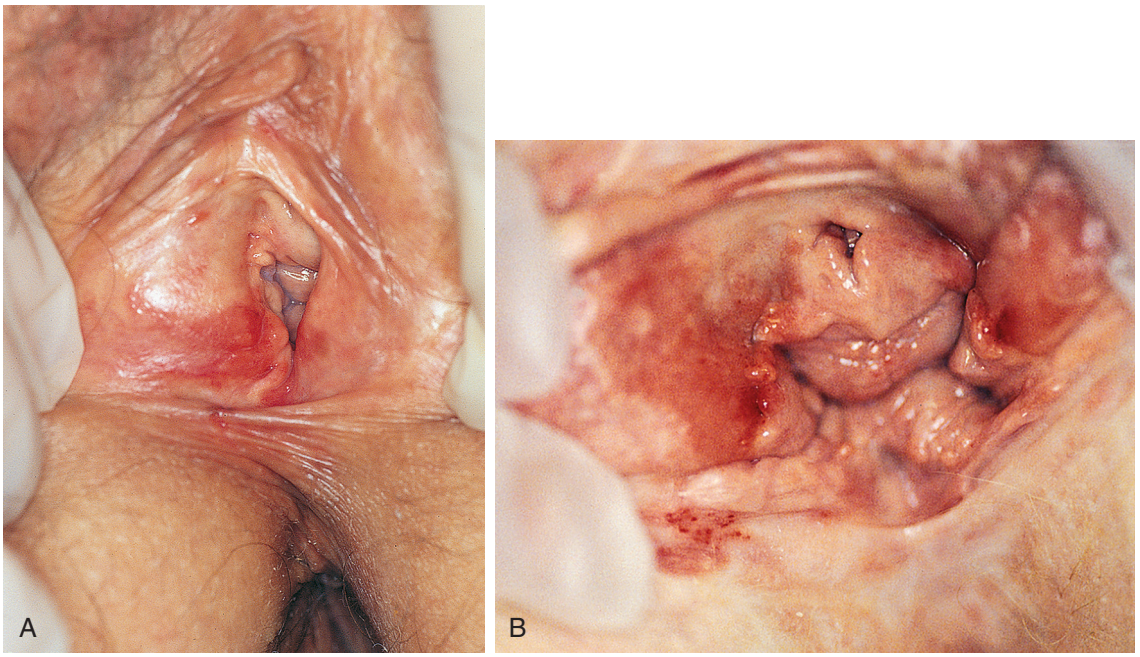

Fig. 18.18 Vulvar vestibulitis. **A,** Redness localized to the right Bartholin duct opening and, below it, vulvar vestibulitis. **B,** Discrete localized periglandular erythema in vulvar vestibulitis in a 60-year-old woman. (From Fisher BK, Margesson LJ. *Genital Skin Disorders: Diagnosis and Treatment.* St. Louis: Mosby; 1998.)

pain is not present without stimulation. The diagnostic maneuver to establish the presence of allodynia is to lightly touch the vulvar vestibule with a cotton-tipped applicator. The vulvar areas most likely to be affected are from the 4 to 8 o'clock positions along the vulvar-vaginal borders. Erythema is not always present, but when present, it is confined to the vulvar vestibule (Fig. 18.18). Additionally, patients with vestibulodynia experience intolerance to pressure in the vulvar region. This pain is neurogenic in origin. The intolerance to pressure may be caused by tampon use, sexual activity, or tight clothing, and the pain is described as raw and burning. It is not a spontaneous pain; it is invoked. However, it is severe in nature. Some authors have suggested that symptoms be present for at least 6 months before establishing the diagnosis. The symptoms may appear around the time of first intercourse, or within the next 5 to 15 years.

Studies of women with vulvar vestibulodynia have found no increased incidence of sexual abuse compared with controls. However, many women are found to have erotophobia. Some even noted an increased nerve density and normal estrogen receptors compared with controls. In contrast, other investigators have noted an increase in alpha-estrogen receptors. Theories regarding the cause cite potential immunologic and infectious factors, though no theory has been proved to date. Oral contraceptive use in younger women and hormone replacement in older women have no association with vestibulodynia.

Vulvar dysesthesia, or vulvodynia, is a nonlocalized pain that is constant (not provoked by touch), mimicking a neuralgia. Allodynia is rarely noted, and erythema is also much less common than in vulvar vestibulodynia. Women with vulvodynia are more often perimenopausal or postmenopausal. Dyspareunia is currently present but has usually not been present before the development of dysesthesia. Similar to women with vulvar vestibulodynia, there is not an increased history of sexual abuse compared with controls. Women with dysesthesia also have an increased incidence of chronic interstitial cystitis. In general, both groups of women have an increased incidence of atopy. In some, a history of inflammation from topical agents may be elicited. These agents have usually either been self-prescribed or prescribed by a professional to treat initially what seems to be infection. Patients are often depressed and anxious, but this is thought to be a secondary reaction to the chronic pain. An outline for evaluating these patients is presented in Box 18.1. Before the diagnosis, one should exclude infection by atypical *Candida* (which may not be obvious on inspection and should be diagnosed by culture) and by group B *Streptococcus.* Some would recommend that before extensive treatment a punch biopsy should be obtained to rule out dermatitis presenting atypically, including lichen sclerosis.

The therapeutic approach for these two conditions emphasizes a sensitivity to the debilitating social aspects of the problem. Similar to other chronic pain syndromes, tricyclic antidepressants or gabapentin have been found to be successful in several series. Doses of gabapentin range from 300 to 3600 mg, usually given with increasing doses every week. Most authors start at 300 mg daily, increase to 300 mg twice daily, then three times a day, then 600 mg three times per day to 900 three times per day,

BOX 18.1 Evaluation of Patients With Vulvar Pain

- Examination of vulva for abnormal redness, erosions, crusting, ulceration, hypopigmentation
- Cotton swab test to identify areas of pain on pressure (e.g., vestibule)
- Sensory neurologic examination for allodynia and symmetric sensation
- Examination for vaginal redness, erosions, pallor, dryness
- Biopsy of specific skin findings for evaluation by dermatopathologist
- Microscopic evaluation of vaginal secretions for yeast, pH, increased white blood cells
- Culture for *Candida* (exclusive of *C. albicans*) and bacteria (especially group B *Streptococcus*)
- Evaluation for depression and impact on quality of life
- Classification of vulvar vestibulitis syndrome or dysesthetic vulvodynia

and so on; the average effective dose is approximately 1800 mg daily. Approximately 66% to 75% of women have a response to treatment with gabapentin. When the medication is discontinued, it should be tapered.

Biofeedback and behavior modification therapy have also produced relief. Topical 5% lidocaine ointment has been described as a local treatment option with limited success.

In the past, women with refractory vulvar vestibulitis have been treated with surgical removal of the vulvar vestibule and reapproximation of tissue. The surgery is difficult, with a significant complication rate, but results are generally good. In one series of 126 women with vulvar vestibulitis, the complication rate was 39%; 89% of women felt that the surgery improved their condition enough to recommend it to other women (Traas, 2006). Importantly, 30% of women have spontaneous relief of their symptoms without any treatment. Reports have indicated that multilevel nerve block given simultaneously for refractory cases has produced some response. Botulinum neurotoxin is also effective in some women, particularly those with concurrent vaginismus and levator ani spasm. Series of treatments and combinations of treatments are often used.

For women with vestibulodynia unresponsive to other therapies, surgery is usually recommended. Vestibulectomy and modified vestibulectomy (partial or limited from 3 to 9 o'clock) have resulted in resolution in 60% to 90% of patients compared with 40% to 80% for nonsurgical interventions (Stockdale, 2014). Surgery has been noted to be most effective in younger women. Some advocate for partial vestibulectomy because most pain and painful skin occur in the lower half of the vestibule. Complications from vestibulectomy include occlusion of the Bartholin gland, leading to development of cysts. This problem requires surgical "unroofing" of the duct.

VAGINA

Urethral Diverticulum

A urethral diverticulum is a permanent, epithelialized, saclike projection that arises from the posterior urethra. Most are thought to be acquired and occur in women between ages 30 and 60 years (Lee, 2005). It often presents as a mass on the anterior vaginal wall, and urethral diverticula represent approximately 84% of periurethral masses (Table 18.1). It is a common problem, being discovered in approximately 1% to 3% of women. Most urogynecologists have noted a decline in the prevalence of this condition since the early 1990s. The majority of cases are initially diagnosed in reproductive-age women, with the peak incidence in the fourth decade of life. The symptoms of a urethral diverticulum are nonspecific and are identical to the symptoms of a lower urinary tract infection. To diagnose this elusive condition, one should suspect urethral diverticulum in any woman with chronic or recurrent lower urinary tract symptoms. The urologic aspects of this condition are discussed in Chapter 21. Histologically the diverticulum is lined by epithelium; however, there is a lack of muscle in the saclike pocket.

Urethral diverticula may be congenital or acquired. Few urethral diverticula are present in children; therefore it is assumed that most diverticula are not congenital. The anatomy of the urethra has been described as a tree with many stunted branches that represent the periurethral ducts and glands. It is assumed that the majority of urethral diverticula result from repetitive or chronic infections of the periurethral glands. The suburethral infection may cause obstruction of the ducts and glands, with subsequent production of cystic enlargement and retention cysts. These cysts may rupture into the urethral lumen and produce a suburethral diverticulum. Persistent inflammation and stasis can lead to stone formation (10%). Malignancy has been reported in 6% to 9% of cases, mostly adenocarcinoma (Foley, 2011). Urethral diverticula are small, from 3 mm to 3 cm in diameter. The majority of urethral diverticula open into the midportion of the urethra (Table 18.2). Occasionally, multiple suburethral diverticula occur in the same woman.

Classically the symptoms associated with the urethral diverticulum are extremely chronic in nature and have not resolved with multiple courses of oral antibiotic therapy. The most common symptoms associated with urethral diverticula are urinary urgency and frequency and dysuria, which is the presenting symptom in about 90% of cases. Approximately 15% of women with urethral diverticula experience hematuria. Other authors have stressed the three *D*s associated with a diverticulum: *dysuria*, *dyspareunia*, and *dribbling* of the urine. Although for years, postvoiding dribbling has been termed a classic symptom of urethral diverticulum, it is reported by fewer than 10% of women with this condition. In Lee's series a palpable, tender mass was discovered in 56 of 108 patients (Lee, 2005). It is interesting that in most large series, approximately 20% of the women are asymptomatic. A classic sign of a suburethral diverticulum is the expression of purulent material from the urethra after compressing the suburethral area during a pelvic examination. Although the sign of producing a discharge by manual expression is specific, its sensitivity is poor.

The foundation of diagnosing urethral diverticulum is the physician's awareness of the possibility of this defect occurring in women with chronic symptoms of lower urinary tract infection. Historically the two most common methods of diagnosing urethral diverticulum have been the voiding cystourethrography and cystourethroscopy. Approximately 70% of urethral diverticula will be filled by contrast material on a postvoiding radiograph with a lateral view. Cystourethroscopy will demonstrate the

TABLE 18.1 Final Diagnosis of Periurethral Mass and Frequency

Diagnosis	N (%)	95% Confidence Interval (%)
Urethral diverticulum	66 (84)	73,91
Diverticulum with malignancy	4 (6)	2,14.8
Vaginal cyst	6 (7)	3,15
Leiomyoma	4 (5)	1,12
Vaginal squamous cell carcinoma	2 (2.5)	0.03,8.8
Ectopic ureter	2 (2.5)	0.03,8.8
Granuloma	1 (1)	0.03,6.8

From Blaivas JG, Flisser AJ, Bleustein CB, Panagopoulos G. Periurethral masses: diagnosis in a large series of women. *Obstet Gynecol.* 2004; 103(5 Pt 1):842-847.

TABLE 18.2 Location of the Ostium in 108 Female Patients With Diverticulum of the Urethra

Site	Number of Patients
Distal (external) third of the urethra	11
Middle third of the urethra	55
Proximal (inner) third of the urethra (including vesical neck)	18
Multiple sites	18
Unknown	6

From Lee RA. Diverticulum of the urethra: clinical presentation, diagnosis, and management. *Clin Obstet Gynecol.* 1984;27:490-498.

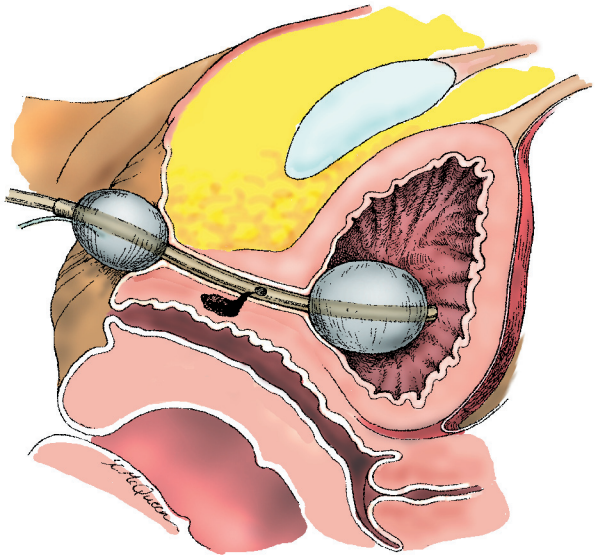

Fig. 18.19 Double-balloon catheter in use for positive-pressure urethrography.

urethral opening of the urethral diverticulum in approximately 6 of 10 cases. Other diagnostic tests used to identify urethral diverticula include urethral pressure profile recordings, transvaginal ultrasound, computed tomography (CT) scans, MRI, and positive-pressure urethrography. For diagnosis of urethral diverticulum, MRI sensitivity is 100% because the resolution is excellent (Tunitsky, 2012). Ultrasonography, done translabially (or introitally), may assist in the assessment of the mass as cystic or solid. Positive-pressure urethrography is done with a special double-balloon urethral catheter (Davis catheter) (Fig. 18.19). Classically the recordings of the pressure profile of the urethra demonstrate a biphasic curve in a woman with a urethral diverticulum. If a woman has a urethral diverticulum and urinary incontinence, performing a stress urethral pressure profile will help differentiate the cause. The differential diagnosis includes Gartner duct cyst, an ectopic ureter that empties into the urethra, and Skene glands cysts.

Several different operations can correct urethral diverticula. Excisional surgery should be scheduled when the diverticulum is not acutely infected. Operative techniques can be divided into transurethral and transvaginal approaches, with most gynecologists preferring the transvaginal approach as described by Lee (Lee, 2005). The majority of diverticula enter into the posterior aspect of the urethra. Diverticula of the distal one-third may be treated by simple marsupialization. After operations, approximately 80% of patients obtain complete relief from symptoms. Some diverticula have multiple openings into the urethra. Complete excision of this network of fistulous connections is important. The recurrence rate varies between 10% and 20%, and many failures are due to incomplete surgical resection. The most serious consequences of surgical repair of urethral diverticula are urinary incontinence and urethrovaginal fistula. Postoperative incontinence usually follows operative repairs of large diverticula that are near the bladder neck. This incontinence may be secondary to damage to the urethral sphincter. The incidence of each of these complications is approximately 1% to 2%.

Inclusion Cysts

Inclusion cysts are the most common cystic structures of the vagina. In a series of 64 women with cystic masses of the vagina, 34 had inclusion cysts (Deppisch, 1975). The cysts are usually discovered in the posterior or lateral walls of the lower third of the vagina. Inclusion cysts vary from 1 mm to 3 cm in diameter. Similar to inclusion cysts of the vulva, inclusion cysts of the vagina are more common in parous women. Inclusion cysts usually result from birth trauma or gynecologic surgery. Often they are discovered in the site of a previous episiotomy or at the apex of the vagina after hysterectomy.

Histologically, inclusion cysts are lined by stratified squamous epithelium. These cysts contain a thick, pale yellow substance that is oily and formed by degenerating epithelial cells. Often these cysts are erroneously called sebaceous cysts in the misbelief that the central material is sebaceous. Similar to vulvar inclusion cysts, the cause is either a small tag of vaginal epithelium buried beneath the surface after a gynecologic or obstetric procedure or a misplaced island of embryonic remnant that was destined to form epithelium.

The majority of inclusion cysts are asymptomatic. If the cyst produces dyspareunia or pain, the treatment is excisional biopsy.

Dysontogenetic Cysts

Dysontogenetic cysts of the vagina are thin-walled, soft cysts of embryonic origin. Whether the cysts arise from the mesonephros (Gartner duct cyst), the paramesonephricum (müllerian cyst), or the urogenital sinus (vestibular cyst) is predominantly of academic rather than clinical importance. The cysts may be differentiated histologically by the epithelial lining (Fig. 18.20). Most mesonephric cysts have cuboidal, nonciliated epithelium. Most perimesonephric cysts have columnar, endocervical-like epithelium. Occasionally pressure produced by the cystic fluid produces flattening of the epithelium, which makes histologic diagnosis less reliable. Although most commonly single, dysontogenetic cysts may be multiple. Usually the cysts are 1 to 5 cm in diameter

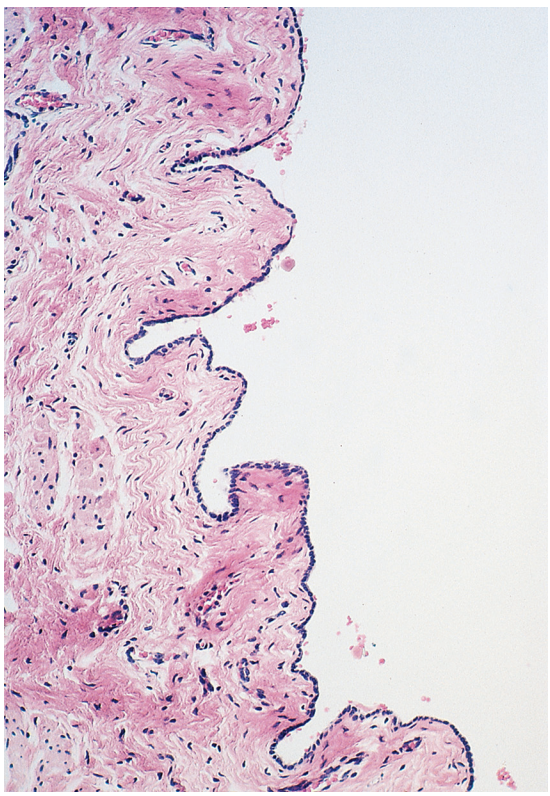

Fig. 18.20 Histologic examination of a Gartner duct cyst from the lateral vaginal wall. The cyst is lined by nonciliated cells. (From Clement PB, Young RH. *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders; 2000.)

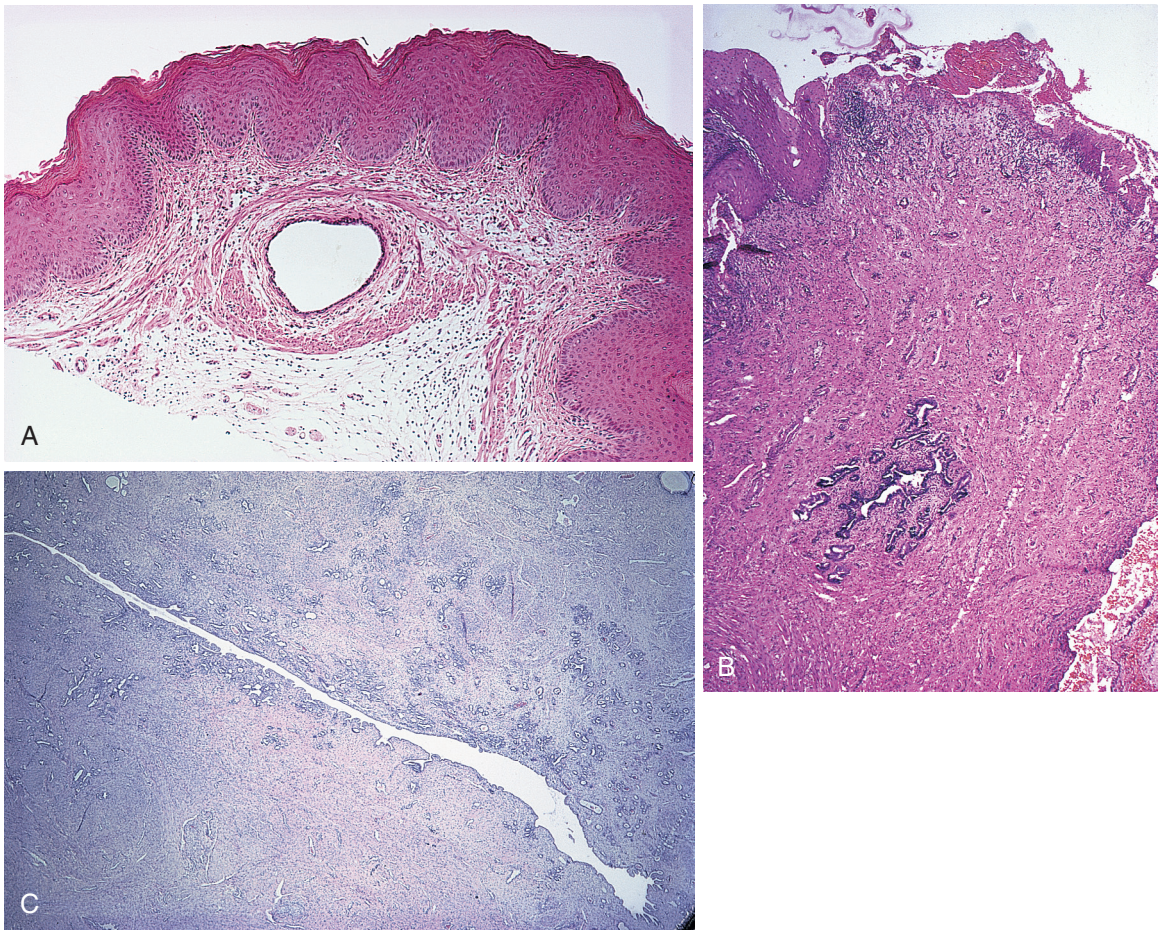

Fig. 18.21 A, Normal mesonephric duct. On cross section it is a single duct in the submucosa surrounded by clusters of smooth muscle bands. **B,** Mesonephric duct. The mother duct, located deep in the wall of the vagina, is surrounded by smaller arborized offshoots. **C,** Elongated mesonephric duct. (From Robboy SJ, Anderson MC, Russell P, et al. The vagina. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

and are discovered in the upper half of the vagina (Fig. 18.21). Sometimes multiple small cysts may present like a string of large, soft beads. A large cyst presenting at the introitus may be mistaken for a cystocele, anterior enterocele, or obstructed aberrant ureter. Approximately 1 in 200 women develop these cysts.

Embryonic cysts of the vagina, especially those discovered on the anterior lateral wall, are usually Gartner duct cysts. In the embryo the distal portion of the mesonephric duct runs parallel with the vagina. It is assumed that a segment of this embryonic structure fails to regress, and the obstructed vestigial remnant becomes cystic. These cysts are most commonly found in the lower one-third of the vagina.

Most of these benign cysts are asymptomatic, sausage-shaped tumors that are discovered only incidentally during pelvic examination. Small asymptomatic Gartner duct cysts may be followed conservatively. In a series of 25 women undergoing operations for symptomatic dysontogenetic cysts, a wide range of symptoms were reported, including dyspareunia, vaginal pain, urinary symptoms, and a palpable mass. Sometimes large cysts interfere with the use of tampons. MRI can be useful in delineating the course and anatomic arrangement of vaginal cysts (Wai, 2004).

Operative excision is indicated for chronic symptoms. Rarely, one of these cysts becomes infected, and if operated on during the acute phase, marsupialization of the cyst is preferred. Excision of the vaginal cyst may be a much more formidable operation than anticipated. The cystic structure may extend up into the broad ligament and anatomically be in proximity to the distal course of the ureter.

Rare tumors of the vagina include fibromas, angiomyxomas, and hemangiomas. All are usually found by the patient and require surgical excision.

Tampon Problems

The vaginal tampon has achieved immense popularity and ubiquitous use. It is not surprising that there are rare associated risks with tampon usage: vaginal ulcers, the "forgotten" tampon, and toxic shock syndrome. The latter, related to toxins elaborated by *Staphylococcus aureus*, is discussed in Chapter 23.

Wearing tampons for a few days has been associated with microscopic epithelial changes. The majority of women develop epithelial dehydration and epithelial layering, and some will develop microscopic ulcers. These minor changes take between 48 hours and 7 days to heal. Using colposcopy to evaluate the vaginal epithelium after tampon use, Friedrich found serial changes of epithelial drying, peeling, layering, and ultimately microulceration in 15% of women wearing tampons only during the time of normal menstruation. No clinical symptoms were associated with these microscopic changes. Theoretically these microulcerations are a potential portal of entry for HIV.

Large macroscopic ulcers of the vaginal fornix have been described in women using vaginal tampons for prolonged times for persistent vaginal discharge or spotting. The ulcers have a base of clean granulation tissue with smooth, rolled edges. One can even find tampon fibers in the biopsy specimens of these ulcers. The pathophysiology of the ulcer is believed to be secondary to drying and pressure necrosis induced by the tampon. Obviously, many of these young women use tampons for the identical symptoms that are associated with a vaginal ulcer—that is, spotting and vaginal discharge. Often the intermenstrual spotting is believed to be breakthrough bleeding from oral contraceptives, and the possibility of a vaginal ulcer from chronic tampon usage is overlooked.

Vaginal ulcers are not uncommon secondary to several types of foreign objects, including diaphragms, pessaries, and medicated silicon rings. Management is conservative because the ulcers heal spontaneously when the foreign object is removed. Any persistent ulcer should be biopsied to establish the cause.

A woman with a "lost" or "forgotten" tampon presents with a classic foul vaginal discharge and occasionally spotting. The tampon is usually found high in the vagina. The odor from a forgotten tampon is overwhelming. The tampon is removed using a "double glove technique" where two gloves are donned on the removal hand and, on grasping the tampon, the outer glove is pulled over the tampon and tied as the tampon is removed. The woman should be treated with an antibiotic vaginal cream or gel (such as metronidazole or clindamycin) for the next 5 to 7 days.

Local Trauma

The most common cause of trauma to the lower genital tract of adult women is coitus. Approximately 80% of vaginal lacerations occur secondary to sexual intercourse. Other causes of vaginal trauma are straddle injuries, penetration injuries by foreign objects, sexual assault, vaginismus, and water-skiing accidents. The management of vulvar and vaginal trauma in children is discussed in Chapter 12.

The predisposing factors believed to be related to coital injury include virginity, the state of the postpartum and postmenopausal vaginal epithelium, pregnancy, intercourse after a prolonged period of abstinence, hysterectomy, and inebriation. In one series of 19 injuries from normal coitus, 12 of the women were between the ages of 16 and 25 and 5 were older than 45 (Smith, 1983). The most common injury is a transverse tear of the posterior fornix. Similar linear lacerations often occur in the right or left vaginal fornices. The location of the coital injury is believed to be related to the poor support of the upper vagina, which is supported only by a thin layer of connective tissue. The most prominent symptom of a coital vaginal laceration is profuse or prolonged vaginal bleeding. Many women experienced sharp pain during intercourse, and 25% noted persistent abdominal pain. The most troublesome but extremely rare complication of vaginal laceration is vaginal evisceration. Coital injury to the vagina should be considered in any woman with profuse or prolonged abnormal vaginal bleeding. Sensitive but thorough history regarding abuse is always appropriate.

