endometriotic tissue and ovarian cancers in some cases, as described below.

MORPHOLOGY

Endometriotic lesions bleed periodically in response to both extrinsic cyclic (ovarian) and intrinsic hormonal stimulation. This bleeding produces nodules with a red-blue to yellow-brown appearance on or just beneath the mucosal and/or serosal surfaces at sites of involvement. When lesions are extensive, organizing hemorrhage causes extensive fibrous adhesions between tubes, ovaries, and other structures and obliterates the pouch of Douglas. The ovaries may become markedly distorted by large cystic masses (3 to 5 cm in diameter) filled with brown fluid resulting from previous hemorrhage; these are often referred to clinically as **chocolate cysts** or **endometriomas**. Aggressive forms of endometriosis can invade tissues and cause fibrosis and subsequent adhesions.

The histologic diagnosis of endometriosis is usually straightforward but may be difficult in long-standing cases in which the endometrial tissue is obscured by secondary fibrosis. The diagnosis is readily made when both endometrial glands and stroma are present (Fig. 22-21*B*), with or without the presence of hemosiderin. In rare cases only stroma is identified. If only glands are present, other diagnoses with different clinical ramifications, such as endosalpingiosis, must be considered.

Atypical endometriosis, the likely precursor to endometriosis-related ovarian carcinoma, has two morphologic appearances. One consists of cytologic atypia of the epithelium lining the endometriotic cyst without major architectural changes. The second is marked by glandular crowding due to excessive epithelial proliferation, often associated with cytologic atypia, producing an appearance that resembles complex atypical endometrial hyperplasia (discussed later).

Clinical Features. Clinical signs and symptoms usually include severe dysmenorrhea, dyspareunia (pain with intercourse), and pelvic pain due to the intrapelvic bleeding and periuterine adhesions. Pain on defecation occurs with rectal wall involvement and dysuria results from involvement of the bladder serosa. Menstrual irregularities are common, and infertility is the presenting complaint in 30% to 40% of women. In addition, although uncommon, malignancies can develop in this setting, suggesting that endometriosis contains "at-risk" epithelium.

A related disorder, *adenomyosis*, is defined as the presence of endometrial tissue within the uterine wall (myometrium). Adenomyosis remains in continuity with the endometrium, presumably signifying downgrowth of endometrial tissue into and between the smooth muscle fascicles of the myometrium. Adenomyosis occurs in up to 20% of uteri. On microscopic examination, irregular nests of endometrial stroma, with or without glands, are arranged within the myometrium, separated from the basalis by at least 2 to 3 mm. Like endometriosis, the clinical symptoms of adenomyosis include menometrorrhagia (irregular and heavy menses), colicky dysmenorrhea, dyspareunia, and pelvic pain, particularly during the premenstrual period. It can coexist with endometriosis.

KEY CONCEPTS

Endometriosis

- Endometriosis is defined as endometrial glands and stroma outside of the uterus. The "ectopic" endometrial tissue may undergo cyclic bleeding.
- Most common sites of endometriosis are within the abdominal cavity, but occasionally it is found at distant sites.
- Several theories (regurgitation, metaplasia, metastasis, and stem cell origin) are proposed to explain the distribution of endometriosis.
- It commonly results in dysmenorrhea, pelvic pain, and infertility.
- Endometriosis may be a precursor to carcinoma (endometrioid and clear cell carcinoma).

Endometrial Polyps

Endometrial polyps are exophytic masses of variable size that project into the endometrial cavity. They may be single or multiple and are usually sessile, measuring from 0.5 to 3 cm in diameter, but are occasionally large and pedunculated. Polyps may be asymptomatic or may cause abnormal bleeding (intramenstrual, menometrorrhagia, or postmenopausal) if they ulcerate or undergo necrosis.

Cytogenetic studies indicate that the stromal cells in endometrial polyps contain certain chromosomal rearrangements that are similar to those found in other benign mesenchymal tumors. These findings suggest that the polyp stroma is neoplastic, and that the associated glands are reactive, merely "coming along for the ride." The glands in polyps may be hyperplastic or atrophic, and may occasionally demonstrate secretory changes (functional polyps). Polyps may by become hyperplastic in association with generalized endometrial hyperplasia and are responsive to estrogen but show little or no response to progesterone (Fig. 22-20*C*). Endometrial polyps have been observed in association with the administration of tamoxifen, which is often used in the therapy of breast cancer due to its anti-estrogenic activity on the breast. However, tamoxifen has weak pro-estrogenic effects in the endometrium. Atrophic polyps, which mainly occur in postmenopausal women, likely represent the atrophic remnants of previously hyperplastic polyps. Rarely, adenocarcinomas arise within endometrial polyps.

Endometrial Hyperplasia

Endometrial hyperplasia is an important cause of abnormal bleeding and a frequent precursor to the most common type of endometrial carcinoma. It is defined as an increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio when compared with normal proliferative endometrium. Clinicopathologic and epidemiologic studies have supported the malignant potential of endometrial hyperplasia and the concept of a continuum of