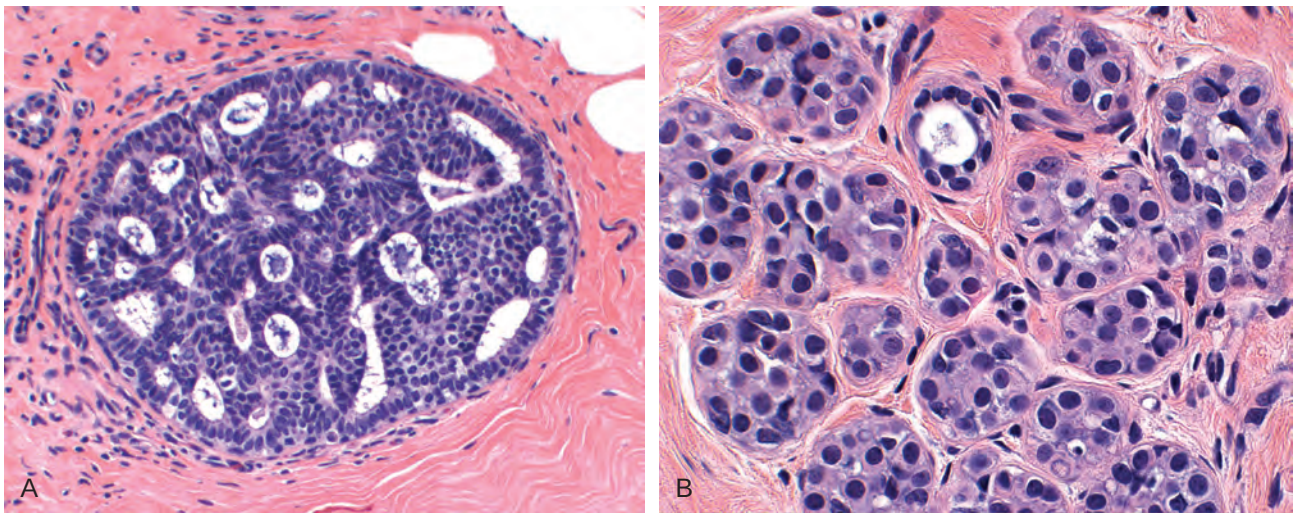

Figure 23-12 **A,** Atypical ductal hyperplasia. A duct is filled with a mixed population of cells consisting of oriented columnar cells at the periphery and more rounded cells within the central portion. Although some of the spaces are round and regular, the peripheral spaces are irregular and slitlike. These features are highly atypical, but fall short of a diagnosis of ductal carcinoma in situ. **B,** Atypical lobular hyperplasia. A population of monomorphic small, round, loosely cohesive cells partially fills a lobule. Although the cells are morphologically identical to the cells of lobular carcinoma in situ, the extent of involvement is not sufficient for this diagnosis.

Atypical ductal and atypical lobular hyperplasias may have acquired chromosomal aberrations such as loss of 16q or gain of 17p, changes also found in carcinoma in situ. Atypical lobular hyperplasia also shows loss of E-cadherin expression, a feature it shares with lobular carcinoma in situ (discussed later). This form of intraepithelial spread is called "pagetoid" because of its resemblance to Paget disease, described later.

Clinical Significance of Benign Epithelial Changes

Epidemiologic studies have established the association of benign histologic changes with the later development of invasive cancer (Table 23-1). Nonproliferative changes do not increase the risk of cancer. Proliferative disease is associated with a 1.5- to two-fold increased risk, while proliferative disease with atypia confers a four- to five-fold increased risk. Both breasts are at increased risk, although the risk to the ipsilateral breast may be slightly higher. Risk reduction can be achieved by bilateral prophylactic mastectomy or treatment with estrogen antagonists, such as tamoxifen. However, fewer than 20% of women with atypical hyperplasia develop breast cancer, and therefore many choose careful clinical and radiologic surveillance over intervention.

KEY CONCEPTS

Benign Epithelial Lesions

- Benign epithelial lesions usually do not cause symptoms but are frequently detected as mammographic calcifications or densities.
- These lesions are classified according to the subsequent risk of cancer in either breast.
- The majority are not precursors of cancer.
- Although risk reduction can be achieved by surgery or chemoprevention, the majority of women will not develop cancer and many women choose surveillance instead of intervention.

Carcinoma of the Breast

Carcinoma of the breast is the most common non-skin malignancy in women and is second only to lung cancer as a cause of cancer deaths. A woman who lives to age 90 has a one in eight chance of developing breast cancer. In 2012, approximately 226,000 women in the United States were diagnosed with invasive breast cancer, 63,000 with carcinoma in situ, and almost 40,000 women died of the

Table 23-1 Epithelial Breast Lesions and the Risk of Developing Invasive Carcinoma

Pathologic Lesion	Relative Risk (Absolute Lifetime Risk)*
Nonproliferative Breast Changes (Fibrocystic changes)	1 (3%)
Duct ectasia Cysts Apocrine change Mild hyperplasia Adenosis Fibroadenoma without complex features	
Proliferative Disease Without Atypia	1.5 to 2 (5%-7%)
Moderate or florid hyperplasia Sclerosing adenosis Papilloma Complex sclerosing lesion (radial scar) Fibroadenoma with complex features	
Proliferative Disease with Atypia	4 to 5 (13%-17%)
Atypical ductal hyperplasia (ADH) Atypical lobular hyperplasia (ALH)	
Carcinoma in Situ	8 to 10 (25%-30%)
Lobular carcinoma in situ (LCIS) Ductal carcinoma in situ (DCIS)	

*Relative risk is the risk compared to women without any risk factors. Absolute lifetime risk is the percentage of patients expected to develop invasive carcinoma if untreated.