Management of coital lacerations involves prompt suturing under adequate anesthesia. Secondary injury to the urinary and gastrointestinal tracts should be ruled out.

CERVIX

Endocervical and Cervical Polyps

Endocervical and cervical polyps are the most common benign neoplastic growths of the cervix, reported in 4% of gynecologic patients. Endocervical polyps are most common in multiparous women in their 40s and 50s. Cervical polyps usually present as a single polyp, but multiple polyps do occur occasionally. The majority are smooth, soft, reddish purple to cherry red, and fragile. They readily bleed when touched. Endocervical polyps may be single or multiple and are a few millimeters to 4 cm in diameter. The stalk of the polyp is of variable length and width (Fig. 18.22). Polyps may arise from either the endocervical canal (endocervical polyp) or ectocervix (cervical polyp). Endocervical polyps are more common than are cervical polyps. Often the terms *endocervical* and *cervical* polyps are used to describe the same abnormality. Polyps whose base is in the endocervix usually have a narrow, long pedicle and occur during the reproductive years, whereas polyps that arise from the ectocervix have a short, broad base and usually occur in postmenopausal women.

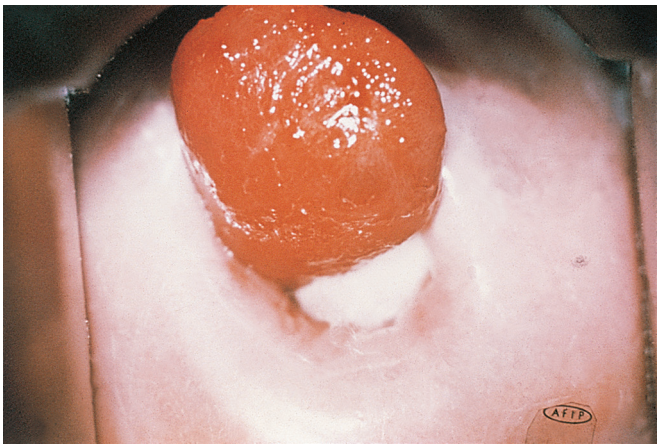

Fig. 18.22 Cervical polyp. A large polyp protrudes from the external cervical os. The surface is red and rough, covered by endocervical epithelium. (From Anderson MC, Robboy SJ, Russell P, et al. The cervix—benign and non-neoplastic conditions. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

The hypothesis of the origin of endocervical polyps is that they are usually secondary to inflammation or abnormal focal responsiveness to hormonal stimulation. Focal hyperplasia and localized proliferation are the response of the cervix to local inflammation. The color of the polyp depends in part on its origin, with most endocervical polyps being cherry red and most cervical polyps grayish white.

The classic symptom of an endocervical polyp is intermenstrual bleeding, especially after contact such as coitus or a pelvic examination. Sometimes an associated leukorrhea emanates from the infected cervix. Many endocervical polyps are asymptomatic and recognized for the first time during a routine speculum examination. Often the polyp seen on inspection is difficult to palpate because of its soft consistency.

Histologically the surface epithelium of the polyp is columnar or squamous epithelium, depending on the site of origin and the degree of squamous metaplasia (Fig. 18.23). The stalk is composed of an edematous, inflamed, loose, and richly vascular connective tissue. Six different histologic subtypes have been described: adenomatous, cystic, fibrous, vascular, inflammatory, and fibromyomatous. Greater than 80% are of the adenomatous type. During pregnancy, focal areas of decidual changes may develop in the stroma. Often there is ulceration of the stalk's most dependent portion, which explains the symptom of contact bleeding. Malignant degeneration of an endocervical polyp is extremely rare; the reported incidence is less than 1 in 200. Considerations in the differential diagnosis include endometrial polyps, small prolapsed myomas, retained products of conception, squamous papilloma, sarcoma, and cervical malignancy. Microglandular endocervical hyperplasia sometimes presents as a

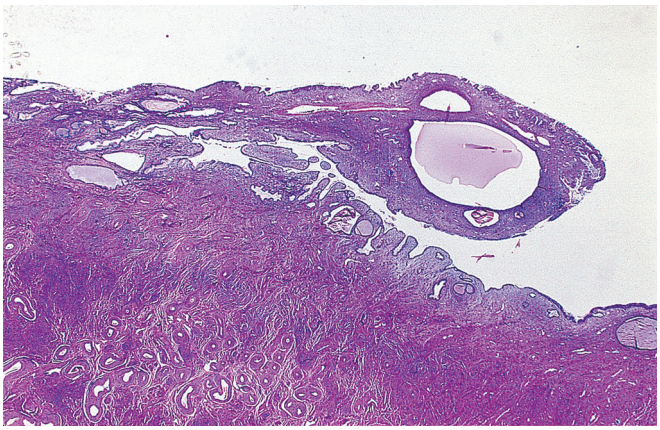

Fig. 18.23 Cervical polyp. The stroma is fibromuscular and the base contains thick-walled blood vessels. Endocervical crypts, some dilated, are present within the polyp. (From Anderson MC, Robboy SJ, Russell P, et al. The cervix—benign and non-neoplastic conditions. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

1- to 2-cm polyp. This is an exaggerated histologic response, usually to oral contraceptives.

Most endocervical polyps may be managed in the office by grasping the base of the polyp with an appropriately sized clamp. The polyp is avulsed with a twisting motion and sent to the pathology laboratory for microscopic evaluation. The polyp is usually friable. If the base is broad or bleeding ensues, the base may be treated with chemical cautery, electrocautery, or cryocautery. After the polyp is removed, the endometrium should be evaluated in women older than 40 who have presented with abnormal bleeding, to rule out coexisting pathologic changes because a significant endometrial pathologic condition is found in approximately 5% of asymptomatic women with endocervical polyps.

Nabothian Cysts

Nabothian cysts are retention cysts of endocervical columnar cells occurring where a tunnel or cleft has been covered by squamous metaplasia. These cysts are so common that they are considered a normal feature of the adult cervix. Many women have multiple cysts. Grossly these cysts may be translucent or opaque whitish or yellow in color, and they vary from microscopic to macroscopic size, with the majority between 3 mm and 3 cm in diameter. Rarely, a woman with several large nabothian cysts may develop gross enlargement of the cervix. These mucous retention cysts are produced by the spontaneous healing process of the cervix. The area of the transformation zone of the cervix is in an almost constant process of repair, and squamous metaplasia and inflammation may block the cleft of a gland orifice. The endocervical columnar cells continue to secrete, and thus a mucous retention cyst is formed. Nabothian cysts are asymptomatic, and no treatment is necessary.

Lacerations

Cervical lacerations may occur during obstetric deliveries. Obstetric lacerations vary from minor superficial tears to extensive full-thickness lacerations at 3 and 9 o'clock, respectively, which may extend into the broad ligament. Lacerations may occur in nonpregnant women with mechanical dilation of the cervix. The atrophic cervix of the postmenopausal woman increases the risk of cervical laceration when the cervix is mechanically dilated for dilation and curettage (D&C) or hysteroscopy.

Acute cervical lacerations bleed and should be sutured. Cervical lacerations that are not repaired may give the external os of the cervix a fish-mouthed appearance; however, they are usually asymptomatic. The use of laminaria tents to slowly soften and dilate the cervix before mechanical instrumentation of the endometrial cavity has reduced the magnitude of iatrogenic cervical lacerations. Furthermore, the practice of routine inspection of the cervix after every second- or third-trimester delivery has enabled physicians to discover and repair extensive cervical lacerations. Extensive cervical lacerations, especially those involving the endocervical stroma, may lead to incompetence of the cervix during a subsequent pregnancy.

Cervical Myomas

Cervical myomas are smooth, firm masses that are similar to myomas of the fundus (Figs. 18.24 and 18.25). A cervical myoma is usually a solitary growth in contrast to uterine myomas, which, in general, are multiple. Depending on the series, 3% to 8% of myomas are categorized as cervical myomas. Because of the relative paucity of smooth muscle fibers in the cervical stroma, the majority of myomas that appear to be cervical actually arise from the isthmus of the uterus.

Most cervical myomas are small and asymptomatic. When symptoms do occur, they are dependent on the direction in which the enlarging myoma expands. The expanding myoma produces symptoms secondary to mechanical pressure on adjacent organs. Cervical myomas may produce dysuria, urgency, urethral or ureteral obstruction, dyspareunia, or obstruction of the cervix. Occasionally a cervical myoma may become pedunculated and protrude through the external os of the cervix. These prolapsed myomas are often ulcerated and infected. A very large cervical myoma may produce distortion of the cervical canal and upper vagina. Rarely a cervical myoma causes dystocia during childbirth.

The diagnosis of a cervical myoma is by inspection and palpation. Grossly and histologically, cervical myomas are identical to and indistinguishable from myomas of the corpus of the uterus. Occasionally the histologic picture of cervical myomas will demonstrate many hyalinized, thick-walled blood vessels that are postulated to be the source of the neoplastic smooth muscle tumor. This latter subtype of cervical myoma is termed a *vascular*

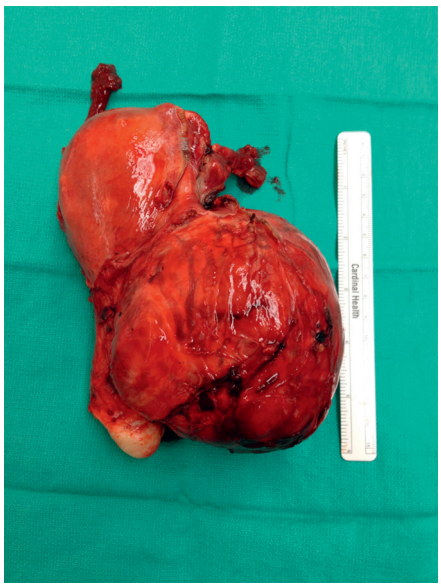

Fig. 18.24 Large fibroid originating from the lateral wall of the cervix and growing into the broad ligament. (Courtesy Fidel A. Valea, MD.)

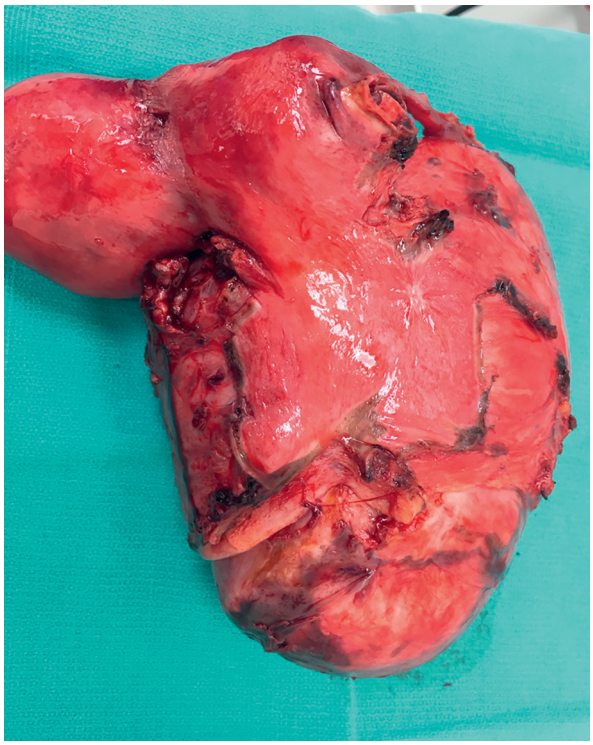

Fig. 18.25 Posterior view of the uterus with a large fibroid that is prolapsing through a very dilated cervix and completely distorts the anatomy of the lower uterine segment. (Courtesy Fidel A. Valea, MD.)

leiomyoma. Management is similar to that of uterine myomas in that asymptomatic, small myomas may be observed for rate of growth. The occurrence and persistence of symptoms from a cervical myoma are an indication for medical therapy with GnRH agonists or myomectomy or hysterectomy, depending on the patient's age and future reproductive plans. Because of both a complex blood supply and involvement with the distal course of the ureter, treatment of cervical myomas that grow laterally may become a challenge if myomectomy is the operation of choice. Cervical myomas may be treated by radiologic catheter embolization. Prolapsed uterine myomas are discussed later in this chapter.

Cervical Stenosis

Cervical stenosis most often occurs in the region of the internal os and may be divided into congenital or acquired types. The causes of acquired cervical stenosis are operative, radiation induced, infectious, neoplastic, or atrophic changes. Loop electrocautery excision procedure (LEEP), cone biopsy, and cautery of the cervix (either electrocautery or cryocoagulation) are the operations most commonly associated with cervical stenosis, which often depends on the volume of tissue removed. The symptoms of cervical stenosis depend on whether the patient is premenopausal or postmenopausal and whether the obstruction is complete or partial. Common symptoms in premenopausal women include dysmenorrhea, pelvic pain, abnormal bleeding, amenorrhea, and infertility. The infertility is usually associated with endometriosis, which is commonly found in reproductive-age women with cervical stenosis. Postmenopausal women are usually asymptomatic for a long time. Slowly they develop a hematometra (blood), hydrometra (clear fluid), or pyometra (exudate).

The diagnosis is established by inability to introduce a 1- to 2-mm dilator into the uterine cavity. If the obstruction is complete, a soft, slightly tender, enlarged uterus is appreciated as a midline mass, and ultrasound examination demonstrating fluid within the uterine cavity. Management of cervical stenosis is dilation of the cervix with dilators under ultrasound guidance. If stenosis recurs, monthly laminaria tents may be used. Similarly, office follow-up and sounding of the cervix of women who have had a cone biopsy or cautery of the cervix is important to establish patency of the endocervical canal. Postmenopausal women with pyometra usually do not need antibiotics. After the acute infection has subsided, endometrial carcinoma and endocervical carcinoma should be ruled out by appropriate diagnostic biopsies. After cervical dilation, it is often useful to leave a T tube or latex nasopharyngeal airway as a stent in the cervical canal for a few days to maintain patency.

UTERUS

Ultrasound

Ultrasound, primarily endovaginal, is the most common and most efficient imaging technique for pelvic structures. For endovaginal ultrasound, transducers are configured on vaginal probes and placed in a sterile sheath, usually a glove or condom, before an examination. During the examination the woman is in a dorsal lithotomy position and has an empty bladder. Because the transducer is closer to the pelvic organs than when a transabdominal approach is employed, endovaginal resolution is usually superior. However, if the pelvic structures to be studied have expanded and extend into the patient's abdomen, the organs are difficult to visualize with an endovaginal probe. Most ultrasound machines are equipped with both types of transducers.

For transabdominal gynecologic examinations, a sector scanner is preferable. It provides greater resolution of the pelvis and an easier examination than the linear array. During abdominal pelvic ultrasound examination, it is helpful for the patient to have a full bladder. This serves as an acoustic window for the high-frequency sound waves. Ultrasound is more than 90% accurate in recognizing the presence of a pelvic mass, but it does not establish a tissue diagnosis.

Ultrasonography employs an acoustic pulse echo technique. The transducer of the ultrasound machine is made up of piezoelectric crystals that vibrate and emit acoustic pulses. Acoustic echoes return from the tissues being scanned and cause the crystals to vibrate again and release an electric charge. A computer within the ultrasound machine then integrates the electric charges to form the image. Present equipment provides resolution of less than 0.2 mm.

Doppler ultrasound techniques assess the frequency of returning echoes to determine the velocity of moving structures. Measurement of diastolic and systolic velocities provides indirect indices of vascular resistance. Muscular arteries have high resistance. Newly developed vessels, such as those arising in malignancies, have little vascular wall musculature and thus have low resistance. Three-dimensional ultrasound is a computer technique in which multiple two-dimensional images are compiled to render either a surface- or volume-based image that appears to occupy space, as opposed to being flat. Three-dimensional ultrasound has of yet not been shown to have a specific diagnostic advantage in gynecology compared with other modalities.

A disadvantage of ultrasound is its poor penetration of bone and air; thus the pubic symphysis and air-filled intestines and rectum often inhibit visualization. Advantages of ultrasound include the real-time nature of the image, the absence of radiation, the ability to perform the procedure in the office before, during, or immediately after a pelvic examination, and the ability to describe the findings to the patient while she is watching. One of the most reassuring aspects of sonography is the absence of adverse clinical effects from the energy levels used in diagnostic studies.

Sonographic evaluation of endometrial pathologic changes involves measurement of the endometrial thickness or stripe. The normal endometrial thickness is 4 mm or less in a postmenopausal woman not taking hormones. The thickness varies in premenopausal women at different times of the menstrual cycle and in women taking hormone replacement (Fig. 18.26), making endometrial thickness measurements less reliable in that setting. The endometrial thickness is measured in the longitudinal plane, from outer margin to outer margin, at the widest part of the endometrium. Ultrasound is not a screening tool in asymptomatic women. However, several studies of postmenopausal women with vaginal bleeding have documented that malignancy is extremely rare in women with an endometrial thickness of 4 mm or less. Systematic reviews have noted that ultrasound may be reliably used to predict 96% to 99% of endometrial cancers in women with postmenopausal bleeding. The flip side of the coin is that 1% to 4% of malignancies will be missed using a cutoff of less than 4 mm (Tabor, 2002). In addition, papillary-serous adenocarcinomas of the endometrium do not always develop the same endometrial stripe thickness as endometrioid cancer. Two caveats for using ultrasound in screening of postmenopausal bleeding are (1) ultrasound does not provide a diagnosis—a tissue specimen is necessary for a diagnosis; and (2) all women with bleeding, no matter the endometrial thickness, should have a tissue biopsy. If an endometrial biopsy obtains inadequate tissue and the endometrial thickness is 5 mm or greater, a repeat biopsy, hysteroscopically directed biopsy, or curettage should be performed.

Sonohysterography is an easily accomplished and validated technique for evaluating the endometrial cavity. The technique involves instilling saline into the uterine cavity. Sonohysterography is an alternative to office hysteroscopy. In this procedure a thin balloon-tipped catheter or intrauterine insemination catheter is inserted through the cervical os, and 5 to 30 mL of warmed saline is slowly injected into the uterine cavity. Meta-analyses of sonohysterography have found the procedure to be successful in obtaining information in 95% of women, with minimal complications. Contraindications are active cervical or uterine infection. Some clinicians will have patients take a dose of ibuprofen before the procedure. Preferably, sonohysterography is performed in the proliferative phase of the cycle when the endometrial lining is at its lowest level. Sonohysterography has also been helpful in the evaluation of polyps, filling defects, submucous myomas, and uterine septae (Fig. 18.27). Importantly, sonohysterography, as with all types of ultrasound, does not make a tissue diagnosis.

Sonography is the method of choice to locate a "missing" intrauterine device (IUD). It will help in diagnosing perforation of the uterus or unrecognized expulsion of the device. Endovaginal ultrasound transducers equipped with needle guides are often used for oocyte aspiration as part of *in vitro* fertilization.

In summary, ultrasound has become an extremely valuable adjunct to the bimanual examination. In many patients, particularly those with obesity, it is superior to perform bimanual examination alone. An endovaginal ultrasound of an early pregnancy has become a mainstay in the evaluation of the pregnant woman with first-trimester vaginal bleeding.

Endometrial Polyps

Endometrial polyps are localized overgrowths of endometrial glands and stroma that project beyond the surface of the endometrium. They are soft, pliable, and may be single or multiple. Most polyps arise from the fundus of the uterus. *Polypoid hyperplasia* is a benign condition in which numerous small polyps are discovered throughout the endometrial cavity. Endometrial polyps vary from a few millimeters to several centimeters in diameter, and it is possible for a single large polyp to fill the endometrial cavity. Endometrial polyps may have a broad base (sessile) or be attached by a slender pedicle (pedunculated). They occur in all age groups but have a peak incidence between the ages of 40 and 49. The prevalence of endometrial polyps in reproductive-age women is 20% to 25%, and they are noted in approximately 10% of women when the uterus is examined at autopsy. The cause of endometrial polyps is unknown. Because polyps are often associated with endometrial hyperplasia, unopposed estrogen has been implicated as a possible cause.

The majority of endometrial polyps are asymptomatic. Those that are symptomatic are associated with a wide range of abnormal bleeding patterns. No single abnormal bleeding pattern is diagnostic for polyps; however, menorrhagia, premenstrual and postmenstrual staining, and scanty postmenstrual spotting are the most common. Occasionally a pedunculated endometrial polyp with a long pedicle may protrude from the external cervical os. Sometimes large endometrial polyps may contribute to infertility.

Polyps are succulent and velvety, with a large central vascular core. The color is usually gray or tan but may occasionally be red or brown. Histologically, an endometrial polyp has three components: endometrial glands, endometrial stroma, and central vascular channels (Fig. 18.28; see Fig. 18.27). Epithelium must be identified on three sides, like a peninsula. Approximately two out of three polyps consist of an immature endometrium that does not respond to cyclic changes in circulating progesterone. This immature endometrium differs from surrounding endometrium and often appears as a "Swiss cheese" cystic hyperplasia during all phases of the menstrual cycle (Fig. 18.29). The other one-third of endometrial polyps consist of functional endometria that will undergo cyclic histologic changes. The tip of a prolapsed polyp often undergoes squamous metaplasia, infection, or ulceration. The clinician cannot distinguish whether the abnormal bleeding originates from the polyp or is secondary to the commonly coexisting endometrial hyperplasia. Approximately one in four reproductive-age women with abnormal bleeding will have endometrial polyps discovered in her uterine cavity.

Malignancy in an endometrial polyp is related to patient's age and is most often of a low stage and grade. In one series of 67 women from the United Kingdom with endometrial polyps, 86% were benign, 13% hyperplastic, and 3% malignant. Another series of 61 women with polyps found 88% were benign and 5% were malignant. In a review and meta-analysis of the oncogenic potential of reported endometrial polyps, the prevalence of premalignant or malignant polyps was 5.42% in postmenopausal women compared with 1.7% in reproductive-age women. Furthermore, the prevalence of endometrial neoplasia within polyps in women with symptomatic bleeding was 4.15% compared with 2.16% for those without bleeding. Among symptomatic postmenopausal women with endometrial polyps, 4.47% had a malignant polyp compared with 1.51% in asymptomatic postmenopausal women (Lee, 2010). The question of an association of endometrial polyps with endometrial carcinoma is still debated. A population-based, case-control study from Sweden estimated that the increased risk of subsequent endometrial carcinoma in women with endometrial polyps is only twofold. It is interesting that benign polyps have been found in approximately 20% of uteri removed for endometrial carcinoma.

Unusual polyps have been described in association with chronic administration of the nonsteroidal antiestrogen tamoxifen. The endometrial abnormalities associated with chronic tamoxifen therapy include polyps, 20% to 35%; endometrial hyperplasia, 2% to 4%; and endometrial carcinoma, 1% to 2%; and often with multiple irregular sonolucencies suggesting the presence of cysts.

Most endometrial polyps are asymptomatic, and the diagnosis is not usually established until the uterus is opened after hysterectomy for other reasons. Endometrial polyps may be discovered by vaginal ultrasound, with or without hydrosonography, hysteroscopy, or hysterosalpingography, during the diagnostic workup of a woman with a refractory case of abnormal uterine bleeding or

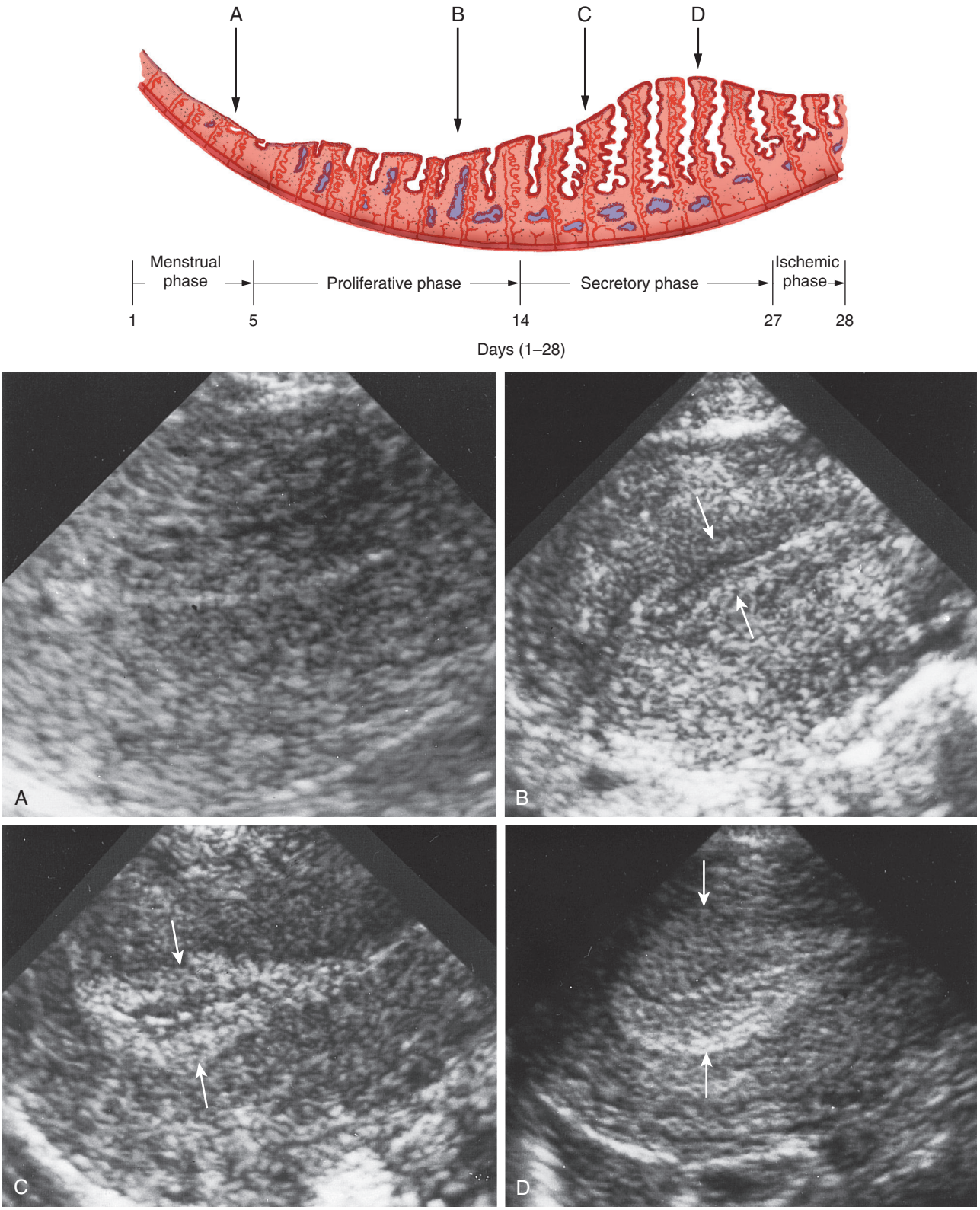

Fig. 18.26 Variation in endometrium during menstrual cycle. **A,** Early proliferative phase. **B,** Late proliferative phase. **C,** Periovulatory phase. **D,** Late secretory phase. Note increase in endometrial thickness throughout the menstrual cycle. Also note multilayered appearance in the late proliferative phase. (From Fleischer AC, Kepple DM. Benign conditions of the uterus, cervix, and endometrium. In: Nyberg DA, Hill LM, Bohm-Velez M, et al, eds. *Transvaginal Ultrasound.* St. Louis: Mosby–Year Book; 1992.)

