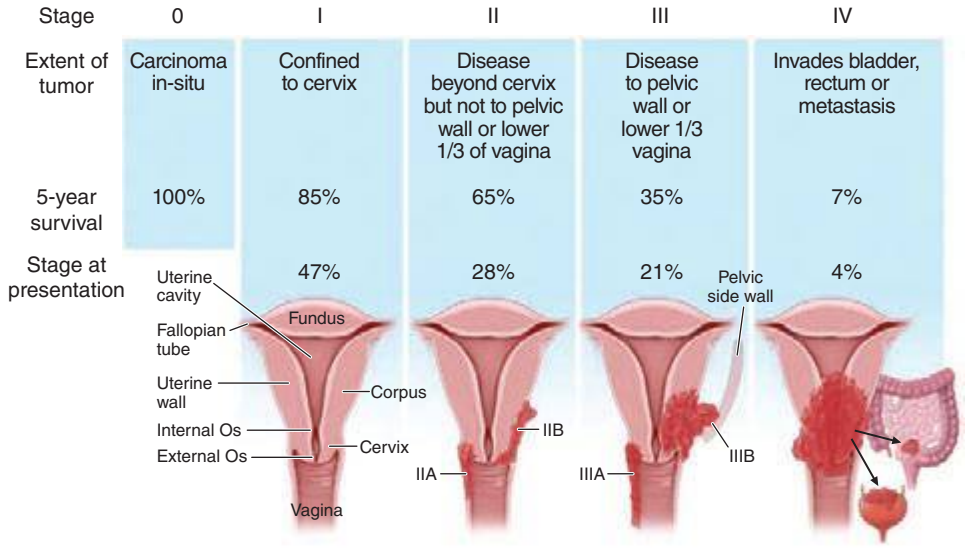

FIGURE 117-1 **Anatomic display of the stages of cervix cancer** defined by location, extent of tumor, frequency of presentation, and 5-year survival.

This technique seems more prognostic and accurate than CT, MRI, or lymphangiogram, especially in the para-aortic region.

Stage I cervical tumors are confined to the cervix, whereas stage II tumors extend into the upper vagina or paracervical soft tissue (Fig. 117-1). Stage III tumors extend to the lower vagina or the pelvic sidewalls, whereas stage IV tumors invade the bladder or rectum or have spread to distant sites. Very small stage I cervical tumors can be treated with a variety of surgical procedures. In young women desiring to maintain fertility, radical trachelectomy removes the cervix with subsequent anastomosis of the upper vagina to the uterine corpus. Larger cervical tumors confined to the cervix can be treated with either surgical resection or radiation therapy in combination with cisplatin-based chemotherapy with a high chance of cure. Larger tumors that extend regionally down the vagina or into the paracervical soft tissues or the pelvic sidewalls are treated with combination chemotherapy and radiation therapy. The treatment of recurrent or metastatic disease is unsatisfactory due to the relative resistance of these tumors to chemotherapy and currently available biological agents, although bevacizumab, a monoclonal antibody that is said to inhibit tumor-associated angiogenesis, has demonstrated clinically meaningful activity in the management of metastatic disease.

UTERINE CANCER

EPIDEMIOLOGY

Several different tumor types arise in uterine corpus. Most tumors arise in the glandular lining and are endometrial adenocarcinomas. Tumors can also arise in the smooth muscle; most are benign (uterine leiomyoma), with a small minority of tumors being sarcomas. The endometrioid histologic subtype of endometrial cancer is the most common gynecologic malignancy in the United States. In 2014, an estimated 52,630 women were diagnosed with cancer of the uterine corpus, with 8590 deaths from the disease. Development of these tumors is a multistep process, with estrogen playing an important early role in driving endometrial gland proliferation. Relative overexposure to this class of hormones is a risk factor for the subsequent development of endometrioid tumors. In contrast, progestins drive glandular maturation and are protective. Hence, women with high endogenous or pharmacologic exposure to estrogens, especially if unopposed by progesterone, are at high risk for endometrial cancer. Obese women, women treated with unopposed estrogens, or women with estrogen-producing tumors (such as granulosa cell tumors of the ovary) are at higher risk for endometrial cancer. In addition, treatment with tamoxifen, which has antiestrogenic effects in breast tissue but estrogenic effects in uterine epithelium, is associated with an increased risk of endometrial cancer. Events such as the loss of the *PTEN* tumor suppressor gene with activation and often additional mutations in the PIK-3CA/AKT pathways likely serve as secondary events in carcinogenesis. The Cancer Genome Atlas Research Network has demonstrated that endometrioid tumors can be divided into four subgroups: ultramutated, microsatellite instability hypermutated, copy number low, and copy number high subgroups. These groups have different natural histories; therapy for these subgroups may eventually be individualized. Serous tumors of the uterine corpus represent approximately 5–10% of epithelial tumors of the uterine corpus and possess distinct molecular characteristics that are most similar to those seen in serous tumors arising in the ovary or fallopian tube.

Women with a mutation in one of a series of DNA mismatch repair genes associated with the Lynch syndrome, also known as hereditary nonpolyposis colon cancer (HNPCC), are at increased risk for endometrioid endometrial carcinoma. These individuals have germline mutations in *MSH2*, *MLH1*, and in rare cases *PMS1* and *PMS2*, with resulting microsatellite instability and hypermutation. Individuals who carry these mutations typically have a family history of cancer and are at markedly increased risk for colon cancer and modestly increased risk for ovarian cancer and a variety of other tumors. Middle-aged women with HNPCC carry a 4% annual risk of endometrial cancer and a relative overall risk of approximately 200-fold as compared to age-matched women without HNPCC.

PRESENTATIONS

The majority of women with tumors of the uterine corpus present with postmenopausal vaginal bleeding due to shedding of the malignant endometrial lining. Premenopausal women often will present with atypical bleeding between typical menstrual cycles. These signs typically bring a woman to the attention of a health care professional, and hence the majority of women present with early-stage disease with the tumor confined to the uterine corpus. Diagnosis is typically established by endometrial biopsy. Epithelial tumors may spread to pelvic or para-aortic lymph nodes. Pulmonary metastases can appear later in the natural history of this disease but are very uncommon at initial presentation. Serous tumors tend to have patterns of spread much more