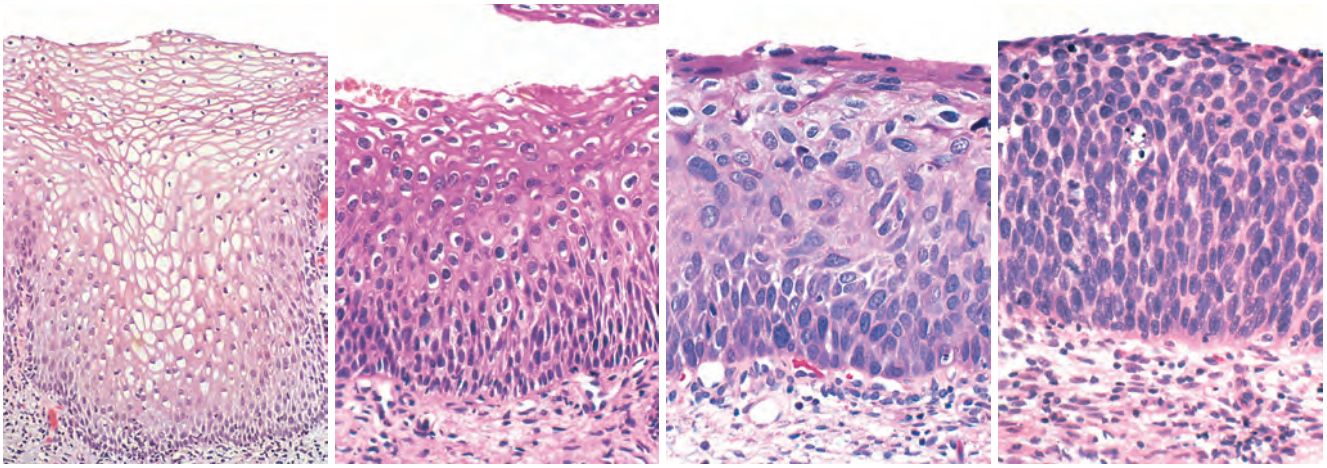

Figure 22-14 Spectrum of cervical intraepithelial neoplasia: normal squamous epithelium for comparison; LSIL (CIN I) with koilocytic atypia; HSIL (CIN II) with progressive atypia and expansion of the immature basal cells above the lower third of the epithelial thickness; HSIL (CIN III) with diffuse atypia, loss of maturation, and expansion of the immature basal cells to the epithelial surface.

More than 80% of LSILs and 100% of HSILs are associated with high-risk HPVs, with HPV-16 being the most common HPV type in both categories of lesions. Table 22-2 shows rates of regression and progression of SILs within 2-year follow-up. Although the majority of HSILs develop from LSILs, approximately 20% of cases of HSIL develop de novo, independent of any preexisting LSIL. The rates of progression are by no means uniform, and although HPV type—especially HPV 16—is associated with increased risk, it is difficult to predict the outcome in an individual patient. These findings underscore that the risk of developing precursor lesions and cancer is conferred only in part by HPV type. Progression to invasive carcinoma, when it occurs, takes place over a period of a few years to more than a decade.

Cervical Carcinoma

The average age of patients with invasive cervical carcinoma is 45 years. Squamous cell carcinoma is the most common histologic subtype, accounting for approximately 80% of cases. The second most common tumor type is adenocarcinoma, which constitutes about 15% of cervical cancer cases and develops from a precursor lesion called *adenocarcinoma in situ*. Adenosquamous and neuroendocrine carcinomas are rare cervical tumors that account for the remaining 5% of cases. All of the aforementioned tumor types are caused by high-risk HPVs. The progression time from in situ to invasive adenosquamous and neuroendocrine carcinomas is shorter than in squamous cell carcinoma, and patients with these tumors often

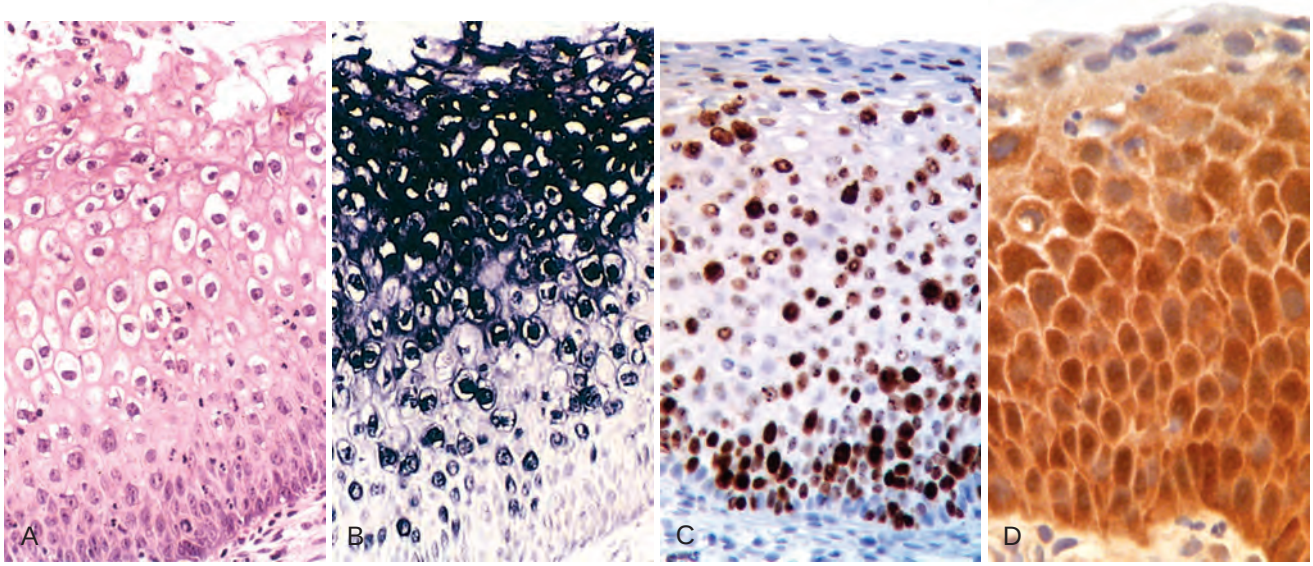

Figure 22-15 **A,** Low-grade squamous intraepithelial lesion (LSIL)—Routine hematoxylin and eosin staining shows marked koilocytic change, seen as perinuclear "halos" in suprabasilar cells. **B,** In situ hybridization test for HPV DNA. The dark granular staining denotes HPV DNA, which is typically most abundant in the koilocytes. **C,** Diffuse positivity for the proliferation marker Ki-67 (seen as brown nuclear staining), illustrates abnormal expansion of the proliferating cells from the normal basal location to the superficial layers of the epithelium. **D,** Upregulation of the cyclin-dependent kinase inhibitor p16 (seen here as brown staining) characterizes high-risk HPV infections.