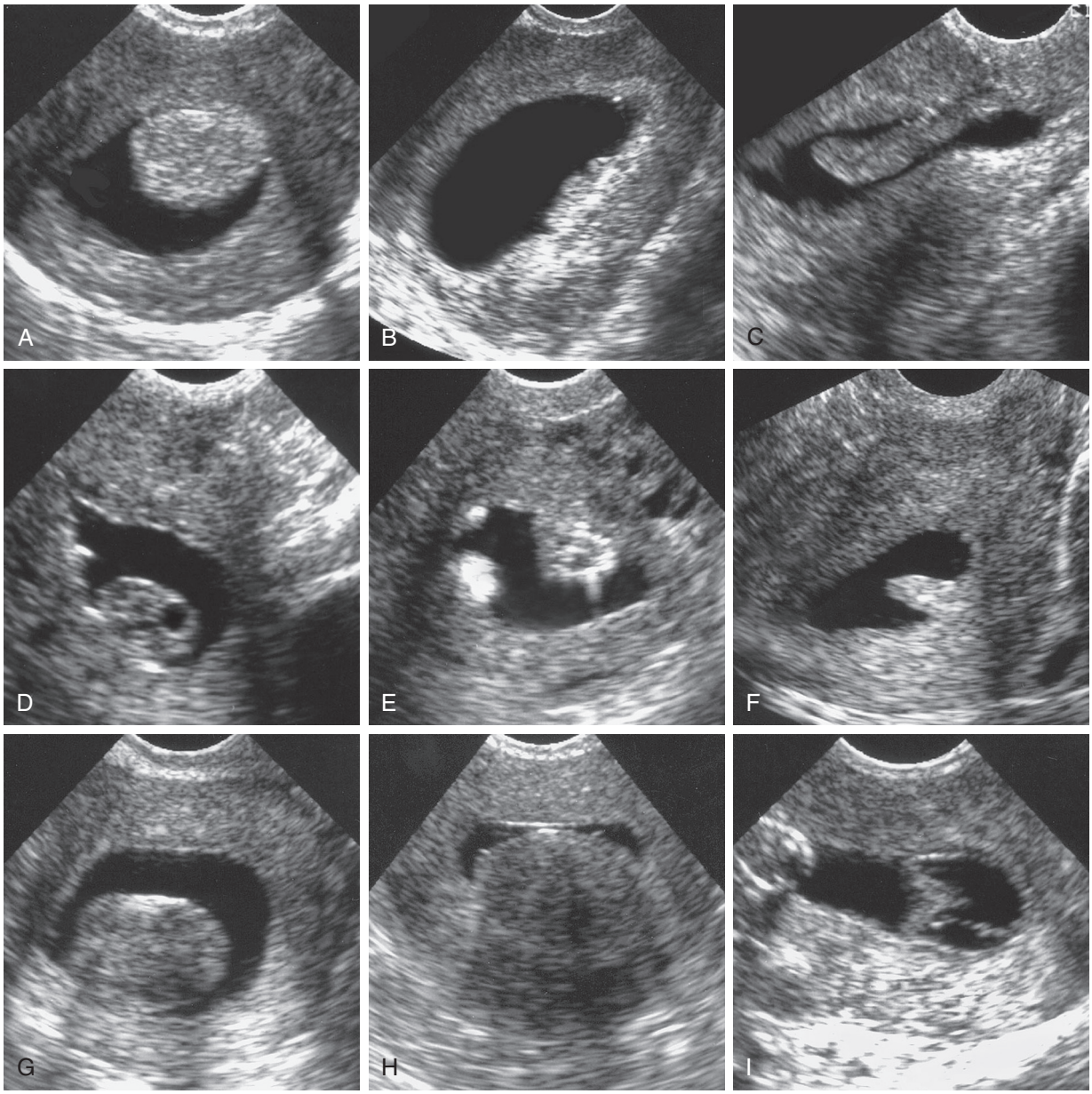

Fig. 18.27 Sonohysterograms. **A,** Well-defined, round echogenic polyp. **B,** Carpet of small polyps. **C,** Polyp on a stalk. **D,** Polyp with cystic areas. **E,** Small polyp. **F,** Small polyp. **G,** Hypoechoic submucosal fibroid. **H,** Hypoechoic attenuating submucosal fibroid. **I,** Endometrial adhesions. Note bridging bands of tissue within fluid-filled endometrial canal. (From Salem S. The uterus and adnexa. In Rumack CM, Wilson SR, Charboneau JW, eds. *Diagnostic Ultrasound.* 2nd ed. St. Louis: Mosby; 1998:538.)

pelvic mass. Endometrial polyps are often confused with endocervical polyps (Fig. 18.30). A well-defined, uniformly hyperechoic mass that is less than 2 cm in diameter, identified by vaginal ultrasound within the endometrial cavity, is usually a benign endometrial polyp (see Fig. 18.27, *A-C*). Most endometrial polyps usually resolve after a few years, although new polyps can form.

The optimal management of endometrial polyps is removal by hysteroscopy with D&C. Because of the common association of endometrial polyps and other endometrial pathologic conditions, it is important to examine histologically both the polyp and the associated endometrial lining. Polyps, because of their mobility, often tend to elude the curette. Postcurettage hysteroscopic studies have demonstrated that routine use of a long, narrow polyp forceps at the time of curettage at best results in discovery and removal of only approximately one in four endometrial polyps. The differential diagnosis of endometrial polyps includes submucous leiomyomas, adenomyomas, retained products of conception, endometrial hyperplasia, carcinoma, and uterine sarcomas.

Hematometra

A hematometra is a uterus distended with blood and is secondary to gynatresia, which is partial or complete obstruction of any portion of the lower genital tract. Obstruction of the isthmus of the uterus, cervix, or vagina may be congenital or acquired. The two most common congenital causes of hematometra are an imperforate hymen and a transverse vaginal septum. Among the leading

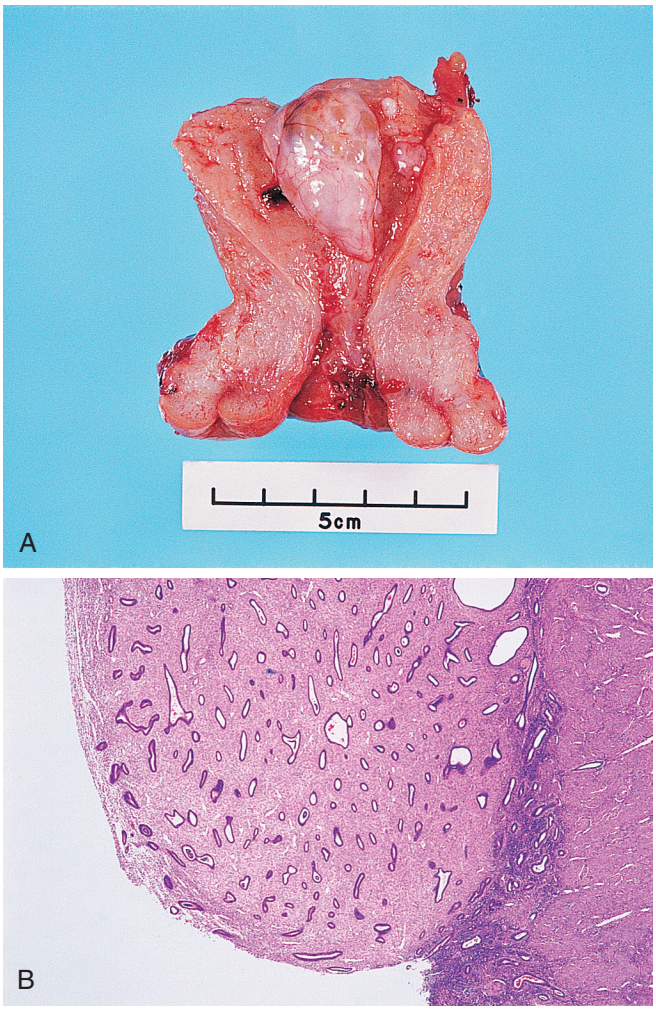

Fig. 18.28 Endometrial polyp. **A,** Note cystic glands in the polyp. **B,** The fibrous stroma of the polyp contrasts with the cellular stroma of the adjacent endometrium. (From Anderson MC, Robboy SJ, Russell P, et al. Endometritis, metaplasias, polyps, and miscellaneous changes. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

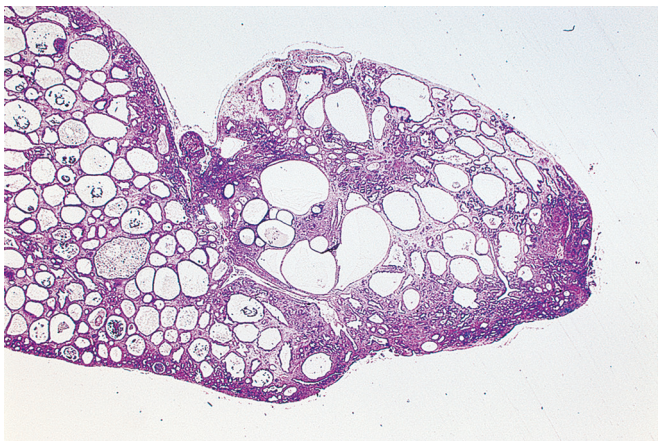

Fig. 18.29 Endometrial polyp showing multiple cystic glands with flattened epithelial lining. (From Anderson MC, Robboy SJ, Russell P, et al. Endometritis, metaplasias, polyps and miscellaneous changes. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

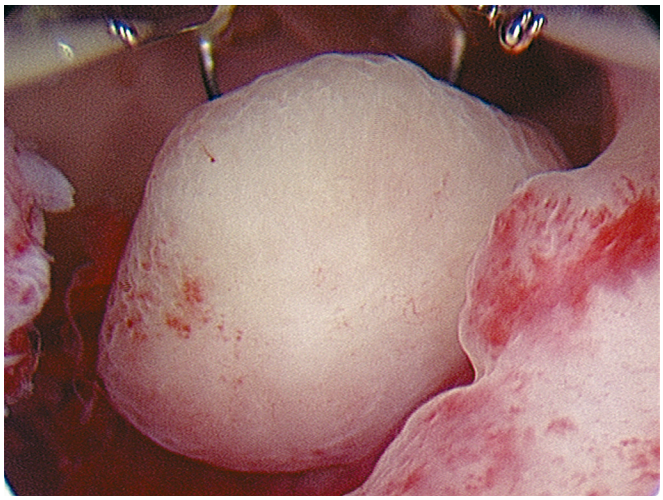

Fig. 18.30 Endocervical polyp was seen at hysteroscopy. (From Goldberg JM, Falcone T. *Atlas of Endoscopic Techniques in Gynecology.* London: WB Saunders; 2000.)

causes of acquired lower tract stenosis are senile atrophy of the endocervical canal and endometrium, scarring of the isthmus by synechiae, cervical stenosis associated with surgery, radiation therapy, cryocautery or electrocautery, endometrial ablation, and malignant disease of the endocervical canal.

The symptoms of hematometra depend on the age of the patient, her menstrual history and the rapidity of the accumulation of blood in the uterine cavity, and the possibility of secondary infection producing pyometra. Thus common symptoms of hematometra include primary or secondary amenorrhea and possibly cyclic lower abdominal pain. During the early teenage years, the combination of primary amenorrhea and cyclic, episodic cramping lower abdominal pains suggests the possibility of a developing hematometra. Occasionally the obstruction is incomplete, and there is associated spotting of dark brown blood. Hematometra in postmenopausal women may be entirely asymptomatic. On pelvic examination a mildly tender, globular uterus is usually palpated. Ultrasound may be used to confirm the diagnosis.

The diagnosis of hematometra is generally suspected by the history of amenorrhea and cyclic abdominal pain. The diagnosis is usually confirmed by vaginal ultrasound or probing the cervix with a narrow metal dilator, with release of dark brownish black blood from the endocervical canal. Sometimes the blood retained inside the uterus becomes secondarily infected and has a foul odor.

Management of hematometra depends on operative relief of the lower tract obstruction. Treatment of congenital obstruction is discussed in Chapter 11. Appropriate biopsy specimens of the endocervical canal and endometrium should be obtained to rule out malignancy when the cause of hematometra is not obvious. If the uterus is significantly enlarged or if there is any suspicion that the retained fluid is infected, drainage should be accomplished first. Biopsy should be postponed for approximately 2 weeks to diminish the chances of infection or uterine perforation. Hematometra after operations or cryocautery usually resolves with cervical dilation. Rarely, a hematometra may form after a first-trimester abortion. This is treated by repeat suction aspiration of the products of conception that are blocking the internal os.

Leiomyomas

Leiomyomas, also called *myomas*, are benign tumors of muscle cell origin. These tumors are often referred to by their popular names, *fibroids* or *fibromyomas*, but such terms are semantic misnomers if one is referring to the cell of origin. Most leiomyomas

contain varying amounts of fibrous tissue, which is believed to be secondary to degeneration of some of the smooth muscle cells.

Leiomyomas are the most common benign neoplasms of the uterus. The lifetime prevalence of leiomyomas is greater than 80% among African American women and approaches 70% among white women (Baird, 2003). In general, a third of myomas will become symptomatic, causing abnormal and excessive uterine bleeding, pelvic pain, pelvic pressure, bowel and bladder dysfunction, infertility, recurrent miscarriage, and abdominal protrusion. Leiomyomas are a tremendous public health burden and the most common indication for hysterectomy in the United States. Approximately 42 per 1000 women are hospitalized annually because of fibroids, but African American women have higher rates of hospitalization, myomectomies, and hysterectomies compared with white women (relative risk [RR] of 3.5, 6.8, and 2.4, respectively) (Wechter, 2011). In black women, vitamin D deficiency has been linked with increased fibroid risk (Baird, 2013). Why some women develop myomas and others do not is unknown. Therefore effective treatment is limited by the poor understanding of their pathogenesis.

Risk factors associated with the development of myomata include increasing age, early menarche, low parity, tamoxifen use, obesity, and in some studies a high-fat diet. Smoking has been found to be associated with a decreased incidence of myomata, believed to be due to relative estrogen deficiency. African American women have the highest incidence, whereas Hispanic and Asian women have similar rates to white women. There appears to be a familial tendency to develop myoma. Studies of twins have noted that when identical and fraternal twins are compared, a significant proportion of myoma tend to have an inherited basis. Rare genetic conditions such as hereditary leiomyomatosis and renal cell cancer (Launoned, 2001) and Alport syndrome (Uliana, 2011) feature development of myomas. The growth of myomas is dependent on gonadal steroids, and there are increased numbers of steroid receptors in myomas compared with normal myometrium. They have a limited malignant potential with less than 1% transformation into malignancy. Cytogenetically, most fibroids are chromosomally normal and arise from a single cell (are clonal). Although fibroids are clonal in nature, heterogeneity exists and they may vary greatly in size, location, and appearance within the same uterus. There is accumulating evidence that suggests hypoxia is implicated in early cellular events that lead to the myometrial smooth muscle cell to transform into leiomyoma (Tal, 2014). Angiogenesis and vascularization are factors that control the growth of tumors. Tal and Segars reviewed the molecular regulation of the growth factors involved in angiogenesis of fibroids and described the potential implications for future therapy (Tal, 2014).

Although leiomyomas arise throughout the body in any structure containing smooth muscle, in the pelvis the majority are found in the corpus of the uterus. Occasionally, leiomyomas may be found in the fallopian tube or the round ligament, and approximately 5% of uterine myomas originate from the cervix. Rarely, myomas will arise in the retroperitoneum and produce symptoms secondary to "mass effects" on adjacent organs.

Myomas may be single but most often are multiple. They vary greatly in size from microscopic to multinodular uterine tumors that may weigh more than 50 pounds and literally fill the patient's abdomen (Fig. 18.31). Initially most myomas develop from the myometrium, beginning as intramural myomas. As they grow, they remain attached to the myometrium with a pedicle of varying width and thickness. Small myomas are round, firm, solid tumors. With continued growth, the myometrium at the edge of the tumor is compressed and forms a pseudocapsule. Although myomas do not have a true capsule, this pseudocapsule is a valuable surgical plane during a myomectomy.

Myomas are classed into subgroups by their relative anatomic relationship and position to the layers of the uterus (Fig. 18.32).

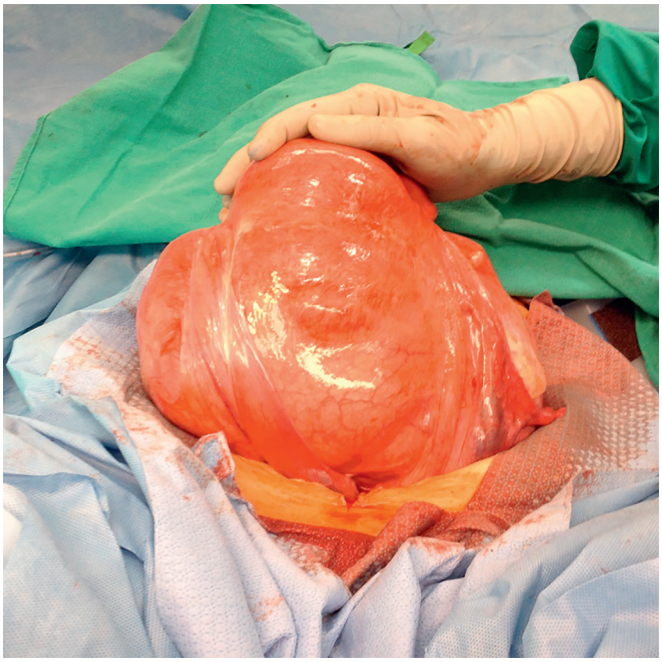

Fig. 18.31 Image of large fibroid uterus before hysterectomy. (Courtesy Fidel A. Valea, MD.)

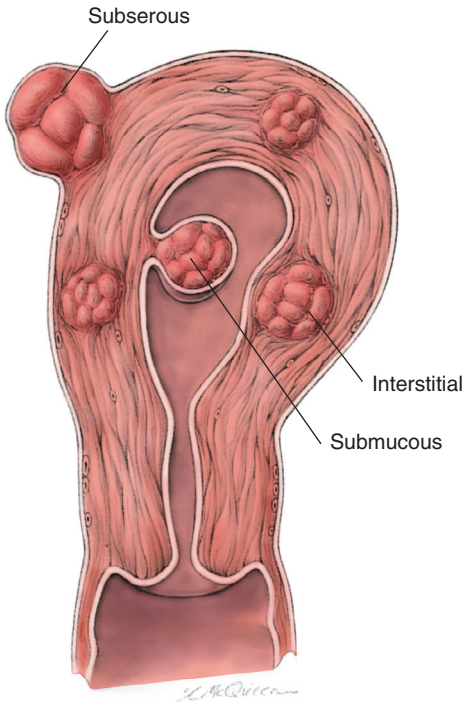

Fig. 18.32 Drawing of cut surface of uterus showing characteristic whorl-like appearance and varying locations of leiomyomas. (From Novak ER, Woodruff JD, eds. *Novak's Gynecologic and Obstetric Pathology.* 6th ed. Philadelphia: WB Saunders; 1967:215.)

The three most common types of myomas are intramural, subserous, and submucous, with special nomenclature for broad ligament and parasitic myomas (Fig. 18.33). Continued growth in one direction determines which myomas will be located just below the endometrium (submucosal) and which will be found just beneath the serosa (subserosal) (Fig. 18.34). Although only 5% to 10% of

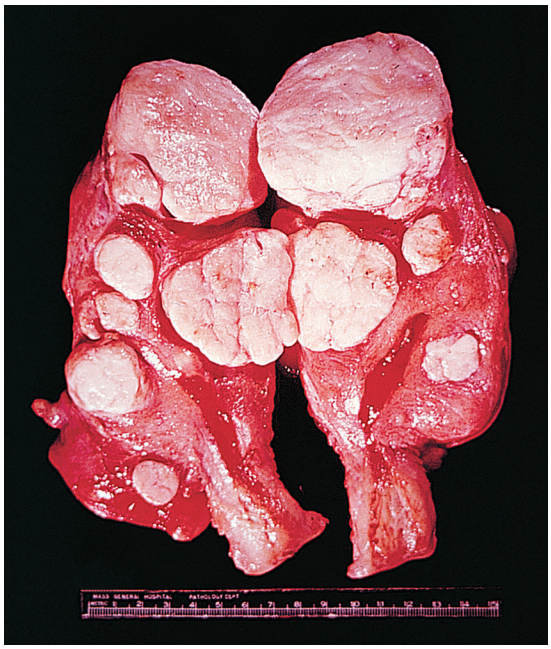

Fig. 18.33 Multiple leiomyomas. These are predominantly intramural. The bulging cut surfaces are clearly shown. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

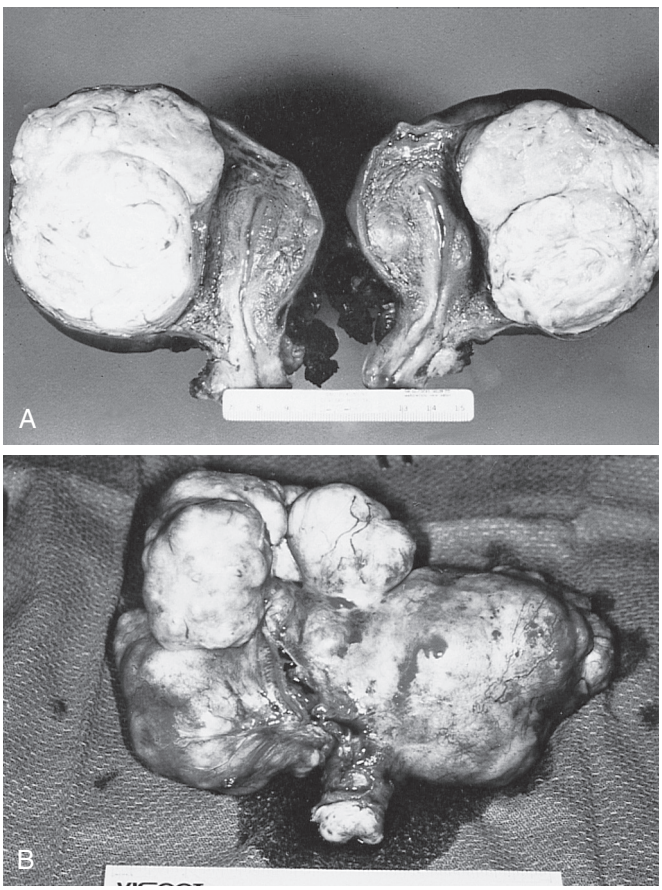

Fig. 18.34 **A,** Large subserosal myoma. **B,** Hysterectomy specimen of myomatous uterus. (Courtesy Vern L. Katz and William Droegemueller.)

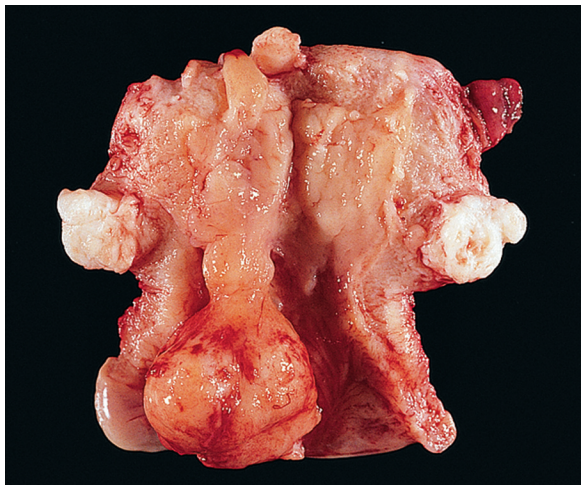

Fig. 18.35 Uterus with multiple myomata. Note the large central submucosal myoma. (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology.* St. Louis: Mosby-Wolfe; 1997.)

myomas become submucosal, they usually are the most troublesome clinically (Fig. 18.35). These submucosal tumors may be associated with abnormal vaginal bleeding or distortion of the uterine cavity that may produce infertility or miscarriage. Rarely, a submucosal myoma enlarges and becomes pedunculated. The uterus will try to expel it, and the prolapsed myoma may protrude through the external cervical os (see Fig. 18.25).

Subserosal myomas give the uterus its knobby contour during pelvic examination. Further growth of a subserosal myoma may lead to a pedunculated myoma wandering into the peritoneal cavity. This myoma may outgrow its uterine blood supply and obtain a secondary blood supply from another organ, such as the omentum, and become a parasitic myoma. Growth of a myoma in a lateral direction from the uterus may result in a broad ligament myoma (see Fig. 18.24). The clinical significance of broad ligament myomas is that they are difficult to differentiate on pelvic examination from a solid ovarian tumor. Large, broad ligament myomas may produce a hydroureter as they enlarge.

