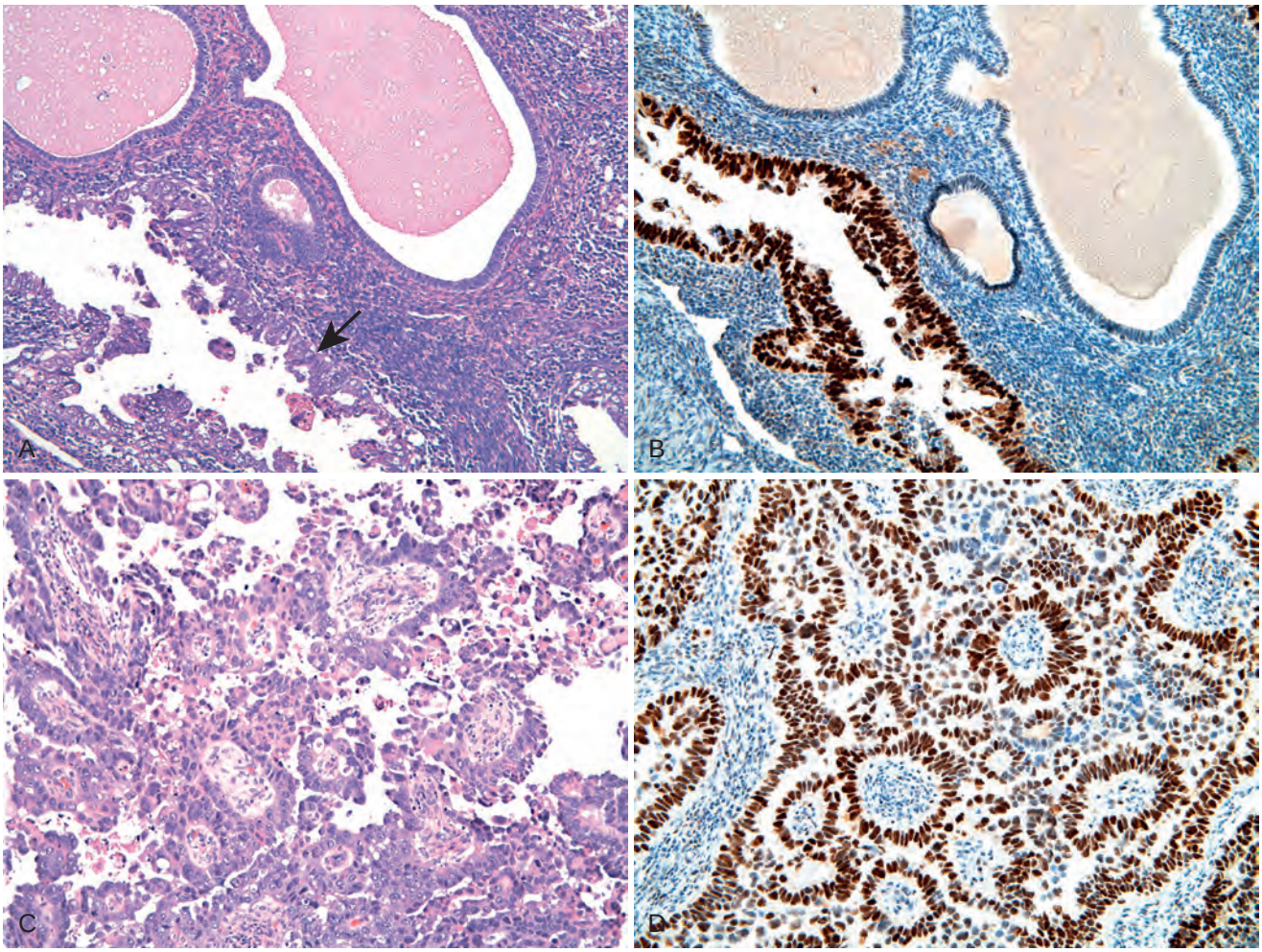

Figure 22-26 Type II endometrial carcinoma. **A,** Endometrial intraepithelial carcinoma, the precursor to serous carcinoma showing malignant cells *(arrow)* with morphologic features identical to serous carcinoma lining the surfaces of the endometrial glands without obvious stromal invasion. **B,** Strong, diffuse expression of p53 as detected by immunohistochemistry in endometrial intraepithelial carcinoma. **C,** Serous carcinoma of the endometrium with papillary growth pattern consisting of malignant cells with marked cytologic atypia including high nuclear-to-cytoplasmic ratio, atypical mitotic figures, and hyperchromasia. **D,** As with the previous lesion, there is an accumulation of p53 protein in the nucleus.

Pathologic staging of both type I and II endometrial adenocarcinoma and malignant mixed müllerian tumors (described later) is as follows:

Stage I—Carcinoma is confined to the corpus uteri itself.

Stage II—Carcinoma involves the corpus and the cervix.

Stage III—Carcinoma extends outside the uterus but not outside the true pelvis.

Stage IV—Carcinoma extends outside the true pelvis or involves the mucosa of the bladder or the rectum.

Type II (Serous) Carcinoma. These generally occur in women who are about 10 years older than those with type I carcinomas, and in contrast to type I carcinoma they usually arise in the setting of *endometrial atrophy* (Fig. 22-24*B*). Type II tumors are by definition poorly differentiated (grade 3) tumors and account for approximately 15% of cases of endometrial carcinoma. The most common subtype is *serous carcinoma*, referred to as such because of morphologic and biologic overlap with ovarian serous carcinoma. Several less common histologic subtypes (clear cell carcinoma and malignant mixed müllerian tumor) are also included within this category.

Mutations in the tumor suppressor *TP53* are present in at least 90% of serous endometrial carcinoma. The majority are missense mutations that result in an accumulation of the altered protein (Fig. 22-26*B* and *D*). The precursor of serous carcinoma, serous endometrial intraepithelial carcinoma, consists of cells identical to those of serous carcinoma but lacks identifiable stromal invasion. Mutations in *TP53* are also found in approximately 75% of endometrial intraepithelial carcinoma, suggesting that mutation of *TP53* is an early event in the evolution of serous endometrial carcinoma. Thus, serous carcinoma presumably begins as a surface epithelial neoplasm that extends into adjacent gland structures and later invades endometrial stroma. Their generally poorer prognosis is thought to be a consequence of a propensity to exfoliate, travel through the fallopian tubes, and implant on peritoneal surfaces like their ovarian counterparts. They have often spread outside of the uterus at the time of diagnosis. Recent whole-exome sequencing studies have detected mutations in a number of