



**Figure 22-10** Paget disease of the vulva. **A**, The epidermis is infiltrated by large cells with pale-pink cytoplasm that are spreading along the basal portion of the squamous epithelium. There is inflammation in the underlying dermis. **B**, Immunostaining for cytokeratin 7 highlights the intraepidermal Paget cells.

## VAGINA

The vagina is a portion of the female genital tract that is remarkably free from primary disease. In the adult, inflammation often affects the vulva and perivulvar structures and spreads to the cervix without significant involvement of the vagina. Primary lesions of the vagina are rare, the most serious being vaginal squamous cell carcinoma; they are discussed only briefly here.

### Developmental Anomalies

*Septate, or double, vagina* is an uncommon anomaly that arises from a failure of müllerian duct fusion and is accompanied by a double uterus (uterus didelphys). These and other anomalies of the external genitalia may be the manifestations of genetic syndromes, in utero exposure to diethylstilbestrol (DES, used to prevent threatened abortions in the 1940s through 1960s), or other unknown factors that perturb reciprocal epithelial-stromal signaling during fetal development.

During embryonal development, the vagina is initially covered by columnar, endocervical-type epithelium. This is normally replaced by squamous epithelium advancing upwards from the urogenital sinus. Small patches of residual glandular epithelium may persist into adult life and is recognized as *vaginal adenosis*. It presents clinically as red, granular areas that stand out from the surrounding normal pale-pink vaginal mucosa. On microscopic examination, adenosis consists of columnar mucinous epithelium indistinguishable from endocervical epithelium. Adenosis is found in only a small percentage of adult women, but has been reported in 35% to 90% of women exposed to DES in utero. Rare cases of clear cell carcinoma arising in DES-related adenosis were recorded in teenagers and young adult women in the 1970s and 1980s, resulting in discontinuation of DES treatment.

*Gartner duct cysts* are relatively common lesions found along the lateral walls of the vagina and are derived from

wolffian (mesonephric) duct rests. They are 1- to 2-cm fluid-filled cysts that occur in the submucosal location. Other cysts, including mucus cysts, which occur in the proximal vagina, are derived from müllerian epithelium. Another müllerian-derived lesion, endometriosis (described later), may occur in the vagina and clinically simulate a neoplasm.

### Premalignant and Malignant Neoplasms of the Vagina

Most of the benign tumors of the vagina occur in reproductive-age women and include stromal tumors (stromal polyps), leiomyomas, and hemangiomas. The most common malignant tumor to involve the vagina is carcinoma spreading from the cervix, followed by primary squamous cell carcinoma of the vagina. Infants may develop a unique, rare malignancy—embryonal rhabdomyosarcoma (sarcoma botryoides).

### Vaginal Intraepithelial Neoplasia and Squamous Cell Carcinoma

**Virtually all primary carcinomas of the vagina are squamous cell carcinomas associated with high risk HPVs.** It is an extremely uncommon cancer (about 0.6 per 100,000 women yearly) that accounts for about 1% of malignant neoplasms in the female genital tract. The greatest risk factor is a previous carcinoma of the cervix or vulva; 1% to 2% of women with an invasive cervical carcinoma eventually develop a vaginal squamous cell carcinoma. Squamous cell carcinoma of the vagina arises from a premalignant lesion, *vaginal intraepithelial neoplasia*, analogous to cervical squamous intraepithelial lesions (SILs, see under “Cervix”). Most often the invasive tumor affects the upper vagina,