Though the origin of uterine leiomyomas is incompletely understood, cytogenetic studies have yielded some clues to how and why myomas develop. Each tumor develops from a single muscle cell a progenitor myocyte, thus each myoma is monoclonal. Cytogenetic analysis has demonstrated that myomas have multiple chromosomal abnormalities. (Each myoma would have cells with the same abnormality.) Sixty percent are normal, 46XX. The larger the myoma, the more an abnormal karyotype will be detected. Interestingly, the chromosomal anomalies of myomata have a remarkable clustering of changes. Twenty percent of abnormalities involve translocations between chromosomes 12 and 14. Seventeen percent involve a deletion of chromosome 7. Twelve percent involve a deletion of chromosome 12, and some are trisomy 12. The affected regions on chromosome 12 are also abnormal in many other types of solid tumors. The regions of chromosome 12 and 7 involve genes that may regulate growth-inducing proteins and cytokines, including transforming growth factor beta (TGF-β), epidermal growth factor (EGF), insulin-like growth factors (IGF) 1 and 2, and platelet-derived growth factor (PDGF) (Fig. 18.36). Many of these cytokines have been found in significantly higher concentrations in myomas than in the surrounding myometrium. Current theory holds that the neoplastic transformation from normal myometrium to leiomyomata is the result of a somatic mutation in the single progenitor cell. The mutation then affects cytokines that affect cell growth. The growth may also be influenced by the relative levels of estrogen

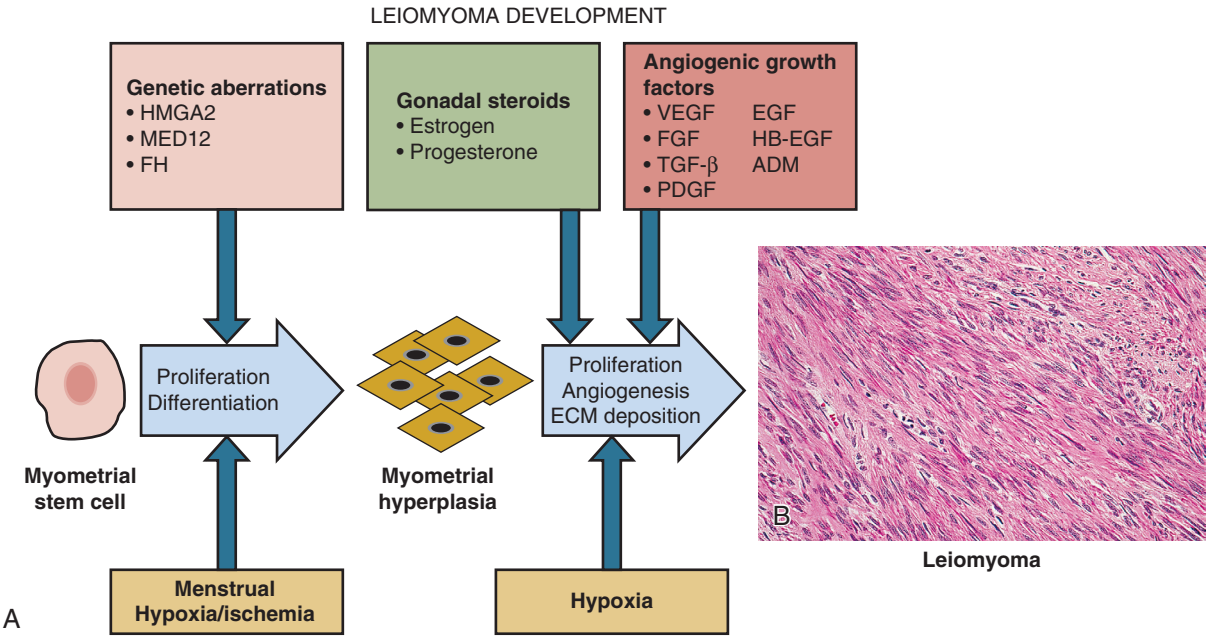

Fig. 18.36 A, Leiomyoma development. **B,** Leiomyoma. The smooth muscle cells are markedly elongated and have eosinophilic cytoplasm and elongated, cigar-shaped nuclei. The nuclei are uniform and mitotic figures absent or sparse. *EGF,* epidermal growth factor; *PDGF,* platelet-derived growth factor; *TGF-β*, transforming growth factor beta; *VEGF,* vascular endothelial growth factor. (**A,** Modified from Tal R, Segars JH. The role of angiogenic factors in fibroid pathogenesis: potential implications for future therapy. *Hum Reprod Update.* 2014;20(2):194-216. **B,** From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

or progesterone. Both estrogen and progesterone receptors are found in higher concentrations in uterine myomas, as are other genomic changes that potentiate cellular proliferation. There also appear to be similarities between fibroids and keloid formation. Interestingly, Ishikawa and colleagues noted that myoma cells have an increased expression of aromatase, which further potentiates more local estrogen, and that African American women had the highest levels of aromatase in myoma cells (Ishikawa, 2009).

Myomas are rare before menarche, and most myomas diminish in size after menopause with the reduction of a significant amount of circulating estrogen. Myomas often enlarge during pregnancy and occasionally enlarge secondary to oral contraceptive therapy. Medically induced hypoestrogenic states produce reductions in the size of myomas. Many women, though, have small myomas that do not grow under the influence of high circulating estrogen levels. Thus the relationship between estrogen and progesterone levels and myoma growth is complex.

Grossly a myoma has a lighter color than the normal myometrium. On a cut surface, the tumor has a glistening, pearl-white appearance, with the smooth muscle arranged in a trabeculated or whorled configuration. Histologically there is a proliferation of mature smooth muscle cells. The nonstriated muscle fibers are arranged in interlacing bundles. Between bundles of smooth muscle cells are variable amounts of fibrous connective tissue, especially toward the center of any large tumor (see Fig. 18.36). The amount of fibrous tissue is proportional to the extent of atrophy and degeneration that has occurred over time. The intracellular structure of myoma cells is different from the surrounding normal myometrium. The abnormal cells contain more collagen and what has been described as a "stiffer" cytoskeleton secondary to the intracellular pressure generated by the densely packed surrounding myoma. Less than 5% of myomas exhibit hypercellularity, and these are termed *cellular leiomyomata.* Cellular leiomyomata tend to be larger in size and solitary. There is less accompanying adenomyosis or other uterine pathologic changes. The clinical presentation of cellular leiomyoma is more similar to that of a sarcoma (leiomyosarcoma). Other authors have noted a genomic expression that is similar, as well, to leiomyosarcomas. However, cellular leiomyomata are not precursors to sarcoma and have a benign prognosis.

The eventual fate of some myomas is determined by their relatively poor vascular supply. This supply is found in one or two major arteries at the base or pedicle of the myoma. The arterial supply of myomas is significantly less than that of a similarly sized area of normal myometrium. Thus with continued growth, degeneration occurs because the tumor outgrows its blood supply. The severity of the discrepancy between the myoma's growth and its blood supply determines the extent of degeneration: hyaline, myxomatous, calcific, cystic, fatty, or red degeneration and necrosis. The mildest form of degeneration of a myoma is hyaline degeneration (Fig. 18.37). Grossly in this condition the surface of the myoma is homogeneous with loss of the whorled pattern. Histologically, with hyaline degeneration, cellular detail is lost as the smooth muscle cells are replaced by fibrous connective tissue.

The most acute form of degeneration is red, or carneous, infarction (Fig. 18.38). This acute muscular infarction causes severe pain and localized peritoneal irritation. This form of degeneration occurs during pregnancy in approximately 5% to 10% of gravid women with myomas. The condition is best treated with nonsteroidal antiinflammatory agents for 72 hours, as long as the woman is less than 32 weeks' gestation. The ultrasound appearance of painful myomas is one of mixed echodense and echolucent areas. Serial ultrasound examinations have also demonstrated that most myomas (80%) do not change size during pregnancy; if a change in size does occur, it is usually not

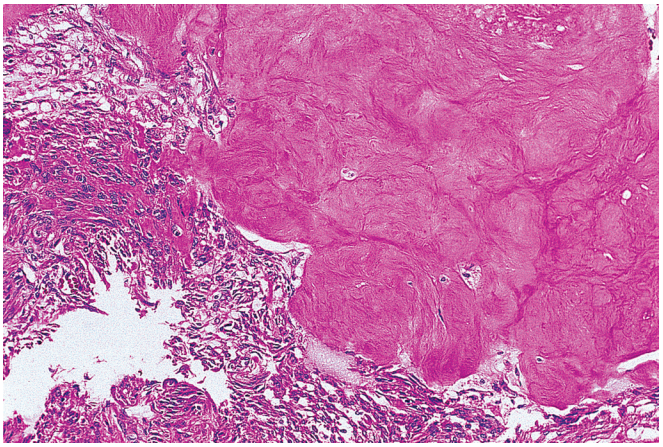

Fig. 18.37 Hyaline degeneration is a leiomyoma. There is an eosinophilic ground-glass appearance. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

associated with painful symptomology. During pregnancy this complication should be treated medically because attempts at operative removal may result in profuse blood loss. If the patient is not pregnant, acute degeneration is not a contraindication to myomectomy. The more advanced forms of degenerating myomas may become secondarily infected, especially when large necrotic areas exist. The histologic changes of degeneration are found more commonly in larger myomas. However, two-thirds of all myomas show some degree of degeneration, with the three most common types being hyaline degeneration (65%), myxomatous degeneration (15%), and calcific degeneration (10%).

The literature emphasizes that the incidence of malignant degeneration is estimated to be between 0.3% and 0.7%. The term *malignant degeneration* is incorrect. It is unknown as to whether myomas degenerate into sarcomas. Given the very high prevalence of myomas, most investigators believe that sarcomas arise spontaneously in myomatous uteri. The possibility of a uterine tumor being a leiomyoma sarcoma is 10 times greater in a woman in her 60s than in a woman in her 40s.

The most common symptoms related to myomas are pressure from an enlarging pelvic mass; pain, including dysmenorrhea; and abnormal uterine bleeding. The severity of symptoms is usually related to the number, location, and size of the myomas. However, more than two-thirds of women with uterine myomas are asymptomatic.

One of three women with myomas experiences pelvic pain or pressure. Acquired dysmenorrhea is one of the most common complaints. Various forms of vascular compromise, either acute degeneration or torsion of the pedicle, produce severe pelvic pain. Mild pelvic discomfort is described as pelvic heaviness or a dull, aching sensation that may be secondary to edematous swelling in the myoma. An enlarged myoma or myomas often produce pressure symptoms similar to those of an enlarging pregnant uterus. Sometimes a woman will notice that her abdominal girth is increasing without appreciable change in weight. Alternatively, an anterior myoma pressing on the bladder may produce urinary frequency and urgency. In general, urinary symptoms are more common than rectal symptoms. Extremely large myomas and broad ligament myomas may produce a unilateral or bilateral hydroureter.

Abnormal bleeding is experienced by 30% of women with myomas. The most common symptom is menorrhagia, but intermenstrual spotting and disruption of a normal pattern are other common complaints. Wegienka and colleagues evaluated the bleeding pattern of 596 women with myomas. Compared with a control group, bleeding was more often described as gushing. Menses were longer in duration and heavier. In this study, symptoms of bleeding were related to the size of myomas. Interestingly, the location of the myomas, submucous versus intramural, was not related to bleeding symptoms (Wegienka, 2003). The exact cause-and-effect relationship between myomas and abnormal bleeding is difficult to determine and is poorly understood. The explanation is straightforward when there are areas of ulceration over submucous myomas. However, ulceration is a rare finding. The most popular theory is that myomas result in an abnormal microvascular growth pattern and function of the vessels in the adjacent endometrium. The older theory that the amount of menorrhagia is directly related to an increase of endometrial surface area has been disproved. One of three women with abnormal bleeding and submucous myomas also has endometrial hyperplasia, which may be the cause of the symptom.

Occasionally, myomas are the only identifiable abnormality after a detailed infertility investigation. Because the data relating

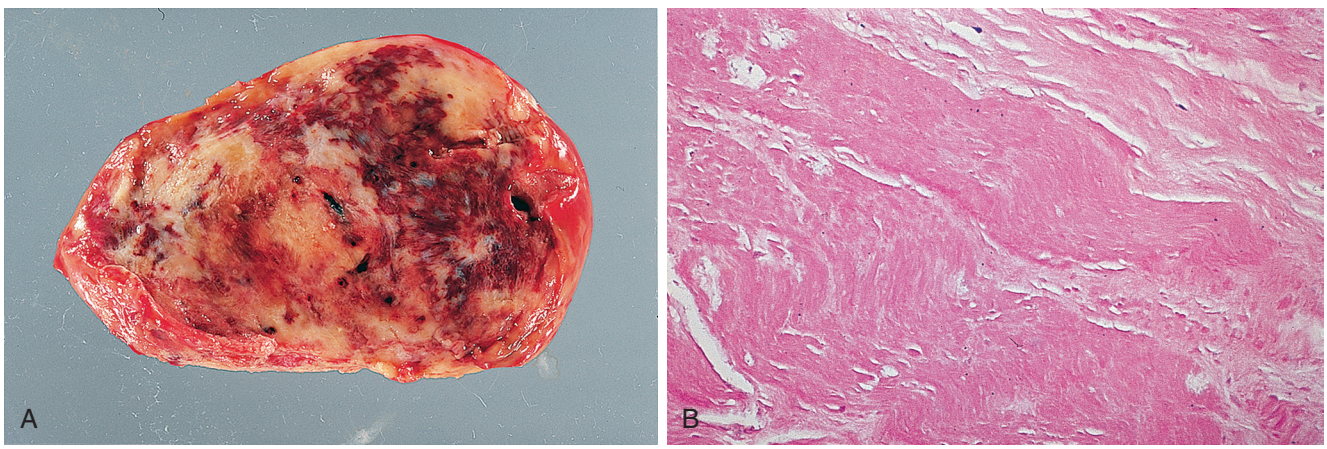

Fig. 18.38 **A,** Gross view of an infarcted leiomyoma. **B,** Red degeneration; the ghosts of the muscle cells and their nuclei remain. (**A,** From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002. **B,** From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology.* St. Louis: Mosby-Wolfe; 1997.)

myomas to infertility are weak, myomectomy is indicated only in long-standing infertility and recurrent abortion after all other potential factors have been investigated and treated. Studies suggest that submucous myomas that distort the uterine cavity are the myomas that may affect reproduction. Successful full-term pregnancy rates of 40% to 50% have been reported after a myomectomy. The success of an operation is most dependent on the age of the patient, the size of the myomas, and the number of compounding factors that affect the couple's fertility. A Cochrane review of the surgical treatment of fibroids for subfertility noted "insufficient evidence from randomized controlled trials to evaluate the role of myomectomy to improve fertility" (Metwally, 2012).

Rapid growth of a uterine myoma after menopause is a disturbing symptom. This is the classic symptom of a leiomyosarcoma; however, fibroids can have growth spurts, and most (but not all) guidelines suggest rapid growth is not necessarily an indication for treatment (Stewart, 2015). Rarely, a secondary polycythemia is noted in women with uterine myomas. This syndrome is related to elevated levels of erythropoietin. The polycythemia diminishes after removal of the uterus.

Clinically the diagnosis of uterine myomas is usually confirmed by physical examination. On palpation, an enlarged, firm, irregular uterus may be felt. The three conditions that commonly enter into the differential diagnosis are pregnancy, adenomyosis, and an ovarian neoplasm. The discrimination between large ovarian tumors and myomatous uteri may be difficult on physical examination because the extension of myomas laterally may make palpation of normal ovaries impossible during the pelvic examination. The mobility of the pelvic mass and whether the mass moves independently or as part of the uterus may be helpful diagnostically. Ultrasound is diagnostic; it can easily differentiate fibroids from a pregnant uterus or adnexal mass (Stewart, 2015). Submucosal myomas may be diagnosed by vaginal ultrasound, sonohysterography, hysteroscopy, or as a filling defect on hysterosalpingography. Occasionally an abdominopelvic radiograph will note concentric calcifications. Several reports promote CT and MRI studies of uterine myomas. However, these imaging techniques are more expensive than ultrasound is. Until CT and MRI can distinguish between benign and malignant myomas, they will rarely be ordered in routine clinical management of myomas. MRI is helpful in differentiating adenomyosis or an adenomyoma from a single, solitary myoma, especially in a woman desiring preservation of her fertility. MRI with gadolinium contrast can also provide information on devascularized (degenerated) fibroids and more detail on the location of fibroids with respect to endometrial, intramural, or serosal (Stewart, 2015). Serial ultrasound examinations have been used to evaluate progression in the size of myomas or response to therapy, although there is a strong correlation between pelvic examination results and ultrasound in determining the size of myomas.

The management of small, asymptomatic myomas is judicious observation. When the tumor is first discovered, it is appropriate to perform a pelvic examination at 6-month intervals to determine the rate of growth. The majority of women will not need surgery, especially those women in the perimenopausal period, where the condition usually improves with diminishing levels of circulating estrogens.

Cases of abnormal bleeding and leiomyomas should be investigated thoroughly for concurrent problems such as endometrial hyperplasia. If symptoms do not improve with conservative management, operative therapy may be considered. The choice between a myomectomy and hysterectomy is usually determined by the patient's age, parity, and, most important, future reproductive plans. Myomectomy is associated with longer hospital stays and more pelvic adhesions than hysterectomy. Studies suggest that myomectomy results in approximately 80% resolution of symptoms. Hysterectomy is associated with a greater than 90% patient satisfaction rate, though hysterectomy has a higher rate of urinary tract injuries, particularly abdominal hysterectomy. When myomectomies are performed to preserve fertility, care must be taken to avoid adhesions, which may compromise the goal of the operation. In the past, full-thickness myomectomies (surgeries that entered the endometrial cavity) were considered an indication for cesarean delivery before labor; however, most clinicians now recommend strong consideration for cesarean section for all degrees of myomectomy other than removal of a pedunculated leiomyomata or small hysteroscopic resection.

Classic indications for a myomectomy include persistent abnormal bleeding, pain or pressure, or enlargement of an asymptomatic myoma to more than 8 cm in a woman who has not completed childbearing. The causal relationship of myomas and adverse reproductive outcomes is poorly understood. Long-standing infertility or repetitive abortion directly related to myomas is rare. Contraindications to a myomectomy include pregnancy, advanced adnexal disease, malignancy, and a situation in which enucleation of the myoma would severely reduce endometrial surface so that the uterus would not be functional. The choice between the two operations is not always an easy one.

Within 20 years of the myomectomy operation, one in four women subsequently has a hysterectomy performed, the majority for recurrent leiomyomas. Myomectomy can be performed in select women using laparoscopic techniques. Similar to the open myomectomy, women undergoing a laparoscopic myomectomy should have a multilayer closure and consideration of the use of antiadhesive barriers. These myomas can be extirpated through extension of the umbilical incision, via minilaparotomy, or vaginally through a colpotomy. Submucous myomas may be resected via the cervical canal using the hysteroscope. Although preliminary studies using laser surgery have been reported, most investigators advocate using an operative resectoscope or tissue removal system. Three out of four women have long-term relief of their menorrhagia secondary to uterine myomas after hysteroscopic resection of the myomas.

The indications for hysterectomy for myomas are similar to indications for myomectomy, with a few additions. Some gynecologists selectively perform a hysterectomy for asymptomatic myomas when the uterus has reached the size of a 14- to 16-week gestation. The hypothesis is that most myomas of this size will eventually produce symptoms. However, it is impossible to predict which individual woman will develop symptoms. Rapid growth of a myoma after menopause warrants investigation and consideration for surgery. Prolapse of a myoma through the cervix is optimally treated by vaginal removal and ligation of the base of the myoma, with antibiotic coverage. Hysteroscopic resection aids the transvaginal removal of a prolapsed myoma.

There has been much controversy regarding the prevalence of undiagnosed uterine cancers among women with presumed benign fibroids at the time of hysterectomy. The risk of unexpected leiomyosarcoma at the time of hysterectomy has been reviewed in multiple publications, including the 2017 Agency for Healthcare Research and Quality report, and was found to be less than 1 in 770 to 1 in 10,000 surgeries for symptomatic leiomyomas (ACOG, 2019b). Morcellation is the process by which a large portion of tissue is divided into smaller pieces. The benefit of morcellation is the ability to perform a hysterectomy or myomectomy in a minimally invasive fashion, avoiding an open abdominal incision and the associated longer recovery time and higher mortality rate. This can be accomplished manually (i.e., with a scalpel or scissors) or via a rapidly rotating blade known as a *power morcellator*. The use of power morcellation may spread unsuspected cancer during surgery for treatment of symptomatic fibroids. The Food and Drug Administration (FDA) recommends against the use of laparoscopic power morcellators in the majority of women undergoing myomectomy or hysterectomy for treatment of fibroids, thereby significantly limiting the use of

morcellation to hysterectomy in premenopausal women who are not candidates for en bloc resection, and only after counseling women about the risks of power morcellation and the potential spread of cancer and offering alternatives such as morcellation in a contained system, such as a laparoscopic retrieval bag (USFDA, 2014). The use of an intraperitoneal bag for morcellation has been proposed to reduce tissue dissemination. Unfortunately, the intraperitoneal bags are not designed for concurrent use with a power morcellator (ACOG, 2019b).

For women undergoing minimally invasive surgery for symptomatic fibroids, preoperative considerations must be made regarding age, menopausal status, hereditary factors, uterine size, rapid uterine growth, endometrial sampling, cervical cytologic test results, and pelvic imaging. Informed consent for these procedures should include a discussion of the risks and benefits of power morcellation. If after careful review malignancy is strongly suspected or known, then power morcellation must be avoided. The impact of the FDA warning on clinical practice has become quickly evident. A survey of American Association of Gynecologic Laparoscopists (AAGL) and American College of Obstetricians and Gynecologists (ACOG) members showed nearly half of the respondents had increased their rate of laparotomy and nearly three-quarters stopped using power morcellation during hysterectomy and myomectomy primarily because of hospital mandates, although they did not believe it resulted in improved patient outcomes (Lum, 2016). Ultimately the physician and the patient must participate in shared decision making about the route of hysterectomy, after detailed discussion of the rare risk of encountering a leiomyosarcoma with its associated mortality and the increased morbidity of the abdominal hysterectomy compared with minimally invasive approaches (ACOG, 2019b).

It is possible to treat leiomyomas medically by reducing the circulating level of estrogen and progesterone. GnRH agonists, medroxyprogesterone acetate (Depo-Provera), danazol, aromatase inhibitors, and the antiprogesterone RU 486 have undergone clinical trials. Randomized controlled trials of 5 and 10 mg of mifepristone (RU486) have shown significant reduction in size, bleeding, and improvement in quality of life. Mifepristone acts through inhibition of progesterone receptors. Daily administration of 5 mg and 10 mg has shown uterine volume reductions of 48% and 52% after 1 year for both doses. Amenorrhea occurred in 65% of the women in 6 months and in 705 within a year. However, long-term use is controversial because of the potential of inducing endometrial pathology (Eisinger, 2005). The use of GnRH agonists, sometimes with add-back hormonal therapy, has also been successful in treating myomas. A Cochrane review on add-back therapy with GnRH analogs for uterine fibroids concluded there was low or moderate evidence that tibolone, raloxifene, estriol, and ipriflavone help preserve bone density and medroxyprogesterone acetate (MPA) and tibolone may reduce vasomotor symptoms. The studies assessed only short-term (within 12 months) effectiveness and safety. Larger uterine volume was an adverse effect associated with some of the therapies (MPA, tibolone, and conjugated estrogens) (Moroni, 2015). Reductions in mean uterine volume and myoma size by 40% to 50% have been documented. However, individual responses vary greatly. With medical treatments, most of the size reductions occur within the first 3 months. After cessation of therapy, myomas gradually resume their pretreatment size. By 6 months after treatment, most myomas will have returned to their original size. During treatment, Doppler flow studies have demonstrated increased resistance in the uterine arteries and in the smaller arteries feeding the myoma. Also during treatment, the proliferative activity of the myoma and the binding of epidermal growth factor are reduced. The use of medical suppressive therapies such as GnRH agonists for women with large myomas and those with anemia may reduce blood loss at the time of hysterectomy or myomectomy. However, one study found that tourniquets at the time of myomectomy were as effective as pretreatment with GnRH agonists in decreasing blood loss.

Therapies for Heavy Menstrual Bleeding

In women who have heavy menstrual bleeding as the primary symptom, limited data support the effectiveness of medical therapies, including tranexamic acid and the levonorgestrel-releasing intrauterine device (Stewart, 2015). Tranexamic acid is an oral fibrinolytic agent that may decrease bleeding when taken only during heavy menstrual bleeding. Because its mechanism of action is concerning for increased thrombotic risk, it should not be taken concomitantly with oral contraceptives. The levonorgestrel-releasing intrauterine device decreased menstrual bleeding while providing contraception; however, the rate of expulsion among women with submucosal fibroids may be as high as 12% (Stewart, 2015). Oral contraceptives reduce menstrual bleeding in women with fibroids according to observational data. In addition, nonsteroidal antiinflammatory drugs decrease heavy menstrual bleeding and menstrual pain. Oral progestogens have not been shown to reduce fibroid size or fibroid-related symptoms

Future Options for Medical Treatment

No validated medical treatment is yet able to eliminate fibroids; therefore surgery is the most effective treatment for symptomatic fibroids. However, there are emerging medical treatments such as ulipristal acetate that may be an option for women who wish to avoid surgery or, before surgery, to reduce the extent of the operation by reducing the size of the fibroids.

Ulipristal acetate is a selective progesterone receptor modulator that on binding to the progesterone receptor in target tissues displays antagonist and partial agonist effects (McKeage, 2011). The efficacy of ulipristal acetate has been demonstrated in three European phase III studies evaluating PGL4001 (Ulipristal Acetate) Efficacy Assessment in Reduction of Symptoms Due to Uterine Leiomyomata (PEARL I, II, and III) (Donnez, 2014). It has been approved for medical treatment of fibroids in Canada and Europe, but it is not FDA approved for treatment of fibroids in the United States.

Aromatase inhibitors block the synthesis of estrogen. They have been shown to reduce uterine fibroid size (up to 71% in 2 months) and ameliorate uterine fibroid symptoms, including a reduction in menstrual volume and duration of menstruation, and urinary retention (Shozu, 2003). Table 18.3 summarizes the medical options for the management of patients with uterine leiomyomas.

Uterine Artery Embolization

Uterine myomas may also be treated with uterine artery embolization (UAE) (Fig. 18.39). Multiple embolic materials have been used, including gelatin sponge (Gelfoam) silicone spheres, gelatin microspheres, metal coils, and most commonly polyvinyl alcohol (PVA) particles of various diameters. Postprocedural abdominal and pelvic pain is common for the first 24 hours and may last up to 2 weeks. Most patients remain overnight in the hospital for pain relief and observation; however, some women will go home a few hours after treatment. Large trials, including the EMMY trial (Uterine Artery Embolization for Treatment of Symptomatic Uterine Fibroid Tumors), have consistently documented shorter hospitalizations and shorter recoveries, with a similar complication rate to hysterectomy. Reviews of the large trials and reports find that the need for reoperation within the first few years after embolization is 20% to 30%, with an overall failure rate of 40%, *failure rate* being defined as a return of symptoms and decrement in quality-of-life measures. The 5-year failure rate from the EMMY trial as reported by van der Kooij and associates included

TABLE 18.3 Summary of the Medical Management Options for Patients With Uterine Leiomyomas

Drug Class	Action	Benefits	Risks	Side Effects (%)	Authors*
COC	Inhibits ovulation; inhibits sex steroid secretion	17% decrease in the risk of leiomyoma growth; decreases bleeding and increases hematocrit	Thromboembolic events; hepatocellular adenoma (rare)	Spotting; mastalgia; headache; gastrointestinal upset	Qin et al; Orsini et al
Progestogens	May inhibit ovulation and sex steroid synthesis; decidualizes endometrium, inducing a "pseudopregnancy" state	Improves bleeding in up to 70%; amenorrhea in up to 30%; may decrease uterine volume in up to 50%	Loss of bone mass (prolonged use of depot MPA)	Irregular bleeding/spotting; ovarian follicular cysts	Venkatachalam et al; Ichigo et al
LNG-IUS	Endometrial atrophy	Reduces bleeding intensity in up to 99%; decreases uterine volume in about 40%	Device expulsion	Ovarian cysts; acne	Kriplani et al; Sayed et al
GnRH-a	Hypoestrogenism due to gonadotrophin secretion inhibition	Uterine volume decrease in up to 50%; high rates of amenorrhea	Loss of bone mass with prolonged use	Hot flashes (>90%); vaginal atrophy; headache; mood disorders	Friedman et al; Tummon et al; Dawood et al
SPRM	Inhibits ovulation; inhibits progesterone action on fibroid tissue	Improves bleeding in up to 98% of patients; decreases fibroid volume in up to 53%	Long-term endometrial safety is unknown	Benign endometrial changes after short-term use	Donnez et al; Williams et al

From Moroni RM, Vieira CS, Ferriani RA, et al. Pharmacological treatment of uterine fibroids. *Ann Med Health Sci Res.* 2014;4(Suppl 3):S185-S192.
*All citations are from the original source article.
COC, combined oral contraceptive; *GnRH-a,* gonadotropin-releasing hormone analog; *LNG-IUS,* levonorgestrel-releasing intrauterine system; *MPA,* medroxyprogesterone acetate; *SPRM,* selective progesterone receptor modulators.

