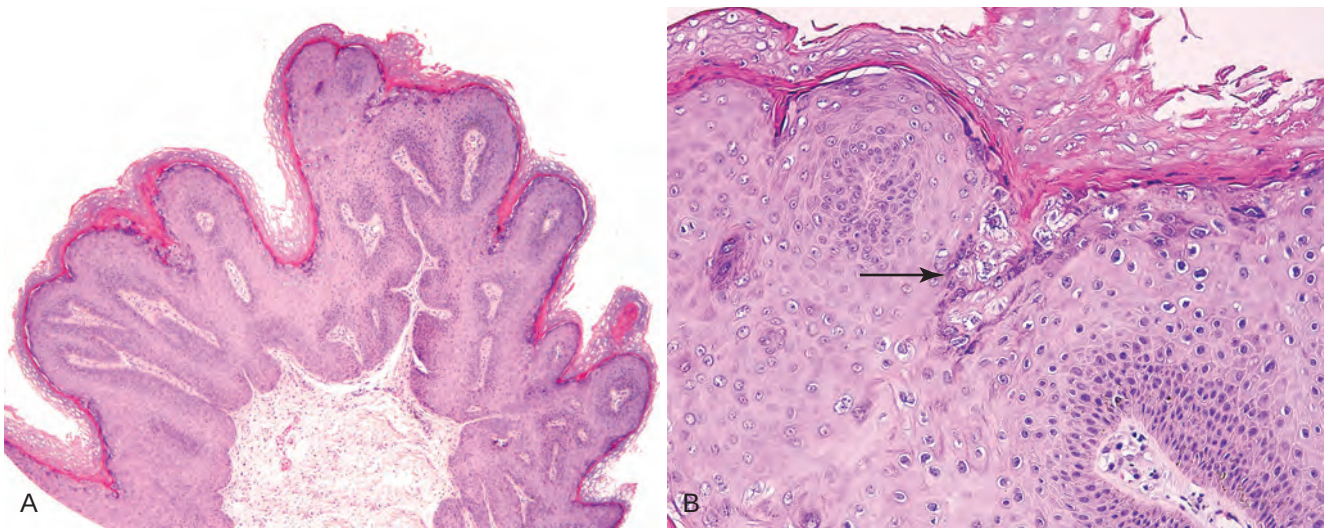

Figure 22-6 Condyloma acuminatum. **A,** Low-power view showing exophytic, papillary architecture. **B,** High-power view reveals HPV cytopathic effect (koilocytic atypia) characterized by atypical, enlarged, hyperchromatic nuclei with perinuclear halos *(arrow).*

fibroepithelial polyps, or skin tags, are similar to skin tags occurring elsewhere on the skin. Vulvar *squamous papillomas* are benign exophytic proliferations covered by nonkeratinized squamous epithelium, which develop on vulvar surfaces and may be single or numerous (vulvar papillomatosis). The etiology of fibroepithelial polyps and squamous papillomas is unknown.

Condyloma Acuminatum

Condylomata acuminata are benign genital warts caused by low oncogenic risk HPVs, mainly types 6 and 11. They may be solitary, but are more frequently multifocal, and may involve vulvar, perineal, and perianal regions as well as the vagina and, less commonly, the cervix. The lesions are identical to those found on the penis and around the anus in males (Chapter 21). On histologic examination, they consist of papillary, exophytic, treelike cores of stroma covered by thickened squamous epithelium (Fig. 22-6*A*). The surface epithelium shows characteristic viral cytopathic changes referred to as *koilocytic atypia* (Fig. 22-6*B*), which manifest as nuclear enlargement, hyperchromasia and a cytoplasmic perinuclear halo (see also "Cervix"). Condylomata acuminata are not precancerous lesions.

Squamous Neoplastic Lesions

Vulvar Intraepithelial Neoplasia and Vulvar Carcinoma

Carcinoma of the vulva is an uncommon malignant neoplasm (approximately one eighth as frequent as cervical cancer) representing about 3% of all genital cancers in the female; approximately two thirds occur in women older than 60 years. Squamous cell carcinoma is the most common histologic type of vulvar cancer. In terms of etiology, pathogenesis, and histologic features, vulvar squamous cell carcinomas are divided into two groups:

- Basaloid and warty carcinomas related to infection with high risk HPVs (30% of cases), most commonly HPV-16. These are less common and occur at younger ages.
- Keratinizing squamous cell carcinomas unrelated to HPV infection (70% of cases). These are more common and occur in older women.

Basaloid and warty carcinomas develop from an in situ precursor lesion called *classic vulvar intraepithelial neoplasia* (VIN). This form of VIN occurs mainly in reproductive age women and includes lesions designated formerly as carcinoma in situ or Bowen disease. The risk factors for VIN are the same as those associated with cervical squamous intraepithelial lesions (e.g., young age at first intercourse, multiple sexual partners, male partner with multiple sexual partners), as both are related to HPV infection. VIN is frequently multicentric, and 10% to 30% of patients with VIN also have vaginal or cervical HPV-related lesions. Spontaneous regression of classic VIN has been reported, usually in younger women. The risk of progression to invasive carcinoma is higher in women older than 45 years of age or in women who are immunosuppressed. The peak age for basaloid and warty vulvar cancer is in the sixth decade.

Keratinizing squamous cell carcinoma occurs most often in individuals with long-standing lichen sclerosus or squamous cell hyperplasia and is not related to HPV. The peak occurrence is in the eighth decade. It arises from a precursor lesion referred to as *differentiated vulvar intraepithelial neoplasia* (differentiated VIN) or *VIN simplex*. It is postulated that chronic epithelial irritation in lichen sclerosus or squamous cell hyperplasia may contribute to a gradual evolution to the malignant phenotype, presumably through acquisition of driver mutations in oncogenes and tumor suppressors. In line with this idea, some investigators have reported a high frequency of *TP53* mutations in differentiated VIN.