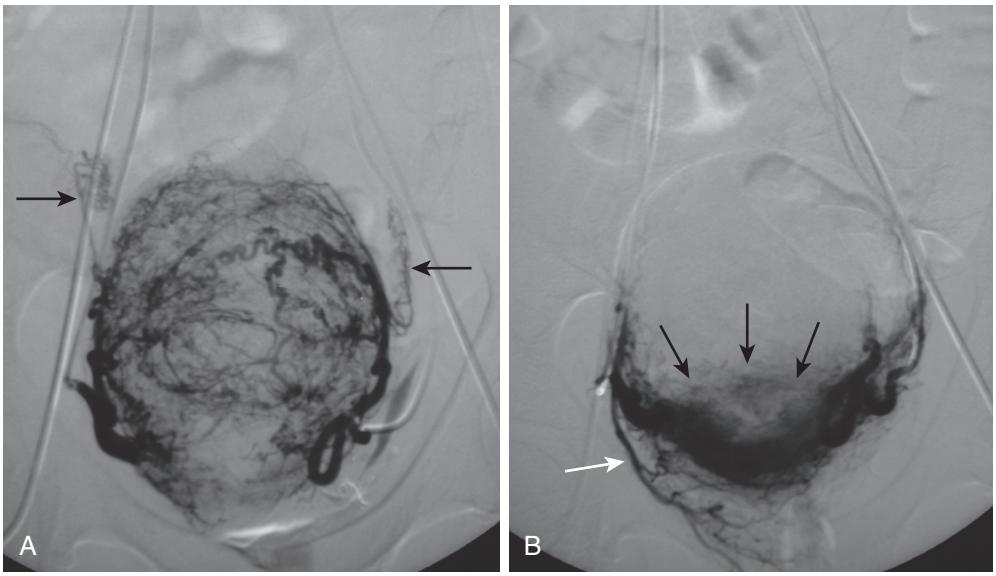

Fig. 18.39 Uterine fibroid embolization. **A,** Angiographic image of uterine leiomyoma before uterine fibroid embolization. *Arrows* point to preembolization uterine artery. **B,** Postembolization image of same devascularized myoma with normal myometrial perfusion maintained *(black arrows). White arrow* points to patent cervicovaginal branch of uterine artery at completion of embolization. (From Spies JB, Czeyda-Pommersheim F. Uterine fibroid embolization. In Mauro MA, Murphy KPJ, Thomson KR, et al, eds. *Image-Guided Interventions.* 2nd ed. Philadelphia: Elsevier; 2014:542-546.)

a 28.4% subsequent hysterectomy rate (van der Kooij, 2010). Risk factors for failure with UAE included younger age at embolization, bleeding as an indication for therapy, multiple myomas, and the finding at the time of imaging of collateral ovarian vessels feeding the myoma. Thus the procedure itself, though a valuable alternative to hysterectomy, is not for all women, with a significant proportion of women needing follow-up procedures.

Fertility after arterial embolization is difficult to quantify. Higher than expected rates of intrauterine growth restriction, preterm delivery, and miscarriage have been reported. In general, women choosing a conservative approach to preserve fertility should have a surgical myomectomy rather than UAE.

Complications of UAE affect about 5% of patients and include postembolization fever; sepsis from infarction of the necrotic myometrium, which may occur several weeks to a few months post procedure; and ovarian failure, affecting up to 3% of cases in women younger than 45 and 15% in women older than 45. This is thought to occur from spread of emboli material into the ovarian circulation. There is, in general, a decreased ovarian reserve found in older women after embolization. Amenorrhea may

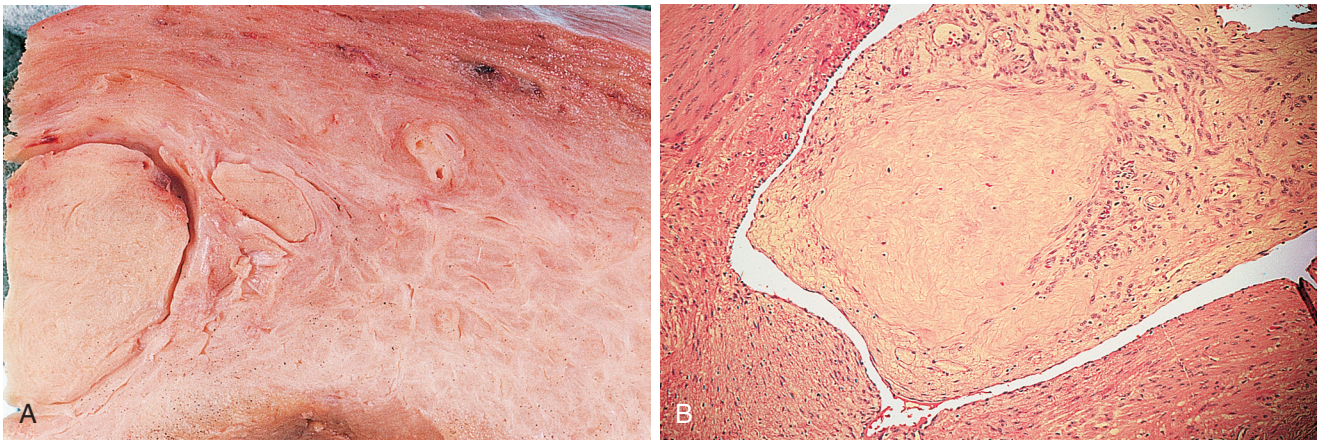

Fig. 18.40 Intravenous leiomyomatosis. **A,** Tumor masses are present within distended blood vessels. **B,** This example shows hyaline degeneration of the intravascular element. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

occur secondary to an endometrial hypoxic injury, as well. Rarely, necrosis of surrounding tissues may present as a complication of embolization.

Another complication of UAE is shedding of necrotic myomata or portions of myomata into the intrauterine cavity. Shedding may lead to infection or abdominal pain as the uterus tries to pass the material. This may require either a uterine curettage or hysteroscopic removal, although some authors have reported removing the necrotic material in the office. Because shedding of necrotic material is a relatively common complication, several authors have recommended that submucous myomata be removed hysteroscopically rather than attempted through UAE because these types of myomata are more at risk to be shed into the uterine cavity. Intraabdominal adhesions, particularly after embolization of larger myomata, are also an uncommon but not rare complication.

Other Minimally Invasive Interventions

Endometrial ablation is used mainly to manage heavy uterine bleeding. It is limited to women with a normal-size uterus and uterine fibroids less than 3 cm in diameter. Compared with hysterectomy, endometrial ablation has a shorter intraoperative time, faster recovery, and fewer adverse events; however, it has inferior reduction in menstrual bleeding and lower patient satisfaction (Lethaby, 2000). Pregnancy after endometrial ablation is not recommended because of the high risk of miscarriage, ectopic pregnancy, and invasive placental disorders that may occur after this procedure.

Myolysis (the destruction of uterine fibroids or their blood supply via ultrasound, laser, cryotherapy, or other methods) has been studied as a conservative alternative for women who want to preserve their uterus but not fertility. Candidates are women with small fibroids (typically less than or equal to 5 cm) or the largest fibroid being less than 10 cm in diameter. Magnetic resonance–guided, focused ultrasound surgery appears to be the most effective and least aggressive; however, this technique is restricted by the need for costly equipment and the limited data regarding efficacy and safety (Marret, 2012).

Two associated but rare diseases should be noted: intravenous leiomyomatosis and leiomyomatosis peritonealis disseminata. *Intravenous leiomyomatosis* is a rare condition in which benign smooth muscle fibers invade and slowly grow into the venous channels of the pelvis (Fig. 18.40). The tumor grows by direct extension and grossly appears like a "spaghetti" tumor. Only 25% of tumors extend beyond the broad ligament. However, case series and reports document tumor growth into the vena cava and right heart. The tumors may present with cardiac symptomology and usually require surgical resection. Series from Zhang and colleagues and Worley and colleagues noted good results with single-stage surgeries. Most authors recommend antiestrogen therapy with aromatase inhibitors after resection of leiomyomatosis of any degree (Worley, 2009; Zhang, 2010).

Leiomyomatosis peritonealis disseminata (LPD) is a benign disease with multiple small nodules over the surface of the pelvis and abdominal peritoneum. Grossly, LPD mimics disseminated carcinoma (Fig. 18.41). However, histologic examination demonstrates benign-appearing myomas (Fig. 18.42). This disorder is often associated with a recent pregnancy. Also, the use of power morcellation increases the risk of LPD because of intraperitoneal spread of uterine tissue (Kumar, 2008). Therapies with progestogens, selective estrogen receptor modulators (SERMs), and aromatase inhibitors have all been used in management. A rare autosomal syndrome of uterine and cutaneous leiomyomata and renal cell carcinoma also exists. Consideration should be given to renal evaluation in families with this history and with cutaneous leiomyomas.

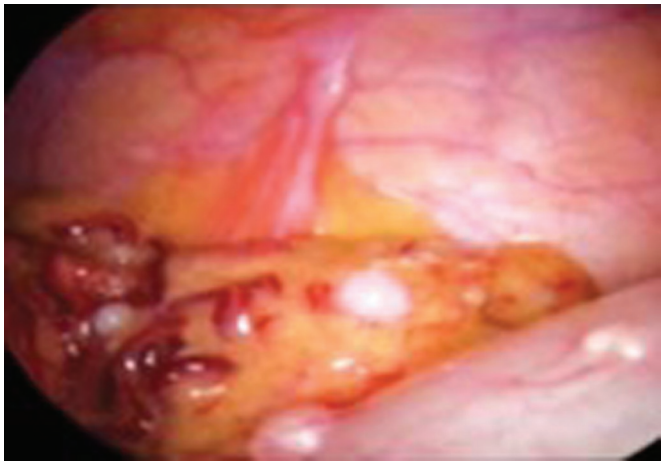

Fig. 18.41 Laparoscopic image of the omental, peritoneal, and intestinal dissemination of leiomyomatosis peritonealis disseminata. (From Honemeyer U, Ross JR, Barnard JJ, et al. Recurrent leiomyomatosis peritonealis disseminata: sonographic and laparoscopic correlation. *Donald School J Ultrasound Obstet Gynecol.* 2012:6;327-332.)

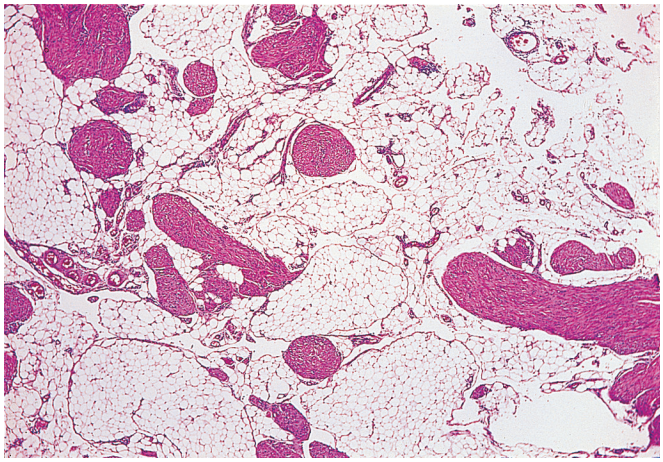

Fig. 18.42 Peritoneal leiomyomatosis. Multiple tiny nodules of smooth muscle are scattered throughout the omentum. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

In summary, leiomyomas are the most common tumor in women, and certainly one of the most common problems facing the gynecologist. Symptoms will present in 30% to 50% of women with myomata. Management is individualized to fit the patient's symptoms and reproductive desires.

ADENOMYOSIS

Adenomyosis has often been referred to as *endometriosis interna*. This term is misleading because endometriosis and adenomyosis are discovered in the same patient in less than 20% of women. More important, endometriosis and adenomyosis are clinically different diseases. The only common feature is the presence of ectopic endometrial glands and stroma. Adenomyosis is derived from aberrant glands of the basalis layer of the endometrium. Therefore these glands do not usually undergo the traditional proliferative and secretory changes that are associated with cyclic ovarian hormone production. The disease is common and may be found in up to 60% of hysterectomy specimens in women in the late reproductive years. Most studies have documented an incidence closer to 30%, with greater than 50% of these women being relatively asymptomatic. The symptoms of menorrhagia and dysmenorrhea form a spectrum and are subjective, thus delineating an incidence of associated symptomology with adenomyosis is problematic.

Adenomyosis is usually diagnosed incidentally by the pathologist examining histologic sections of surgical specimens. The frequency of the histologic diagnosis is directly related to how meticulously the pathologist searches for the disease. Adenomyosis is also a common incidental finding during autopsy. Serial histologic slides confirm the continuity of benign growth of the basalis layer of the endometrium into the myometrium. Thus the histogenesis of adenomyosis is direct extension from the endometrial lining.

The disease is associated with increased parity, particularly uterine surgeries and traumas. The pathogenesis of adenomyosis is unknown but is theorized to be associated with disruption of the barrier between the endometrium and myometrium because one series noted a 1.7 RR (1.1 to 2.6) of a dilation and curettage with an SAB in women with adenomyosis versus control subjects (Parazzini, 1997). Other studies have found a higher rate of induced abortion with presumed curettage in women with adenomyosis versus controls. These studies and experimental work in animals strongly support the theory that trauma to the endometrial-myometrial interface is a significant factor in the cause of this condition. However, because adenomyosis was described well before uterine curettage and may occur (though uncommonly) in nulliparous women, the full pathogenesis is yet to be determined.

Pathology

There are two distinct pathologic presentations of adenomyosis. The most common is a diffuse involvement of both anterior and posterior walls of the uterus. The posterior wall is usually involved more than the anterior wall (Fig. 18.43). The individual areas of adenomyosis are not encapsulated. The second presentation is a focal area or adenomyoma. This results in an asymmetric uterus, and this special area of adenomyosis may have a pseudocapsule. Diffuse adenomyosis is found in two-thirds of cases.

In the more common, diffuse type of adenomyosis the uterus is uniformly enlarged, usually two to three times normal size. It is often difficult to distinguish on physical examination from uterine leiomyomas. However, the ultrasound appearance of leiomyomata helps to distinguish the two. Similarly on visual inspection the two entities are quite different. When a knife transects the myometrium, the cut surface protrudes convexly and has a spongy appearance. The cut surface of a uterus with adenomyosis is darker than the white surface of a myoma. Sometimes there are discrete areas of adenomyosis that are not densely encapsulated and contain small, dark cystic spaces. There is not a distinct cleavage plane around focal adenomyomas as there is with uterine myomas.

Histologic examination will note benign endometrial glands and stroma are within the myometrium. These glands rarely undergo the same cyclic changes as the normal uterine endometrium. Studies have demonstrated both estrogen and progesterone receptors in tissue samples from adenomyosis.

The standard criterion used in diagnosis of adenomyosis is the finding of endometrial glands and stroma more than one low-powered field (2.5 mm) from the basalis layer of the endometrium. The small areas of adenomyosis have the same general appearance as the basalis layers of the endometrium. Histologically the glands exhibit an inactive or proliferative pattern. Rarely one can also see cystic hyperplasia or a pseudodecidual pattern. In general, there is a lack of inflammatory cells surrounding the fossae of adenomyosis. Although the areas do not undergo full menstrual-type changes, bleeding may occur in these ectopic areas, as evidenced by both gross and microscopic findings. It is not unusual to see histologic variability in several different areas

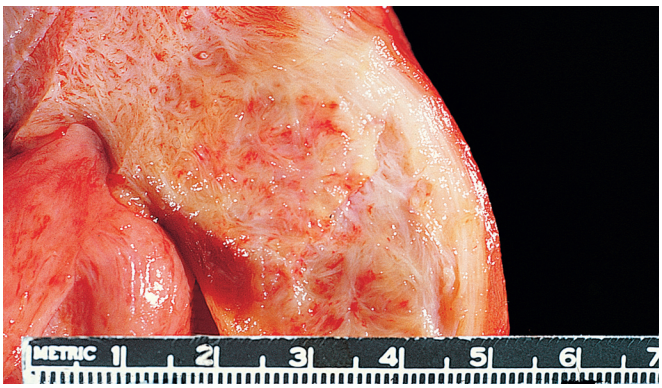

Fig. 18.43 Adenomyosis. The myometrial wall is distorted and thickened by poorly circumscribed trabeculae that contain pinpoint hemorrhagic cysts. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

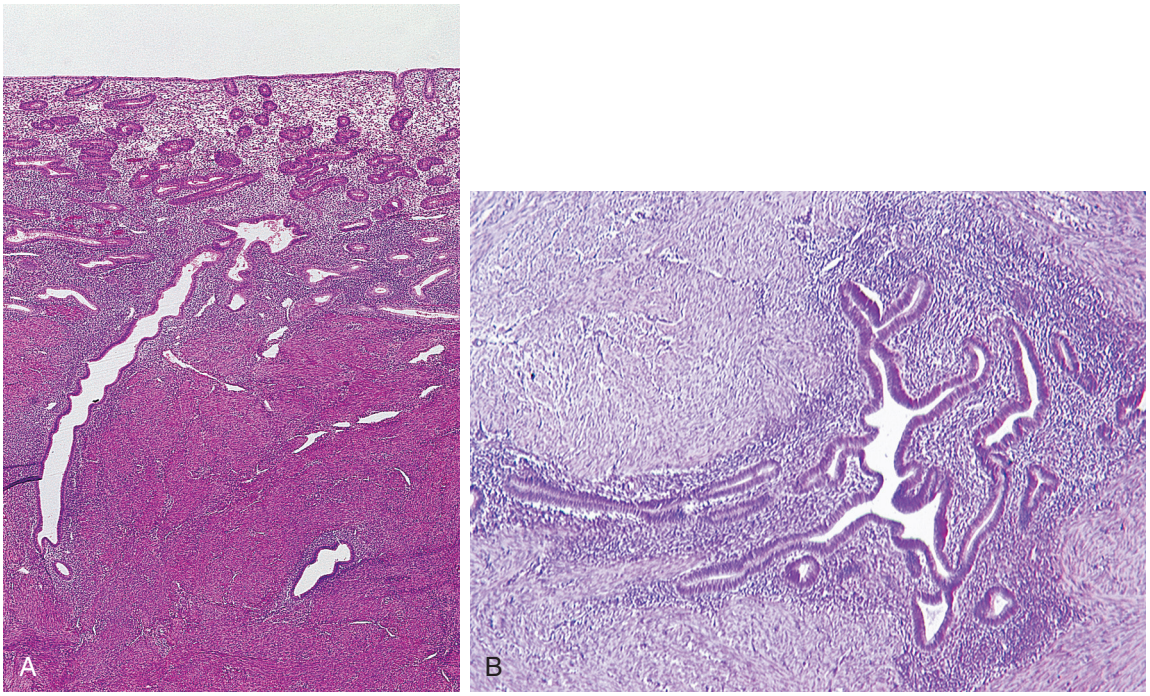

Fig. 18.44 Adenomyosis, histologic appearance. **A,** Endometrial tissue infiltrates into the myometrium. **B,** The infiltrating islands of endometrium consist of both glands and stroma. The glands are inactive and of basal pattern. (From Anderson MC, Robboy SJ, Russell P. Uterine smooth muscle tumors. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

deep in the walls of the myometrium from the same uterus. Some fossae of adenomyosis undergo decidual changes either during pregnancy or during estrogen-progestin therapy for endometriosis. The reaction of the myometrium to the ectopic endometrium is hyperplasia and hypertrophy of individual muscle fibers (Fig. 18.44; see 18.43). Surrounding most foci of glands and stroma are localized areas of hyperplasia of the smooth muscle of the uterus. This change in the myometrium produces the globular enlargement of the uterus (Fig. 18.45).

Clinical Diagnosis

More than 50% of women with adenomyosis are asymptomatic or have minor symptoms that do not annoy them enough to seek medical care. They attribute the increase in dysmenorrhea or menstrual bleeding to the aging process and tolerate the symptoms. Symptomatic adenomyosis usually presents in women between the ages of 35 and 50. The severity of pelvic symptoms increases proportionally to the depth of penetration and the total volume of disease in the myometrium.

The classic symptoms of adenomyosis are secondary dysmenorrhea and menorrhagia. The acquired dysmenorrhea becomes increasingly more severe as the disease progresses. Occasionally the patient complains of dyspareunia, which is midline in location and deep in the pelvis. On pelvic examination the uterus is diffusely enlarged, usually two to three times normal size. It is most unusual for the uterine enlargement associated with adenomyosis to be larger than the size of a 14-week gestation unless the patient also has uterine myomas. The uterus is globular and tender immediately before and during menstruation (see Fig. 18.45).

The diagnosis of adenomyosis is usually confirmed after histologic examination of the hysterectomy specimen. Often the clinical diagnosis is inaccurately assigned to the patient who has chronic pelvic pain. Traditionally the patient will have endometrial sampling to rule out other organic causes of abnormal bleeding.

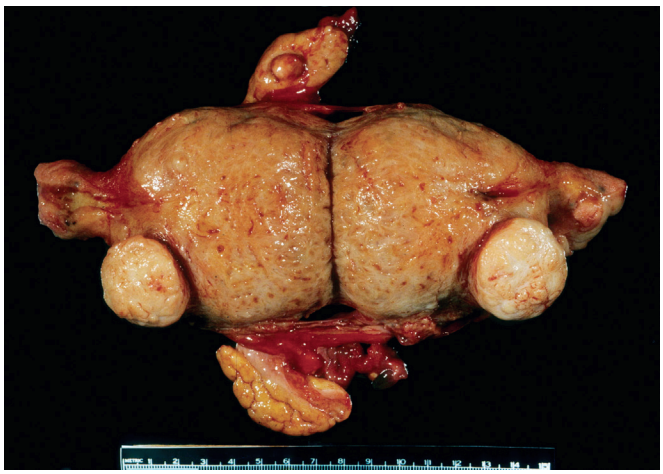

Fig. 18.45 Hysterectomy with adenomyosis. The uterine corpus is thickened and shows prominent trabeculation of the myometrium with multiple small foci of hemorrhage. (From Oliva E. Endometrial stromal tumors, mixed müllerian tumors, adenomyosis, adenomyomas and rare sarcomas. In: Mutter GL, Prat J, eds. *Robboy's Pathology of the Female Reproductive Tract.* 3rd ed. Philadelphia: Elsevier; 2014:425-458.)

Many times adenomyosis is diagnosed retrospectively after a hysterectomy for other indications. Attempts have been made to establish the diagnosis preoperatively by transcervical needle biopsy of the myometrium. However, even with multiple needle biopsies, the sensitivity of the test is too low to be of practical clinical value. Adenomyosis may coexist with both endometrial hyperplasia and endometrial carcinoma. Approximately two of three women with adenomyosis have a coexistent pelvic pathologic condition, most

commonly myomas but also endometriosis, endometrial hyperplasia, and salpingitis isthmica nodosa.

Ultrasound and MRI are both useful to help differentiate between adenomyosis and uterine myomas in a young woman desiring future childbearing. Diagnosing adenomyosis by transvaginal ultrasonography has a reported sensitivity between 53% and 89% and a specificity of 50% to 89%. In some series, MRI is more sensitive, ranging between 88% and 93%, and has a higher specificity (66% to 91%) than ultrasonography in the diagnosis of adenomyosis. Verma and associates reported the addition of sonohysterography with vaginal ultrasound, with an increase in sensitivity and specificity comparable with MRI. T2-weighted images are superior in making the diagnosis and documenting widened junctional zones (Verma, 2009). Studies indicate that three-dimensional transvaginal ultrasound is superior to two-dimensional transvaginal ultrasound and may allow for the diagnosis of early-stage disease (Struble, 2016). Findings of poorly defined junctional zone markings in the endometrial-myometrial interface help confirm the diagnosis. MRI is clinically useful in differentiating adenomyosis from uterine leiomyoma, especially preoperatively in women who desire future fertility or who may choose uterine artery embolization for treatment of myomata. The success of uterine artery embolization for adenomyosis is unproved.

Management

There is no proven satisfactory medical treatment for adenomyosis. Patients with adenomyosis have been treated with GnRH agonists, progestogens, and progesterone-containing IUDs, cyclic hormones, or prostaglandin synthetase inhibitors for their abnormal bleeding and pain. Hysterectomy is the definitive treatment if this therapy is appropriate for the woman's age, parity, and plans for future reproduction. Size of the uterus, degree of prolapse, and presence of associated pelvic pathology determine the choice of surgical approach. Women who become pregnant with adenomyosis are at increased risk of pregnancy complications such as premature labor and delivery, low birthweight, and preterm premature rupture of membranes.

OVIDUCT

Leiomyomas

Both benign and malignant tumors of the oviduct are uncommon compared with other gynecologic neoplasms. Although these tumors are underreported, fewer than 100 women with myomas or leiomyomas of the oviduct are described in the literature. Tubal leiomyomas may be single or multiple and usually are discovered in the interstitial portion of the tubes. They usually coexist with the more common uterine leiomyomas. Myomas may originate from muscle cells in the walls of the tube or blood vessels or from smooth muscle in the broad ligament.

Leiomyomas of the tube present as smooth, firm, mobile, usually nontender masses that may be palpated during the bimanual examination. Similar to uterine myomas, they may be subserosal, interstitial, or submucosal. During laparoscopy the myomas appear as a spherical mass that protrudes from beneath the peritoneal surface. They vary from a few millimeters to 15 cm in diameter. Histologically they are identical to uterine leiomyomas.

The majority of the myomas of the oviduct are asymptomatic. Rarely they may undergo acute degeneration or be associated with unilateral tubal obstruction or torsion. Treatment of a symptomatic tubal leiomyoma is excision.

Adenomatoid Tumors

The most prevalent benign tumor of the oviduct is the *angiomyoma* or *adenomatoid tumor* (Fig. 18.46), a small, gray-white, circumscribed nodule, 1 to 2 cm in diameter. These tumors are usually unilateral, present as small nodules just under the tubal serosa, and do not produce pelvic symptoms or signs. These benign tumors also are found below the serosa of the fundus of the uterus and the broad ligament. Microscopically they are composed of small tubules lined by a low cuboidal or flat epithelium. Histologic studies have established that the thin-walled channels that comprise these tumors are of mesothelial origin (Fig. 18.47). These tumors do not become malignant; however, they may be mistaken for a low-grade neoplasm when initially viewed during a frozen-section evaluation.

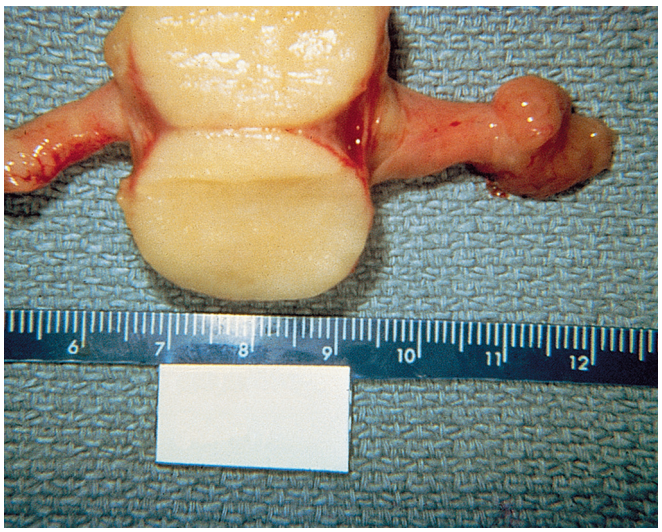

Fig. 18.46 Adenomatoid tumor. (From Anderson MC, Robboy SJ, Russell P. The fallopian tube. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

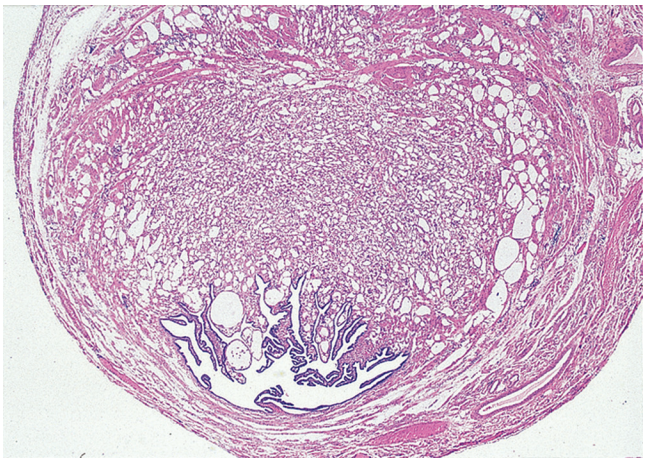

Fig. 18.47 Adenomatoid tumor arising in the fallopian tube. (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology*. St. Louis: Mosby-Wolfe; 1997.)

Paratubal Cysts

Paratubal cysts are often incidental discoveries during gynecologic operations for other abnormalities. They are commonly multiple and may vary from 0.5 cm to more than 20 cm in diameter. Most cysts are small, asymptomatic, and slow growing and are discovered during the third and fourth decades of life. When

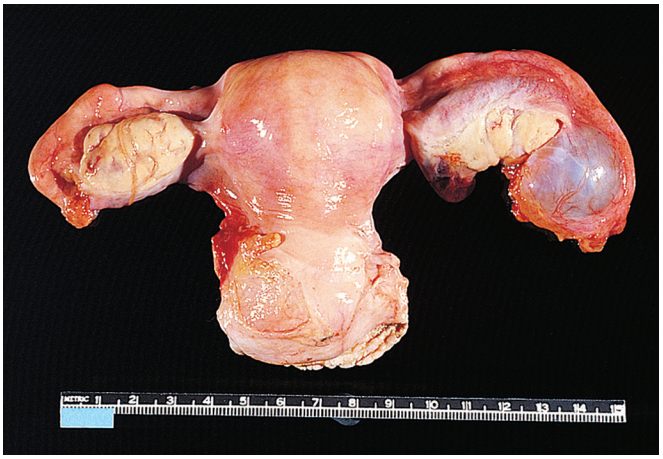

Fig. 18.48 Broad ligament cyst. This parovarian, or paratubal cyst, is thin walled and contains clear watery fluid. (From Anderson MC, Robboy SJ, Russell P. The fallopian tube. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

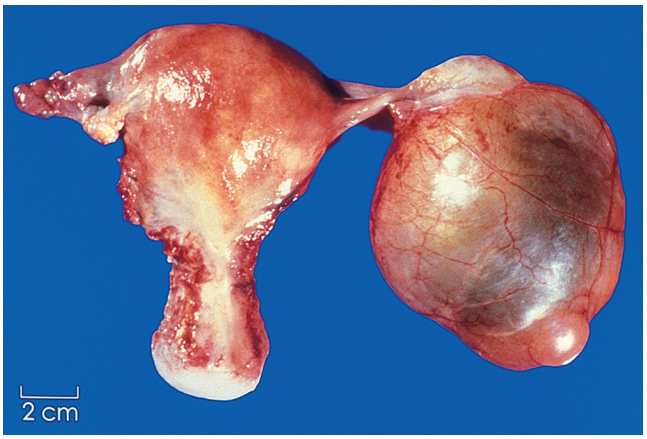

Fig. 18.49 A nonneoplastic cyst with the broad ligament abuts the normal ovary. (From Clement PB, Young RH. *Atlas of Gynecologic Surgical Pathology.* Philadelphia: Saunders; 2000.)

paratubal cysts are *pedunculated* and near the fimbrial end of the oviduct, they are called hydatid cysts of Morgagni (Figs. 18.48 and 18.49). Cysts near the oviduct may be of mesonephric, mesothelial, or paramesonephric origin. Sometimes the histologic differentiation is difficult because of mechanically produced changes in the cells that line the cyst. These cysts are translucent and contain a clear or pale yellow fluid.

The histogenesis of the majority of paratubal cysts had been believed to be from the mesonephric duct, with the cysts arising from the main duct or accessory tubules. These latter cysts often develop between the leaves of the broad ligament in the mesosalpinx, with the ovary being separate. However, a histologic study of 79 paratubal cysts documented that 60 of the cysts were of tubal origin. Thus the majority of grossly identified "paratubal cysts" are in reality accessory lumina of the fallopian tubes. The remaining 19 cysts were of mesothelial origin. Paratubal cysts are thin walled and smooth and contain clear fluid. Often there are multiple small cysts, and occasionally there is a papillomatous proliferation on the internal wall of these cysts. Inflammatory cysts of the peritoneum may be found anywhere in the pelvis.

The majority of paratubal cysts are asymptomatic and are usually discovered incidentally during ultrasound or during gynecologic operations. When paratubal cysts are symptomatic, they generally produce a dull pain. During a pelvic examination it is difficult to distinguish a paratubal cyst from an ovarian mass. At operation the oviduct is often found stretched over a large paratubal cyst. The oviduct should not be removed in these cases because it will return to normal size after the paratubal cyst is excised. In one retrospective 10-year review of 168 women with parovarian tumors, three low-grade malignant neoplasms were found. These malignancies were in women of reproductive age who had cysts greater than 5 cm in diameter with internal papillary projections. The authors cautioned that the differentiation between benign and malignant parovarian masses cannot be made by external examination of the cyst. The practice of aspirating cysts via the laparoscope should be limited to cysts that are completely simple and associated with normal CA-125 levels. More recent theories of epithelial ovarian carcinogenesis suggest that serous, endometrioid, and clear cell carcinomas are derived from the fallopian tube and the endometrium rather than the ovarian surface epithelium (Erickson, 2013). ACOG supports the view that prophylactic salpingectomy may offer clinicians the opportunity to prevent ovarian cancer in their patients, and the surgeon should discuss the potential benefits of the removal of the fallopian tubes during hysterectomy in women at population risk for ovarian cancer. However, they do not encourage altering the planned route of hysterectomy merely to be able to perform an opportunistic salpingectomy (ACOG, 2019a).

Paratubal cysts may grow rapidly during pregnancy, and most of the cases of torsion of these cysts have been reported during pregnancy or the puerperium. Treatment is simple excision.

Torsion

Acute torsion of the oviduct is a rare event; however, it has been reported with both normal and pathologic fallopian tubes. Pregnancy predisposes to this problem. Tubal torsion usually accompanies torsion of the ovary because they have a common vascular pedicle. (See the discussion of ovarian torsion presented later in this chapter.) Torsion of the fallopian tube is secondary to an ovarian mass in approximately 50% to 60% of patients. The right tube is involved more often than is the left (Fig. 18.50). The degree of tubal torsion varies from less than one turn to four complete rotations. Torsion of the oviduct is usually seen in women of reproductive age; however, it occurs also in preadolescent children, especially when part of the tube is enclosed in the sac of a femoral or inguinal hernia.

Tubal torsion may be divided into intrinsic and extrinsic causes. Prominent intrinsic causes include congenital abnormalities, such as increased tortuosity caused by excessive length of the tube, and

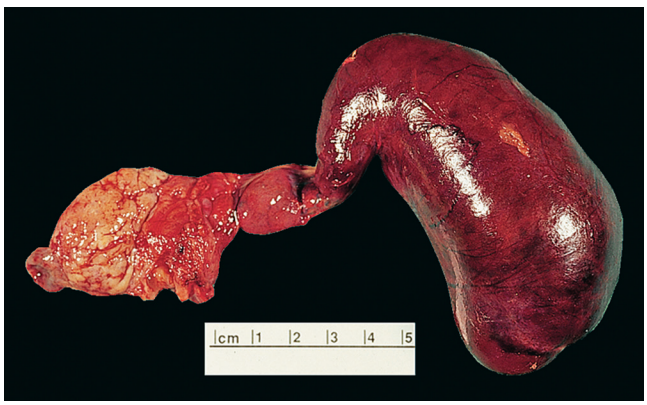

Fig. 18.50 Hematosalpinx with torsion. (From Voet RL. Color Atlas of Obstetric and Gynecologic Pathology. St. Louis: Mosby-Wolfe; 1997.)

pathologic processes, such as hydrosalpinx, hematosalpinx, tubal neoplasms, and previous operation, especially tubal ligation. Torsion of the fallopian tube after tubal ligation is usually of the distal end. Extrinsic causes of tubal torsion are ovarian and peritubal tumors, adhesions, trauma, and pregnancy.

The most important symptom of tubal torsion is acute lower abdominal and pelvic pain. The onset of this pain is usually sudden, but it may also be gradual, and the pain is usually located in the iliac fossa, with radiation to the thigh and flank. The duration of pain is generally less than 48 hours, and it is associated with nausea and vomiting in two-thirds of the cases. Usually the pelvic pain, secondary to hypoxia, is so intense that it is difficult to perform an adequate pelvic examination. Unless there is associated torsion of the ovary, a specific mass is usually not palpable on pelvic examination.

The preoperative diagnosis of tubal torsion is made in less than 20% of reported cases. However, the number of cases diagnosed preoperatively has increased dramatically with the use of vaginal ultrasonography. Because of the severity of the pain, a wide differential diagnosis of abdominal and pelvic pathologic conditions must be considered. The differential diagnosis includes acute appendicitis, ectopic pregnancy, pelvic inflammatory disease, and rupture or torsion of an ovarian cyst.

Exploratory operation determines the extent of hypoxia and the choice of operative techniques. With tubal torsion, usually the tubes are gangrenous and must be excised. The twisted tube is usually filled with a bloody or serous fluid. It may be possible to restore normal circulation to the tube by manually untwisting it. The tube is usually sutured into a secure position to prevent recurrence.

OVARY

Ovarian masses are a common finding on pelvic examination and pelvic imaging. The task of the clinician is to determine whether the mass should be removed or may be managed expectantly. The general factors used to consider removal include the symptoms produces by the mass, the chances that the mass is malignant, and the likelihood of spontaneous resolution.

Functional Cysts

Follicular Cysts

Follicular cysts are by far the most common cystic structures in normal ovaries. They may be found as early as 20 weeks' gestation in female fetuses and throughout a woman's reproductive life. Follicular cysts are often multiple and may vary from a few millimeters to as large as 15 cm in diameter. A normal follicle may develop into a physiologic cyst. A minimum diameter to be considered as a cyst is generally considered to be between 2.5 and 3 cm. Follicular cysts are not neoplastic and are believed to be dependent on gonadotropins for growth. They arise from a temporary variation of a normal physiologic process. Clinically they may present with the signs and symptoms of ovarian enlargement and therefore must be differentiated from a true ovarian neoplasm. Functional cysts may be solitary or multiple. These cysts are found most commonly in young, menstruating women but may be found in postmenopausal women. Solitary cysts may occur during the fetal and neonatal periods and rarely during childhood, but there is an increase in frequency during the perimenarchal period. Large solitary follicular cysts in which the lining is luteinized are occasionally discovered during pregnancy and the puerperium. CA-125 may be used to evaluate such cysts in pregnancy. The values for CA-125 should be within the normal range past 12 weeks' gestation. Multiple follicular cysts in which the lining is luteinized are associated with either intrinsic or extrinsic elevated levels of gonadotropins. Interestingly, reproductive-age women with cystic fibrosis appear to have an increased propensity for developing individual follicular cysts.

Follicular cysts are translucent, thin-walled, and filled with a watery, clear to straw-colored fluid. If a small opening in the capsule of the cyst suddenly develops, the cyst fluid under pressure will squirt out. These cysts are situated in the ovarian cortex, and sometimes they appear as translucent domes on the surface of the ovary. Histologically the lining of the cyst is usually composed of a closely packed layer of round, plump granulosa cells, with the spindle-shaped cells of the theca interna deeper in the stroma. In many cysts the lining of granulosa cells is difficult to distinguish, having undergone pressure atrophy. All that remains is a hyalinized connective tissue lining. The temporary disturbance in follicular function that produces the clinical picture of a follicular cyst is poorly understood. Follicular cysts may result from either the dominant mature follicle's failing to rupture (persistent follicle) or an immature follicle's failing to undergo the normal process of atresia. In the latter circumstance, the incompletely developed follicle fails to reabsorb follicular fluid. Some follicular cysts lose their ability to produce estrogen, and in others the granulosa cells remain productive, with prolonged secretion of estrogens. Occasionally, follicular cysts are better termed *follicular hematomas* because blood from the vascular theca zone fills the cavity of the cyst.

Most follicular cysts are asymptomatic and are discovered during ultrasound imaging of the pelvis or a routine pelvic examination. Ultrasound cannot reliably differentiate a benign from a malignant process. However, several characteristics of ovarian masses correlate with malignancy, including internal papillations (echogenic structures protruding into the mass), loculations, solid lesions or cystic lesions with solid components, thick septations, and smaller cysts adjacent to or part of the wall of the larger cyst–daughter cysts (Fig. 18.51).

Because of their thin walls these cysts may rupture during examination. The patient may experience tenesmus, a transient pelvic tenderness, deep dyspareunia, or no pain whatsoever. Rarely is significant intraperitoneal bleeding associated with the rupture of a follicular cyst. However, women who are chronically anticoagulated or those with von Willebrand disease may bleed. Occasionally, menstrual irregularities and abnormal uterine bleeding may be associated with follicular cysts, which produce elevated blood estrogen levels. The syndrome associated with such follicular cysts consists of a regular cycle with a prolonged intermenstrual interval, followed by episodes of menorrhagia. Some women with larger follicular cysts notice a vague, dull sensation or heaviness in the pelvis.

The initial management of a suspected follicular cyst is conservative observation. The majority of follicular cysts disappear spontaneously by either reabsorption of the cyst fluid or silent rupture within 4 to 8 weeks of initial diagnosis. However, a persistent ovarian mass necessitates operative intervention to differentiate a physiologic cyst from a true neoplasm of the ovary. There is no way to make the differentiation on the basis of signs, symptoms, or the initial growth pattern during early development of either process. Endovaginal ultrasound examination is helpful in differentiating simple from complex cysts and is also helpful during conservative management by providing dimensions to determine whether the cyst is increasing in size. When the diameter of the cyst remains stable for greater than 10 weeks or enlarges, a neoplasia should be ruled out. Oral contraceptives may be prescribed for 4 to 6 weeks for young women with adnexal masses. This therapy removes any influence that pituitary gonadotropins may have on the persistence of the ovarian cyst. It also allows for several weeks of observation. In one series, 80% of cystic masses 4 to 6 cm in size disappeared during the time the patient was taking oral contraceptives. However, randomized prospective trials found no difference in the rate of disappearance of functional ovarian cysts between the group that received oral

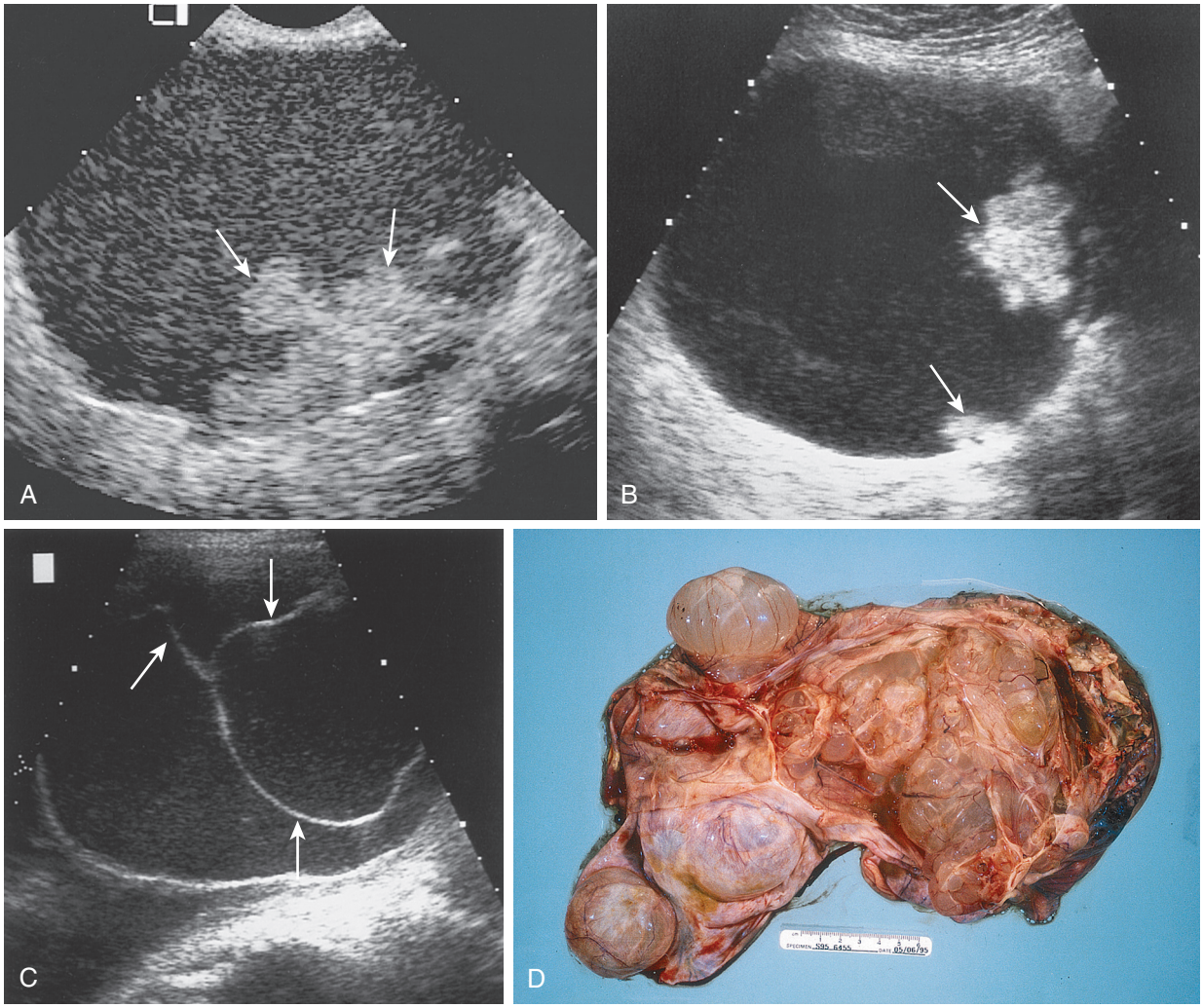

Fig. 18.51 Serous cystadenocarcinoma, varying appearances. **A,** Transvaginal scan shows large cystic mass containing multiple low-level internal echoes and solid echogenic components *(arrows).* **B,** Transabdominal scan shows large cystic mass with irregular solid echogenic mural nodules *(arrows)* and low-level internal echoes. **C,** Mucinous cystadenoma. Transabdominal scan shows large cystic mass with multiple thin septations *(arrows)* and fine low-level internal echoes. **D,** Gross pathologic specimen shows multiple cystic loculations. (From Salem S. The uterus and adnexa. In: Rumack CM, Wilson SR, Charboneau JW, eds. *Diagnostic Ultrasound.* St. Louis: Mosby; 1998:555-556.)

contraceptives and the control group, perhaps because so many cysts will resolve spontaneously.

The evaluation of an asymptomatic cyst, found incidentally, is based on the principle that the cyst should be removed if there is any suspicion of malignancy. Suspicion may develop because of history, including family history, patient age, and other nongynecologic signs and symptoms. The size and physical characteristics of the cyst are as important as are other laboratory parameters. CA-125 is helpful in evaluating the adnexal mass in postmenopausal women. In premenopausal women, CA-125 is rarely helpful unless the mass is extremely suggestive of malignancy. As discussed earlier, measurement of diastolic and systolic velocities provide indirect indices of vascular resistance. Muscular arteries have high resistance. Newly developed vessels, such as those arising in malignancies, have little vascular wall musculature and thus have low resistance. When a color flow Doppler scan demonstrates vascularity, the vascular resistance can be calculated. Low resistance is associated with malignancy, and high resistance usually is associated with normal tissue or benign disease. Although color flow Doppler has been shown to be sensitive in evaluating ovarian neoplasms, it is neither sensitive nor specific enough to be used as a determining study. In most cases, simple small cysts may be observed. In general, complex cysts or persistent simple cysts larger than 10 cm should be evaluated. In women with cysts in pregnancy, if the cyst is simple with a normal CA-125, conservative management is acceptable. (CA-125 is generally not obtained in pregnant women with cysts less than 5 cm if they are simple.)

A cyst in a perimenopausal or postmenopausal woman should be removed if it is anything other than a simple cyst, if the CA-125 is abnormal (>35), or if the cyst is persistent or large (>10 cm), although observation may be reasonable in select cases. A small simple cyst (<5 cm) in a perimenopausal or postmenopausal woman with a normal CA-125 may be observed with follow-up ultrasound and CA-125 testing every 6 months for 2 years. If unchanged at that point, routine monitoring can be stopped. Several studies, including a large prospective series from Greenlee and colleagues, examined the issue of simple cysts in postmenopausal women with simple cysts. These studies have noted that expectant management is safe and reasonable. In the

series by Greenlee, the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, women were followed for 4 years with transvaginal ultrasound. Of 15,735 women, 2217 (14%) had at least one simple cyst. Cysts were more common in women in the 50- to 59-year-old age group and women with hysterectomies before age 40. Cysts were less common among smokers and older women. In all, 54% of cysts were present on scans 1 year later; 8% of women had more than one cyst. Only 0.4% of the entire population developed ovarian cancer, and half of the women who developed cancer did not have cysts. The 14% incidence of cysts in postmenopausal women is similar to rates of simple cysts in other large series. Thus women with simple cysts who are asymptomatic and with negative CA-125 may be reassured and, if desired, followed expectantly (Greenlee, 2010). Management of cysts between 5 and 10 cm that are otherwise not suggestive should be individualized. Cysts with internal structures have a much higher rate of malignancy.

In premenopausal women, operative management of nonmalignant cysts is cystectomy, not oophorectomy. Many clinicians will manage simple cysts laparoscopically. Because this procedure has an accompanying risk of spilling malignant cells into the peritoneal cavity if the cyst is an early carcinoma, strict preoperative criteria should be fulfilled before laparoscopy is attempted. These include the woman's age; size of the mass; and ultrasound characteristics, such as nonadherent, smooth, and thin-walled cysts, without papillae or internal echoes (simple). Higher rates of recurrence, up to 40%, have been reported for simple drainage of multiple types of benign cysts, the point being that drainage or fenestration is effective for follicular cysts and poorly effective for other cysts. When cysts are drained, it is essential to remember that cytologic examination of cyst fluid has poor predictive value and poor sensitivity in differentiating benign from malignant cysts. If there is any suspicion of malignancy, the cyst should be removed as carefully as possible and a histopathologic evaluation obtained. The size of the cyst is not a necessary reason to avoid laparoscopy. Most simple cysts, even those larger than 10 cm, can be managed via minimally invasive surgery.

Corpus Luteum Cysts

Corpus luteum cysts are less common than follicular cysts, but clinically they are more important. This discussion collectively combines corpus luteum cysts and persistently functioning mature corpora lutea (Fig. 18.52). Pathologists are sometimes able to distinguish between a hemorrhagic cystic corpus luteum and a corpus luteum cyst, but at other times this difference cannot be established. All corpora lutea are cystic with gradual reabsorption of a limited amount of hemorrhage, which may form a cavity. Clinically, corpora lutea are not termed *corpus luteum cysts* unless they are a minimum of 3 cm in diameter. Corpus luteum cysts may be associated with either normal endocrine function or prolonged secretion of progesterone. The associated menstrual pattern may be normal, delayed menstruation, or amenorrhea.

Corpora lutea develop from mature graafian follicles. Intrafollicular bleeding does not occur during ovulation. However, 2 to 4 days later, during the stage of vascularization, thin-walled capillaries invade the granulosa cells from the theca interna. Spontaneous but limited bleeding fills the central cavity of the maturing corpus luteum with blood. Subsequently this blood is absorbed, forming a small cystic space. When the hemorrhage is excessive, the cystic space enlarges. If the hemorrhage into the central cavity is brisk, intracystic pressure increases, and rupture of the corpus luteum is a possibility. If rupture does not occur, the size of the resulting corpus luteum cyst usually varies between 3 and 10 cm. Occasionally a cyst may be 11 to 15 cm in diameter. If a cystic central cavity persists, blood is replaced by clear fluid, and the result is a hormonally inactive corpus albicans cyst (Fig. 18.53). A corpus luteum of pregnancy is normally 3 to 5 cm in diameter with a central cystic structure, occupying at least 50% of the ovarian mass.

Most corpus luteum cysts are small, the average diameter being 4 cm. Grossly they have a smooth surface and, depending on whether the cyst represents acute or chronic hemorrhage, are purplish red to brown. When a corpus luteum is cut, the convoluted lining is yellowish orange, and the center contains an organizing blood clot. Both the granulosa and the theca cells undergo luteinization. In chronic corpus luteum cysts, the wall becomes gray-white, and the polygonal luteinized cells usually undergo pressure atrophy.

Corpus luteum cysts vary from being asymptomatic masses to causing catastrophic and massive intraperitoneal bleeding associated with rupture. Many corpus luteum cysts produce dull, unilateral, lower abdominal and pelvic pain. The enlarged ovary is moderately tender on pelvic examination. Depending on the amount of progesterone secretion associated with cysts, the menstrual bleeding may be normal or delayed several days to weeks with subsequent menorrhagia. Halban, in 1915, described a syndrome of a persistently functioning corpus luteum cyst that has clinical features similar to an unruptured ectopic pregnancy. Halban's classic triad was a delay in a normal period followed by

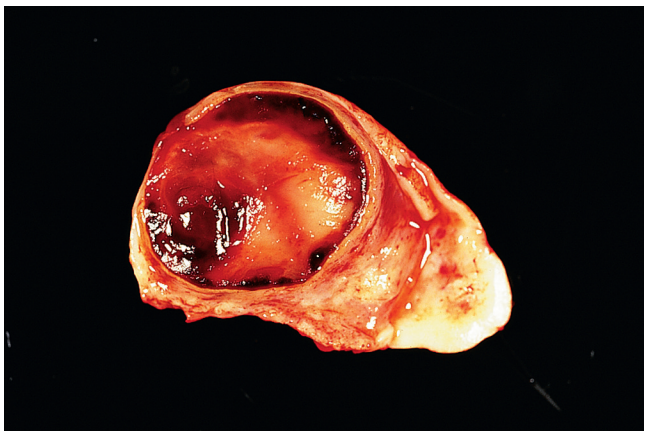

Fig. 18.52 Hemorrhagic corpus luteum with an outer yellow rim and central hemorrhage. (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology*. St. Louis: Mosby-Wolfe; 1997.)

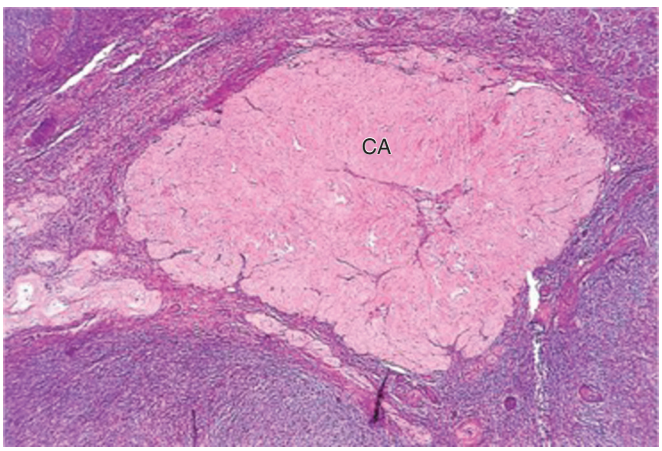

Fig. 18.53 Photomicrograph of an ovary with a corpus albicans (CA) made up of a scar of dense connective tissue at the site of a prior corpus luteum. (From Basicmedical Key Online Library. Available at: https://radiologykey.com/wp-content/uploads/2016/03/B9781416032649500331_f29-07-9781416032649.jpg.)

TABLE 18.4 Symptoms of 173 Women With Ruptured Corpus Luteum

Location	Number	Percentage
Right ovary	114	66
Left ovary	56	32
Unknown	3	2
Abdominal pain	173	100
Right ovary	21	72
Left ovary	8	28
Duration		
Less than 24 hours	94	54
1-7 days	40	23
Over 7 days	14	8
Unknown	25	15
Nausea or vomiting or diarrhea	60	35

From Hallatt JG, Steele CH Jr, Snyder M. Ruptured corpus luteum with hemoperitoneum: a study of 173 surgical cases. *Am J Obstet Gynecol.* 1984;149(1):5-9.

spotting, unilateral pelvic pain, and a small, tender, adnexal mass. This triad of symptomology is similar to the triad of an anomalous period or delay in a normal period, spotting, and unilateral pelvic pain that are exhibited by the classic ectopic pregnancy. The differential diagnosis between these two conditions without a sensitive pregnancy test is difficult.

Corpus luteum cysts may cause intraperitoneal bleeding. The amount of bleeding varies from slight to clinically significant hemorrhage, necessitating blood transfusion. Internal bleeding often follows coitus, exercise, trauma, or a pelvic examination. However, episodes of bleeding usually do not recur, which differs from an ectopic pregnancy. Women with a bleeding diathesis or those undergoing chronic anticoagulation therapy are especially at risk for developing ovarian hemorrhage from a corpus luteum cyst. Bleeding occurs usually between days 20 and 26 of their cycle, and these women have a 31% chance for subsequent hemorrhage from a recurrent corpus luteum cyst. Oral contraceptives are sometimes used to suppress ovulation and avoid recurrent hemorrhage.

Tang and coworkers have also reported a right-sided predominance in the incidence of hemorrhage from corpus luteum cysts. They postulated that the difference is related to a higher intraluminal pressure on the right side because of the differences in ovarian vein architecture (Tang, 1985). Most ruptures occur between days 20 and 26 of the cycle, although in the series of Hallatt and colleagues (Fig 18.4), 28% of the women had a delay in menses not explained by pregnancy.

The differential diagnosis of a woman with acute pain and suspected ruptured corpus luteum cyst includes ectopic pregnancy, a ruptured endometrioma, and adnexal torsion. A sensitive serum or urinary assay for human chorionic gonadotropin (HCG) will help differentiate a bleeding corpus luteum from ectopic pregnancy (see Chapter 17). Vaginal ultrasound is useful in establishing a preoperative diagnosis. Culdocentesis has been used in the past to establish the severity of the hemorrhage, but it is rarely used today. If the hematocrit of the fluid obtained from the posterior cul-de-sac is greater than 15%, operative therapy is recommended. Cystectomy is the operative treatment of choice, with preservation of the remaining portion of the ovary. Unruptured corpus luteum cysts may be followed conservatively. Raziel and coworkers reported on a series of 70 women with ruptured corpora lutea. Ultrasonic evidence of large amounts of peritoneal fluid and severe pain were indications for operative intervention. In 12 of 70 patients with small amounts of intraperitoneal fluid and mild to moderate pain, observation alone was associated with resolution of symptoms (Raziel, 1993).

Theca Lutein Cysts

Theca lutein cysts are by far the least common of the three types of physiologic ovarian cysts (Fig. 18.54), arising from either prolonged or excessive stimulation of the ovaries by endogenous or exogenous gonadotropins or increased ovarian sensitivity to gonadotropins. Unlike corpus luteum cysts, theca lutein cysts are almost always bilateral and produce moderate to massive enlargement of the ovaries. The individual cysts vary in size from 1 cm to 10 cm or more in diameter. The condition of ovarian enlargement secondary to the development of multiple luteinized follicular cysts is termed *hyperreactio luteinalis*. Approximately 50% of molar pregnancies and 10% of choriocarcinomas have associated bilateral theca lutein cysts (see Chapter 35). In these patients the HCG from the trophoblast produces luteinization of the cells in immature, mature, and atretic follicles. The cysts are also discovered in the latter months of pregnancies, often with conditions that produce a large placenta, such as twin gestations, diabetes, and Rh sensitization. It is not uncommon to iatrogenically produce theca lutein cysts in women receiving medications to induce ovulation. Theca lutein cysts are occasionally discovered in association with normal pregnancy, as well as in newborn infants secondary to transplacental effects of maternal gonadotropins. Rarely these cysts are found in young girls with juvenile hypothyroidism.

Grossly the total ovarian size may be voluminous, 20 to 30 cm in diameter, with multiple theca lutein cysts. Bilateral ovarian enlargement is produced by multiple gray to bluish-tinged cysts. The bilateral enlargement is secondary to hundreds of thin-walled locules or cysts, producing a honeycombed appearance. Grossly the external surface of the ovary appears lobulated, and the small cysts contain a clear to straw-colored or hemorrhagic fluid. Histologically the lining of the cyst is composed of theca

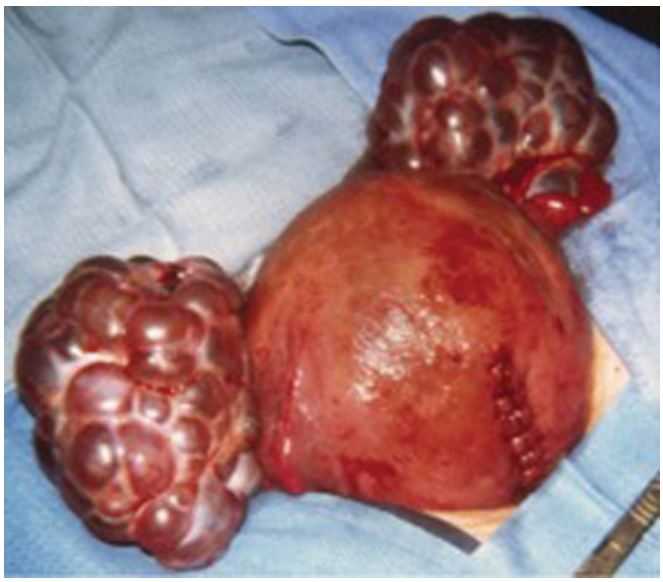

Fig. 18.54 Postgravid uterus with bilateral theca lutein cysts. (From Peter Callen: *Ultrasonography in Obstetrics and Gynecology*, 5th Edition, 2007; Yee B, Tu B, Platt LD: Coexisting hydatidiform mole with a live fetus presenting as a placenta previa on ultrasound. *Am J Obstet Gynecol.* 144:726, 1982.)

lutein cells (paralutein cells), believed to originate from ovarian connective tissue. Occasionally there is also luteinization of granulosa cells. These voluminous and congested ovaries are slow growing, and the majority of women with smaller cysts are asymptomatic. Generally only the larger cysts produce vague symptoms, such as a sense of pressure in the pelvis. Ascites and increasing abdominal girth have been reported with hyperstimulation from exogenous gonadotropins. Associated adnexal torsion or bleeding may occur less than 1% of the time. Some theca lutein cysts persist for weeks after HCG levels normalize.

The presence of theca lutein cysts is established by palpation and often confirmed by ultrasound examination. Treatment is conservative because these cysts gradually regress. If these cysts are discovered incidentally at cesarean delivery, they should be handled delicately. No attempt should be made to drain or puncture the multiple cysts because of the possibility of hemorrhage. Bleeding is difficult to control in these cases because of the thin walls that constitute the cysts.

A condition related to theca lutein cysts is the luteoma of pregnancy. The condition is rare and not a true neoplasm but rather a specific, benign, hyperplastic reaction of ovarian theca lutein cells (Figs. 18.55 and 18.56). These nodules do not arise from the corpus luteum of pregnancy. Fifty percent of luteomas are multiple, and approximately 30% of those reported have bilateral nodules. In appearance they are discrete and brown to reddish brown and may be solid or cystic.

The majority of patients with luteomas are asymptomatic. The solid, fleshy, often hemorrhagic nodules are discovered incidentally at cesarean delivery or postpartum tubal ligation. Most cases have been reported in multiparous African American women. Masculinization of the mother occurs in 30% of cases, and masculinization of the external genitalia of the female fetus may sometimes occur. These tumors regress spontaneously after completion of the pregnancy.

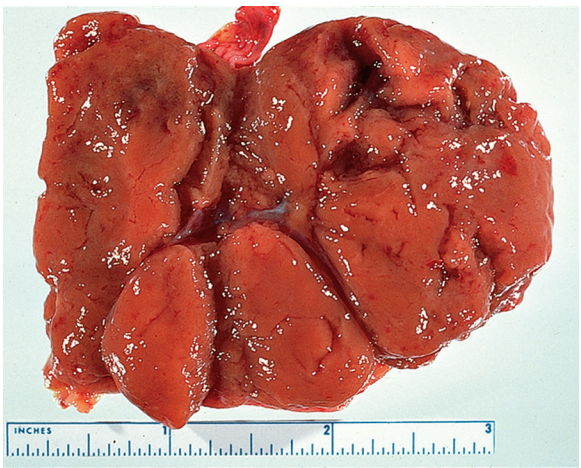

Fig. 18.55 Luteoma of pregnancy with numerous solid brown nodules. (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology.* St. Louis: Mosby-Wolfe; 1997.)

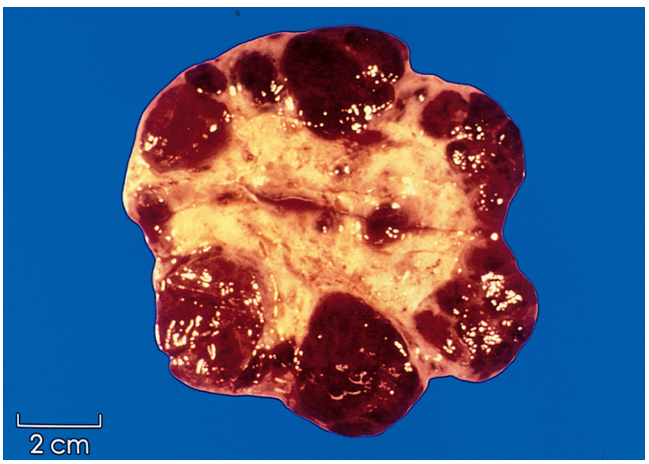

Fig. 18.56 Luteoma with multiple reddish nodules. (From Clement PB, Young RH. *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders; 2000.)

Benign Neoplasms of the Ovary

Benign Cystic Teratoma (Dermoid Cyst, Mature Teratoma)

Benign ovarian teratomas are usually cystic structures that on histologic examination contain elements from all three germ cell layers. The word *teratoma* was first advanced by Virchow and translated literally means "monstrous growth." Teratomas of the ovary may be benign or malignant. Although *dermoid* is a misnomer, it is the most common term used to describe the benign cystic tumor, composed of mature cells, whereas the malignant variety is composed of immature cells (immature teratoma). *Dermoid* is a descriptive term in that it emphasizes the preponderance of ectodermal tissue with some mesodermal and rare endodermal derivatives. Malignant teratomas that are immature are usually solid with some cystic areas and histologically contain immature or embryonic-appearing tissue. (See Chapter 33, for further discussion of malignant teratomas.) Benign teratomas may contain a malignant component, usually in women older than 40 (mean age 48). The malignant component is generally a squamous carcinoma and is found in less than 1% of cases. Nonovarian teratomas may arise in any midline structure of the body where the germ cell has resided during embryonic life.

Benign teratomas are among the most common ovarian neoplasms. They account for more than 90% of germ cell tumors of the ovary. These slow-growing tumors occur from infancy to the postmenopausal years. Depending on the series, dermoids represent 20% to 25% of all ovarian neoplasms and approximately 33% of all benign tumors, if follicular and corpus luteum cysts are excluded. Dermoids are the most common ovarian neoplasm in prepubertal girls and are also common in teenagers. More than 50% of benign teratomas are discovered in women between the ages of 25 and 50 years. In one series of 118 women with dermoids, 86% of the women were younger than 40, and 3.4% had recurrences (Fig. 18.57). With routine obstetric ultrasound, the mean age at diagnosis is expected to fall. In most large series of benign tumors in postmenopausal women, dermoids account for approximately 20% of the neoplasms.

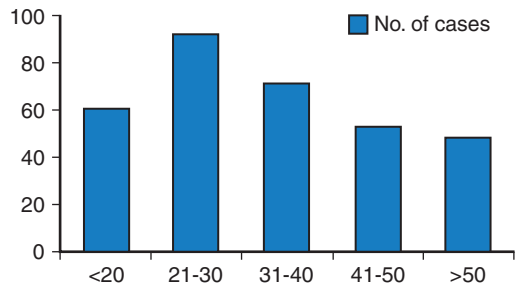

Fig. 18.57 Age distribution of all the mature cystic teratoma in a study of 223 cases. (From Rathore R, Sharma S, Arora D. Clinicopathological evaluation of 223 cases of mature cystic teratoma, ovary: 25-year experience in a single tertiary care centre in India. *J Clin Diagn Res.* 2017;11(4):EC11-EC14.)

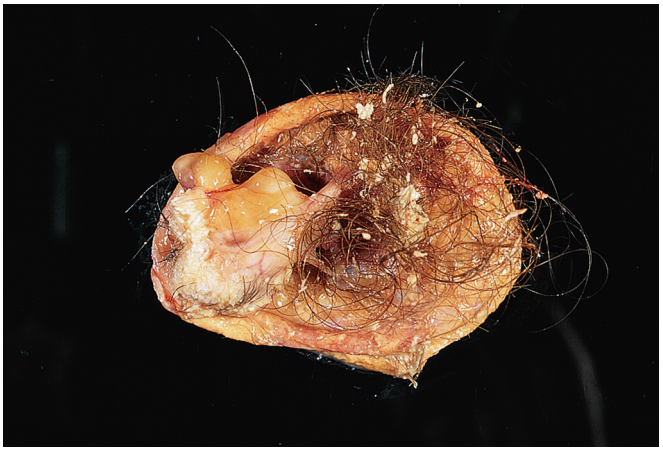

Fig. 18.58 Mature cystic teratoma (dermoid cyst) filled with hair and keratinous debris with one solid nodular area (Rokitansky protuberance). (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology.* St. Louis: Mosby-Wolfe; 1997.)

Dermoids vary from a few millimeters to 25 cm in diameter, although they have been reported to weigh as much as 7657 g in an asymptomatic woman. However, 80% are less than 10 cm. These tumors may be single or multiple, with as many as nine individual dermoids having been reported in the same ovary. Benign teratomas occur bilaterally 10% to 15% of the time. Often, dermoid cysts are pedunculated. These cysts make the ovary heavier than normal, and thus they are usually discovered either in the cul-de-sac or anterior to the broad ligament. On palpation these tumors, which have both cystic and solid components, have a doughy consistency.

The cysts are usually unilocular. The walls of the cyst are a smooth, shiny, opaque white color. When they are opened, thick sebaceous fluid pours from the cyst, often with tangled masses of hair and firm areas of cartilage and teeth (Figs. 18.58 and 18.59). The sebaceous material is a thick fluid at body temperature but solidifies when it cools in room air.

Benign teratomas are believed to arise from a single germ cell after the first meiotic division. Therefore they develop from totipotential stem cells, and they are neoplastic sequelae from a transformed germ cell. Dermoids have a chromosomal makeup of 46,XX and the chromosomes of dermoids were different from the chromosomes of the host, leading one to postulate that dermoids began by parthenogenesis from secondary oocytes. An alternative hypothesis was that the dermoid resulted from fusion of the second polar body with the oocyte. One thing is certain—dermoids do not arise from somatic cells nor from an oogonium before the first stage of meiosis. The first meiotic division occurs at approximately 13 weeks' gestation. Thus dermoids begin in fetal life sometime after the first trimester.

Histologically, benign teratomas are composed of mature cells, usually from all three germ layers (Fig. 18.60). A combination of skin and skin appendages, including sebaceous glands, sweat glands, hair follicles, muscle fibers, cartilage, bone, teeth, glial cells, and epithelium of the respiratory and gastrointestinal tracts, may be visualized. Teeth are predominantly premolar and molar forms. The fluid in dermoid cysts is usually sebaceous. Most solid elements arise and are contained in a protrusion or nipple (mammilla) in the cyst wall, termed the *prominence or tubercle of Rokitansky.* This prominence may be visualized by ultrasound as an echodense region, thus aiding in the sonographic diagnosis. If malignancy occurs, it is almost always found in this nest of cells. The wall of the cyst will often contain granulation tissue, giant cells, and pseudoxanthoma cells.

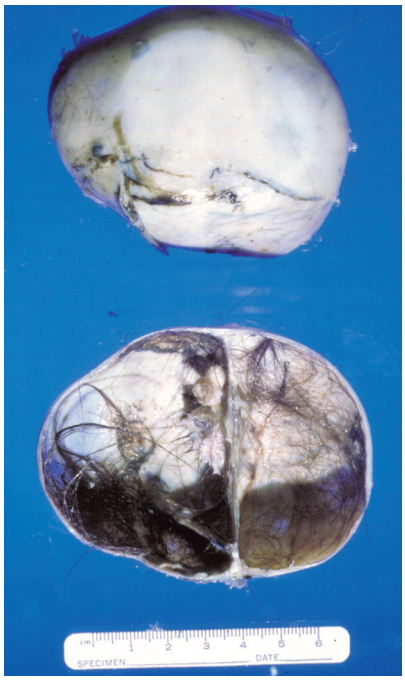

Fig. 18.59 Bilateral mature cystic teratomas in pregnancy. The cyst is bilocular. Dermal papillae are noted. Teeth are also present in the left lobule. (From Russell P, Robboy SJ, Anderson MC. Germ cell tumors of the ovaries. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

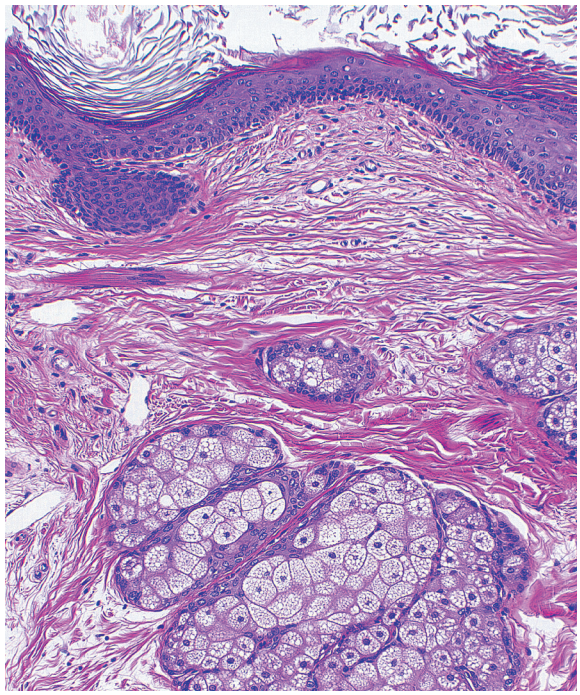

Fig. 18.60 Mature cystic teratoma. This cyst is lined with mature epidermis and is subtended by connective tissue containing exuberant dermal appendages (pilosebaceous follicles). (From Russell P, Robboy SJ, Anderson MC. Germ cell tumors of the ovaries. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

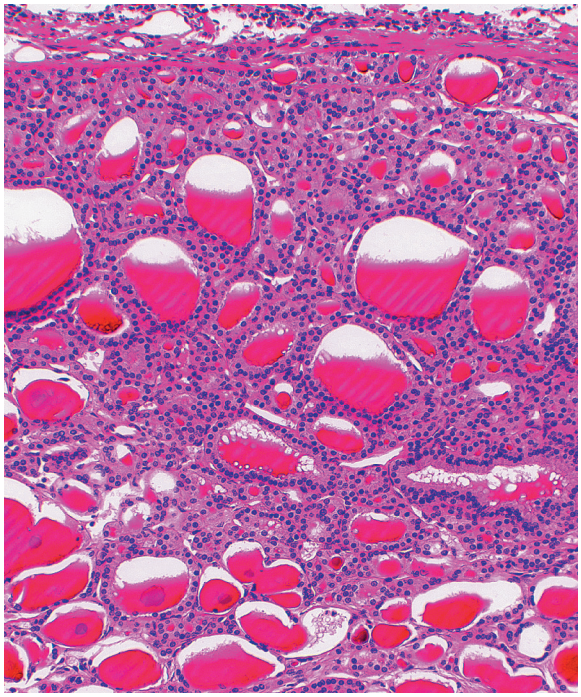

Fig. 18.61 Struma ovarii. Variably sized banal thyroid follicles. (From Russell P, Robboy SJ, Anderson MC. Germ cell tumors of the ovaries. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

From 50% to 60% of dermoids are asymptomatic and are discovered during a routine pelvic examination, coincidentally visualized during pelvic imaging, or found incidentally at laparotomy. Presenting symptoms of dermoids include pain and the sensation of pelvic pressure. Specific complications of dermoid cysts include torsion, rupture, infection, hemorrhage, and malignant degeneration. Three medical diseases also may be associated with dermoid cysts: thyrotoxicosis, carcinoid syndrome, and autoimmune hemolytic anemia, the latter two being quite rare.

Adult thyroid tissue is discovered microscopically in approximately 12% of benign teratomas. Struma ovarii is a teratoma in which the thyroid tissue has overgrown other elements and is the predominant tissue (Fig. 18.61). Strumae ovarii constitute 2% to 3% of ovarian teratomas. These tumors are usually unilateral and measure less than 10 cm in diameter. Less than 5% of women with strumae ovarii develop thyrotoxicosis, which may be secondary to the production of increased thyroid hormone by either the ovarian or the thyroid gland.

Another rare finding with dermoids is the presence of a primary carcinoid tumor from the gastrointestinal or respiratory tract epithelium contained in the dermoid. One of three of these tumors is associated with the typical carcinoid syndrome even without metastatic spread. If the carcinoid is functioning, it may be diagnosed by measuring serum serotonin levels or urinary levels of 5-hydroxyindoleacetic acid. The autoimmune hemolytic anemia associated with dermoids is the rarest of the three medical complications.

Rupture or perforation of the contents of a dermoid into the peritoneal cavity or an adjacent organ is a potentially serious complication. The incidence varies between 0.7% and 4.6%. However, most series report less than 1%. Rupture is more common in pregnancy. If a rupture occurs during surgery, the abdomen should be copiously irrigated with saline, with careful removal of any particulate matter. Chemical peritonitis is reported in less than 1% of ruptured dermoids. Rupture may occur either catastrophically, which produces an acute abdomen, or by a slow leak of the sebaceous material. The latter is clinically more common, with the sebaceous material producing a severe chemical granulomatous peritonitis. Some warn that this possibility should be considered and a frozen section obtained so that the true diagnosis is established. Thus a young woman will not be mistakenly treated for suspected ovarian carcinoma with metastasis because of the identical gross appearance of a slow-leaking dermoid cyst. Infection, hemorrhage, and malignant degeneration are all unusual complications of dermoids, occurring in less than 1% of patients.

Torsion of a dermoid is the most common complication, occurring in 3.5% to 11% of cases. Because of its weight, the benign teratoma is often pedunculated, which may predispose to torsion. Torsion is more common in younger women. Small dermoid cysts, less than 6 cm in diameter, grow slowly at an approximate rate of 2 mm per year.

The diagnosis of a dermoid cyst is often established when a semisolid mass is palpated anterior to the broad ligament. Approximately 50% of dermoids have pelvic calcifications on radiographic examination. Often an ovarian teratoma is an incidental finding during radiologic investigation of the genitourinary or gastrointestinal tract. Most dermoids have a characteristic ultrasound picture. These characteristics include a dense echogenic area within a larger cystic area, a cyst filled with bands of mixed echoes, and an echoic dense cyst. Unfortunately, only one of three dermoids has this "typical picture." In one series of 45 patients with 51 biopsy-proved dermoid cysts, 24% of the dermoid cysts were predominantly solid, 20% were almost entirely cystic, and 24% were not visible. Ultrasound has a more than 95% positive predictive value and a less than 5% false-positive rate (Laing, 1981).

Operative treatment of benign cystic teratomas is cystectomy with preservation of as much normal ovarian tissue as possible. Laparoscopic cystectomy is an accepted approach. Rates of spillage are comparable with that from open laparotomy. However, adequate irrigation in such cases is essential and often more time consuming. Many authors use a 10-cm diameter cutoff as the upper limit for a laparoscopic approach.

When a teratoma is diagnosed incidentally during pregnancy, conservative management is acceptable. Though dermoids have a higher incidence of torsion and potential for rupture during pregnancy, most large series have not shown that an aggressive approach to asymptomatic teratomas less than 10 cm confers any advantage for the mother or pregnancy. Though laparoscopy is safe during pregnancy, a small periumbilical minilaparotomy may be a faster, less traumatic approach. The treatment is cystectomy, and with the recommendation for reduced intraoperative time this approach may be preferable during pregnancy.

Endometriomas

Endometriosis of the ovary is usually associated with endometriosis in other areas of the pelvic cavity. Approximately two out of three women with endometriosis have ovarian involvement. Interestingly, only 5% of these women have enlargement of the ovaries that is detectable by pelvic examination; however, because of the prevalence of the disease, endometriosis is one of the most common causes of enlargement of the ovary. Because most authors do not classify endometriosis as a neoplastic disease, the diagnosis of endometriosis may not be given due consideration in the differential diagnosis of an adnexal mass. Ovarian endometriosis is similar to endometriosis elsewhere and is described in greater detail in Chapter 19.

The size of ovarian endometriomas varies from small, superficial, blue-black implants that are 1 to 5 mm in diameter to large, multiloculated, hemorrhagic cysts that may be 5 to 10 cm in diameter (Fig. 18.62). Clinically, large ovarian endometriomas, greater than 20 cm in diameter, are extremely rare. Areas of ovarian endometriosis

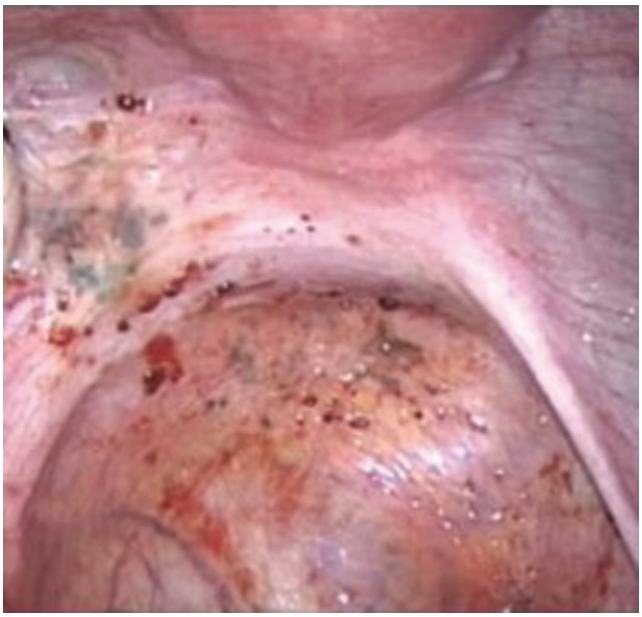

Fig. 18.62 Scattered variable-appearing endometriosis lesions with severe disease in the left pelvis. (From Dun E, Kho K, Morozov V, Kearney S, Zurawin J, Nezhat C. Endometriosis in adolescents. *JSLS.* 2015;19(2):e2015.00019.)

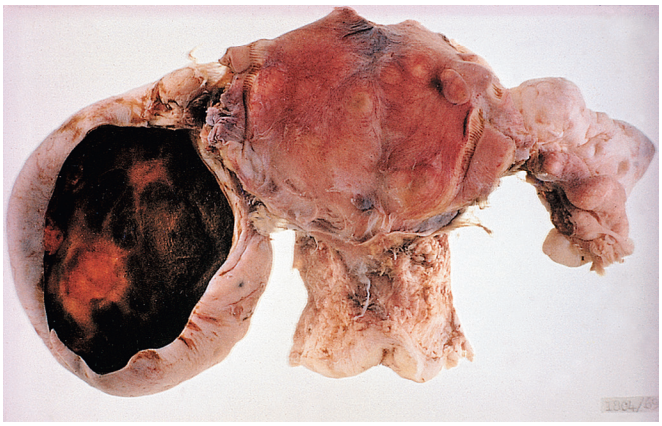

Fig. 18.63 "Chocolate cyst" of the ovary. The endometrioma is large, but it has not yet completely replaced the ovary. (From Robboy SJ. Endometriosis. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

that become cystic are termed *endometriomas.* Rarely, large chocolate cysts of the ovary may reach 15 to 20 cm (Fig. 18.63). Larger cysts are often bilateral. The surface of an ovary with endometriosis is often irregular, puckered, and scarred. Depending on their size, endometriomas replace a portion of the normal ovarian tissue.

Although most women with endometriomas are asymptomatic, the most common symptoms associated with ovarian endometriosis are pelvic pain, dyspareunia, and infertility. Approximately 10% of the operations for endometriosis are for acute symptoms, usually related to a ruptured ovarian endometrioma that was previously asymptomatic. Smaller cysts generally have thin walls, and perforation occurs commonly secondary to cyclic hemorrhage into the cystic cavity.

On pelvic examination the ovaries are often tender and immobile, secondary to associated inflammation and adhesions. Most commonly the ovaries are densely adherent to surrounding structures, including the peritoneum of the pelvic sidewall, the oviduct, the broad ligament, and sometimes the small or large bowel. Endometrial glands, endometrial stroma, and large phagocytic cells containing hemosiderin may be identified histologically (see Fig. 19.11). Pressure atrophy may lead to the loss of architecture of the endometrial glands. The ultrasound characteristics include a thick-walled cyst with a relatively homogeneous echo pattern that is somewhat echolucent. This appearance confers a greater than 95% positive predictive value in some studies.

The choice between medical and operative management depends on several factors, including the patient's age, future reproductive plans, and severity of symptoms. Medical therapy is rarely successful in treating ovarian endometriosis if the disease has produced ovarian enlargement. Often surgical therapy is complicated by formation of *de novo* and recurrent adhesions.

On pathologic examination, it is important to distinguish endometriosis from benign endometrial tumors, which are usually adenofibromas. The latter tumor is a true neoplasm, and there is a malignant counterpart.

Fibroma

Fibromas are the most common benign, solid neoplasms of the ovary. Their malignant potential is low, less than 1%. These tumors make up approximately 5% of benign ovarian neoplasms and approximately 20% of all solid tumors of the ovary.

Fibromas vary in size from small nodules to huge pelvic tumors weighing 50 pounds. One of the predominant characteristics of fibromas is that they are extremely slow-growing tumors. The average diameter of a fibroma is approximately 6 cm; however, some tumors have reached 30 cm in diameter. In most series, less than 5% of fibromas are greater than 20 cm in diameter. The diameter of a fibroma is important clinically because the incidence of associated ascites is directly proportional to the size of the tumor. Many ovarian fibromas are misdiagnosed and are believed to be leiomyomas before operation. Ninety percent of fibromas are unilateral; however, multiple fibromas are found in the same ovary in 10% to 15% of cases. The average age of a woman with an ovarian fibroma is 48, and thus this tumor, which arises from the undifferentiated fibrous stroma of the ovary, often presents in postmenopausal women. Bilateral ovarian fibromas are commonly found in women with the rare genetic transmitted basal cell nevus syndrome.

The pelvic symptoms that develop with growth of fibromas include pressure and abdominal enlargement, which may be secondary to both the size of the tumor and ascites. Smaller tumors are asymptomatic because they do not elaborate hormones, and thus there is no change in the pattern of menstrual flow. Fibromas may be pedunculated and therefore easily palpable during one examination yet difficult to palpate during a subsequent pelvic examination. Sometimes on pelvic examination the fibromas appear to be softer than a solid ovarian tumor because of the edema or occasional cystic degeneration.

Meigs syndrome is the association of an ovarian fibroma, ascites, and hydrothorax. Both the ascites and the hydrothorax resolve after removal of the ovarian tumor. The ascites is caused by transudation of fluid from the ovarian fibroma; the incidence of ascites is directly related to the size of the fibroma. Fifty percent of patients have ascites if the tumor is greater than 6 cm; however, true Meigs syndrome is rare, occurring in less than 2% of ovarian fibromas. The hydrothorax develops secondary to a flow of ascitic fluid into the pleural space via the lymphatics of the diaphragm. Statistically the right pleural space is involved in 75% of reported cases, the left in 10%, and both sides in 15%. The clinical features of Meigs syndrome are not unique to fibromas, and a similar clinical picture is found with many other ovarian tumors.

Grossly, fibromas are heavy, solid, well encapsulated, and grayish white. The cut surface usually demonstrates a homogeneous

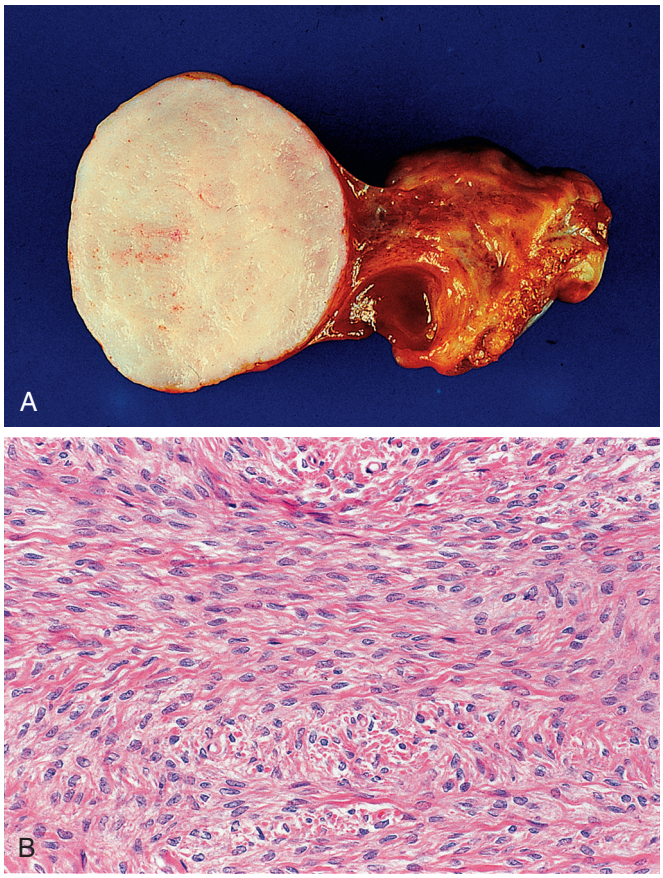

Fig. 18.64 A, Fibroma of the ovary with a well-circumscribed light tan mass. **B,** Histologic view of fibroma of the ovary demonstrating bland fibrous differentiation. (From Voet RL. *Color Atlas of Obstetric and Gynecologic Pathology.* St. Louis: Mosby-Wolfe; 1997.)

white or yellowish white solid tissue with a trabeculated or whorled appearance similar to that of myomas. The majority of fibromas are grossly edematous (Fig. 18.64). Less than 10% of fibromas have calcifications or small areas of hyaline or cystic degeneration. Histologically, fibromas are composed of connective tissue, stromal cells, and varying amounts of collagen interposed between the cells. The connective tissue cells are spindle-shaped, mature fibroblasts arranged in an imperfect pattern. A few smooth muscle fibers may be occasionally identified. It is sometimes difficult to distinguish fibromas from nonneoplastic thecomas. Histologically the pathologist must differentiate fibromas from stromal hyperplasia and fibrosarcomas and also look for epithelial elements of an associated Brenner tumor.

The management of fibromas is straightforward because any woman with a solid ovarian neoplasm should have an exploratory operation soon after the tumor is discovered. Simple excision of the tumor is all that is necessary. After excision of the tumor, there is resolution of all symptoms, including ascites. Because these tumors are commonly discovered in postmenopausal women, often a bilateral salpingo-oophorectomy and total abdominal hysterectomy are performed. Conversely, it is important to note that most women who preoperatively have the combination of a solid ovarian tumor and ascites are found to have ovarian carcinoma.

Transitional Cell Tumors: Brenner Tumors

Brenner tumors are rare, small, smooth, solid, fibroepithelial ovarian tumors that are generally asymptomatic and usually occur in women ages 40 to 60 years. The semantic classification of neoplasms changes, and the current preferred term for benign Brenner tumor is *transitional cell tumor.* The benign, proliferative (low malignant potential), and malignant forms together constitute approximately 2% of ovarian tumors. Approximately 30% of transitional cell tumors are discovered as small, solid tumors in association with a concurrent serous cystic neoplasia, such as serous or mucinous cystadenomas of the ipsilateral ovary. Some are microscopic, with the entire tumor contained in a single low-powered microscopic field, and others may reach a diameter of 20 cm; the majority are less than 5 cm in diameter. The tumor is unilateral 85% to 95% of the time.

The Brenner tumor was first described in 1898. In 1932, Robert Meyer postulated that it was a distinct, independent neoplasm from granulosa cell tumors. Since that time there has been a controversy in the gynecologic pathology literature regarding the histogenesis of the neoplasm. Presently, most authorities accept the theory that most of these tumors result from metaplasia of coelomic epithelium into uroepithelium. Detailed three-dimensional histologic studies have demonstrated a downward growth in a cordlike fashion of epithelium from the surface of the ovary to deeper areas in the ovarian cortex. Others have postulated that sometimes the solid nests of epithelial cells of the tumor originate from the rete ovarii or Walthard rests. Electron microscopy confirmed the histologic and ultrastructural similarity between the epithelium in Brenner tumors and transitional epithelium. These authors argue that because of the histogenesis from coelomic inclusion cysts and also the mixture of müllerian-type epithelium in 30% of Brenner tumors, it might be appropriate to classify Brenner tumors in the epithelial group of ovarian neoplasms.

Approximately 90% of these small neoplasms are discovered incidentally during a gynecologic operation, although large tumors may produce unilateral pelvic discomfort. Postmenopausal bleeding is sometimes associated with Brenner tumors because endometrial hyperplasia is a coexisting abnormality in 10% to 16% of cases. It is postulated that luteinization of the stroma produces estrogen with resulting hyperplasia that leads to classic findings of ovarian Brenner tumors on CT or MRI. The extensive fibrous content of these tumors results in lower signal intensity in T2-weighted images. During CT scanning, Brenner tumors characteristically demonstrate a finding of extensive amorphous calcification within the solid components of the ovarian mass.

Grossly, Brenner tumors are smooth, firm, gray-white, solid tumors that grossly resemble fibromas, and similar to fibromas, transitional cell tumors are slow growing. On sectioning, the tumor usually appears gray; however, occasionally there is a yellowish tinge with small cystic spaces (Fig. 18.65). Approximately 1% to 2%

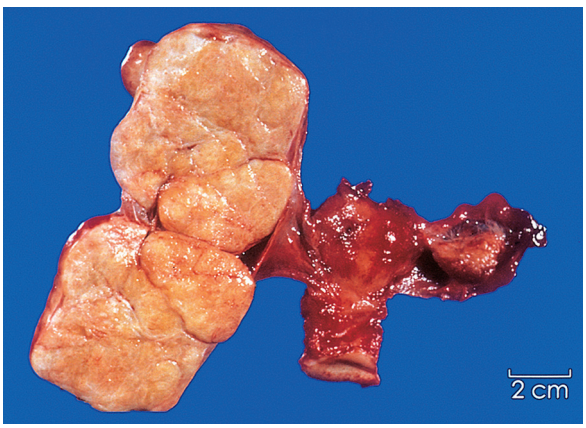

Fig. 18.65 Brenner tumor. (From Clement PB, Young RH: *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders; 2000.)

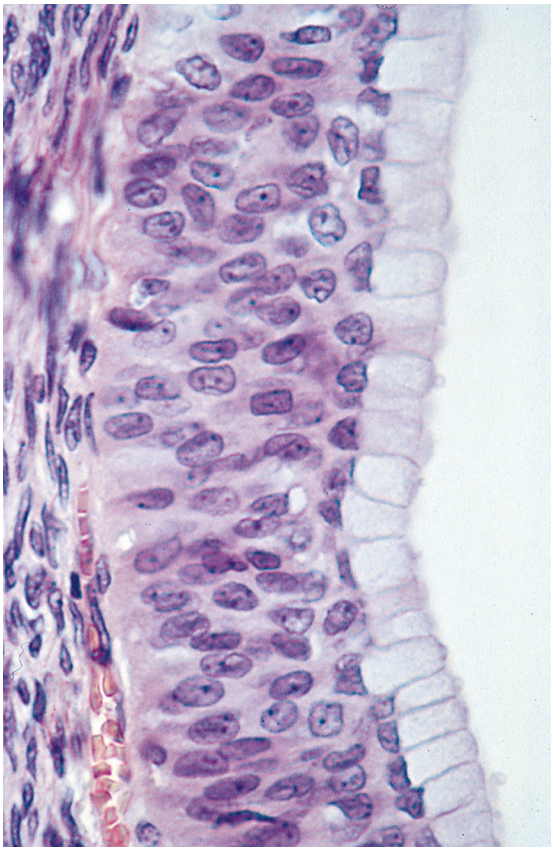

Fig. 18.66 Benign Brenner tumor. A cyst in the Brenner tumor is lined by an inner layer of endocervical-type mucinous cells and an outer layer of stratified transitional cells, a few of which have grooved nuclei. (From Clement PB, Young RH. *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders, 2000.)

of these tumors undergo malignant change (see Chapter 33). Histologically, Brenner tumors have two principal components: solid masses or nests of epithelial cells and a surrounding fibrous stroma. The epithelial cells are uniform and do not appear anaplastic (Fig. 18.66). The histologic characteristics and ultrastructure of the epithelial cells of a Brenner tumor are similar to transitional epithelium of the urinary bladder. The pale epithelial cells have a coffee bean–appearing nucleus, which is also described as a longitudinal groove in the cell's nucleus.

Electron microscopy has demonstrated that the longitudinal groove during routine microscopy is produced by prominent indentation of the nuclear membrane. An additional ovarian neoplasm, such as a serous or mucinous cystadenoma or teratoma, is often found in association with Brenner tumors.

Management of Brenner tumors is operative, with simple excision being the procedure of choice. However, as with ovarian fibromas, the patient's age is often the principal factor in deciding the extent of the operation.

Adenofibroma and Cystadenofibroma

Adenofibromas and cystadenofibromas are closely related. Both these benign firm tumors consist of fibrous and epithelial components. The epithelial element is most commonly serous but histologically may be mucinous and endometrioid or clear cell. They differ from benign epithelial cystadenomas in that there is a preponderance of connective tissue. Most pathologists emphasize that at least 25% of the tumor consists of fibrous connective tissue. Obviously, cystadenofibromas have microscopic or occasional macroscopic areas that are cystic. The varying degree of fibrous stroma and epithelial elements produces a spectrum of tumors, which have resulted in a confusing nomenclature with terms such as *papillomas*, *fibropapillomas*, and *fibroadenomas.*

Adenofibromas are usually small fibrous tumors that arise from the surface of the ovary. They are bilateral in 20% to 25% of women, usually occur in postmenopausal women, and are 1 to 15 cm in diameter. Grossly they are gray or white tumors, and it is difficult to distinguish them from fibromas. Papillary adenofibromas, which project from the surface of the ovary, at first glance may appear to be external excrescences of a malignant tumor. Histologically, small precursors of adenofibromas are identified in many normal ovaries. Under the microscope, true cystic gland spaces lined by cuboidal epithelium are characteristic. However, differing from serous cystadenomas, the fibrous connective tissue surrounding the cystic spaces is abundant and is the predominant tissue of the tumor.

Smaller tumors are asymptomatic and are only discovered incidentally during abdominal or pelvic operations. Large tumors may cause pressure symptoms or, rarely, undergo adnexal torsion. A small series of the MRI features of these tumors has been reported. Similar to Brenner tumors, the fibrous component produces a very low signal intensity on T2-weighted images. This interest in imaging results from an attempt to distinguish, before operation, whether a predominantly solid ovarian mass is benign or malignant. Because adenofibromas are usually discovered in postmenopausal women, the treatment of choice is bilateral salpingo-oophorectomy and total abdominal hysterectomy. Because these tumors are benign and because malignant transformation is rare, simple excision of the tumor and inspection of the contralateral ovary are appropriate in younger women.

Torsion

Torsion of the ovary or both the oviduct and the ovary (adnexal torsion) is uncommon but an important cause of acute lower abdominal and pelvic pain. Torsion may cause up to 3% of all acute abdomens presenting to emergency departments. Torsion of the ovary may occur separately from torsion of the fallopian tube, but most commonly the two adnexal structures are affected together.

Adnexal torsion occurs most commonly during the reproductive years, with the average patient being in her mid-20s. However, adnexal torsion is also a complication of benign ovarian tumors in the postmenopausal woman. Pregnancy appears to predispose women to adnexal torsion. Approximately one in five women are pregnant when the condition is diagnosed. Most susceptible are ovaries that are enlarged secondary to ovulation induction during early pregnancy. The most common cause of adnexal torsion is ovarian enlargement by an 8- to 12-cm benign mass of the ovary, although smaller ovaries may also undergo torsion. Ovarian tumors are discovered in 50% to 60% of women with adnexal torsion. Torsion of a normal ovary or adnexum is also possible and occurs more commonly in children. Dermoids are the most commonly reported tumors in women with adnexal torsion. However, the relative risk of adnexal torsion is higher with parovarian cysts, solid benign tumors, and serous cysts of the ovary. The right ovary has a greater tendency to twist than does the left ovary. Torsion of a malignant ovarian tumor is comparatively rare.

Patients with adnexal torsion present with acute, severe, unilateral, lower abdominal and pelvic pain. Often the patient relates the onset of the severe pain to an abrupt change of position. A unilateral, extremely tender adnexal mass is found in more than 90% of patients. Approximately two-thirds of patients have associated nausea and vomiting. These associated gastrointestinal symptoms sometimes lead to a preoperative diagnosis of acute appendicitis or small intestinal obstruction. Many patients have

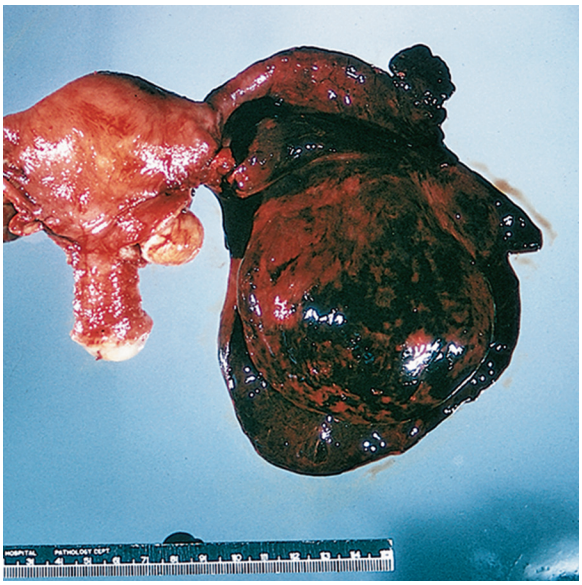

Fig. 18.67 Adnexal torsion with hemorrhagic infarction. A benign cyst was found in the ovary. (From Clement PB, Young RH: *Atlas of Gynecologic Surgical Pathology.* Philadelphia: WB Saunders; 2000.)

noted intermittent previous episodes of similar pain for several days to several weeks. The hypothesis is that previous episodes of pain were secondary to partial torsion, with spontaneous reversal without significant vascular compromise. With progressive torsion, initially venous and lymphatic obstruction occurs. This produces a cyanotic, edematous ovary that on pelvic examination presents as a unilateral, extremely tender adnexal mass. Further progression of the torsion interrupts the major arterial supply to the ovary, resulting in hypoxia, adnexal necrosis, and a concomitant low-grade fever and leukocytosis. Fever is more common in women who have developed necrosis of the adnexa. Approximately 10% of women with adnexal torsion have a repetitive episode affecting the contralateral adnexa.

Most patients with adnexal torsion present with symptoms and signs severe enough to demand operative intervention (Fig. 18.67). Some authors have reported the successful use of Doppler ultrasound to evaluate ovarian arterial blood flow to help diagnose torsion. Abnormal color Doppler flow is highly predictive of torsion of the ovary. However, approximately 60% of women with surgically confirmed adnexal torsion will have a normal Doppler flow study (Sasaki, 2014). The false-negative rate is high enough that normal Doppler studies should never trump clinical suspicion. Women with ovarian torsion may be treated via laparoscopic surgery. The most common gynecologic conditions that may be confused with adnexal torsion are a ruptured corpus luteum or an adnexal abscess. In series emphasizing the early diagnosis of adnexal torsion, conservative operative management has been possible in 75% of cases.

Because the majority of cases of adnexal torsion occur in young women, a conservative operation is ideal. The clinician should maintain a high index of suspicion for adnexal torsion so that early and conservative surgery is possible. Even with severe vascular compromise, the appropriate operation in young women is to untwist the pedicle and preserve ovarian function. If unilateral salpingo-oophorectomy is to be performed, the vascular pedicle should be clamped with care so as not to injure the ureter, which may be tented up by the torsion.

Although salpingo-oophorectomy has been the routine treatment for ovarian torsion, large series of conservative management have been reported. Conservative surgery either through the laparoscope or via laparotomy entails gentle untwisting of the pedicle, possibly cystectomy, and stabilization of the ovary with sutures. The increasing use of detorsion may result in retorsion. A review noted that the risk of retorsion in pregnancy was as high as 19.5% to 37.5%; among fertile women it was 28.6%. Based on observational studies, detorsion and fixation of the ovary is a safe procedure that reduces the risk of recurrence (Hyttel, 2015).

The risk of pulmonary embolus (PE) with adnexal torsion is small, approximately 0.2%. One series noted the risk of PE to be similar when torsion was managed by conservative surgery with untwisting or adnexal removal without untwisting (McGovern, 1999).

Ovarian Remnant Syndrome

Chronic pelvic pain secondary to a small area of functioning ovarian tissue after intended total removal of both ovaries is termed *ovarian remnant syndrome*. Most of the women who develop this condition had endometriosis or chronic pelvic inflammatory disease and extensive pelvic adhesions discovered during previous surgical procedures. A more recently described risk factor is laparoscopic oophorectomy.

The chronic pelvic pain is usually cyclic and exacerbated after coitus. Approximately half of women present with pain, and half with a pelvic mass. Usually the masses are small, approximately 3 cm in diameter, and most commonly located in the retroperitoneal space immediately adjacent to either ureter. Histologically the mass contains both ovarian follicles and stroma (Fig. 18.68). If the mass cannot be palpated during pelvic examination, imaging studies such as vaginal ultrasound or MRI are often helpful. Premenopausal levels of follicle-stimulating hormone or estradiol help establish the diagnosis in a woman who has a history of a bilateral salpingo-oophorectomy. However, sometimes a small area of ovarian tissue does not produce enough circulating estrogen to suppress gonadotropins. Difficult cases have been diagnosed by challenging and stimulating the suspected ovarian remnant with either clomiphene citrate or a GnRH agonist.

Once the diagnosis is suspected, the most effective treatment is surgical removal of the ovarian remnant. The tissue should be removed by laparoscopy or laparotomy with wide excision of the mass using meticulous techniques so as to protect the integrity of the ureter. Removal of an ovarian remnant is associated with a high complication rate. However, a retrospective review reported that laparoscopic and robotic surgery for the treatment of ovarian remnant syndrome had less blood loss, lower postoperative complications, and a shorter length of stay than laparotomy (Zapardiel, 2012).

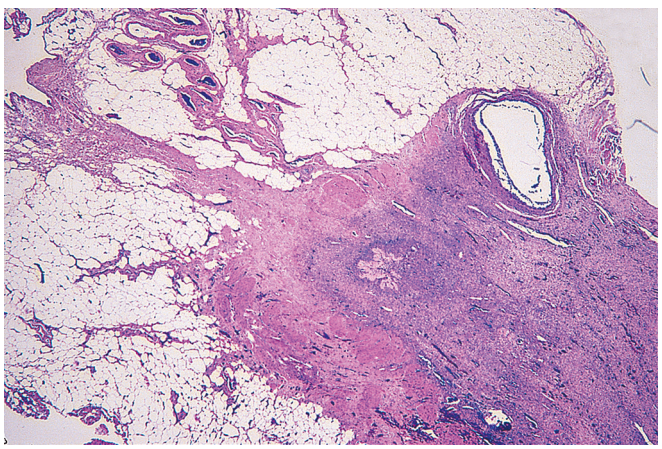

Fig. 18.68 Ovarian remnant syndrome. Ovarian tissue that was left behind at the time of oophorectomy has regrown and is functional. (From Robboy SJ, Bentley RC, Russell P, et al. The peritoneum. In: Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract.* Edinburgh: Churchill Livingstone; 2002.)

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