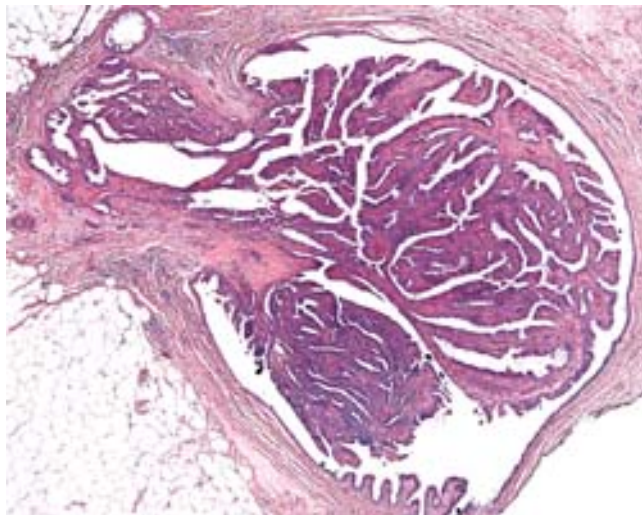


Papillomas.

Papillomas are composed of multiple branching fibrovascular cores, each having a connective tissue axis lined by luminal and myoepithelial cells ([Fig. 23-11](#)). Growth occurs within a dilated duct. Epithelial hyperplasia and apocrine metaplasia are frequently present. Large duct papillomas are usually solitary and situated in the lactiferous sinuses of the nipple. Small duct papillomas are commonly multiple and located deeper within the ductal system.

Small duct papillomas have been shown to be a component of proliferative breast disease and increase the risk of subsequent carcinoma. It is less clear whether or not large duct papillomas carry the same risk



PROLIFERATIVE BREAST DISEASE WITH ATYPIA

Proliferative disease with atypia includes atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH). ADH is present in 5% to 17% of biopsies performed for calcifications and is found less frequently in biopsies for mammographic densities or palpable masses.

CLINICAL SIGNIFICANCE OF BENIGN EPITHELIAL CHANGES

Nonproliferative changes do not increase the risk of cancer. Proliferative disease is associated with a mild increase in risk. Proliferative disease with atypia (ADH and ALH) confers a moderate increase in risk.

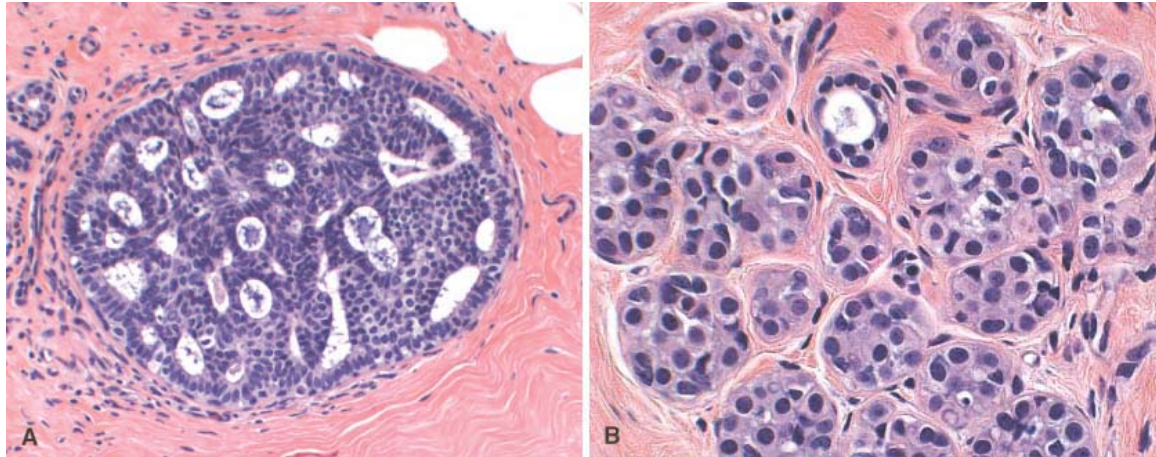


Figure 23-12 *A*, Atypical ductal hyperplasia. A duct is filled with a mixed population of cells consisting of oriented columnar cells at the periphery and more rounded cells within the central portion. Although some of the spaces are round and regular, the peripheral spaces are irregular and slitlike.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

Carcinoma of the Breast

Carcinoma is the most common malignancy of the breast, and breast cancer is the most common non-skin malignancy in women

Risk Factors.

- ***Age.***
- ***Age at Menarche.***
- ***First Live Birth.***
- ***First-Degree Relatives with Breast Cancer.***
- ***Breast Biopsies.***
- ***Race.***
- ***Estrogen Exposure.***
- ***Radiation Exposure.***
- ***Carcinoma of the Contralateral Breast or Endometrium.***
- ***Geographic Influence***
- ***Diet.***
- ***Obesity.***
- ***Breast-Feeding.***

Hereditary Breast Cancer

About 25% of familial cancers (or around 3% of all breast cancers) can be attributed to two highly penetrant autosomal dominant genes: BRCA1 and BRCA2. The probability of breast cancer associated with a mutation in these genes increases if there are multiple affected first-degree relatives

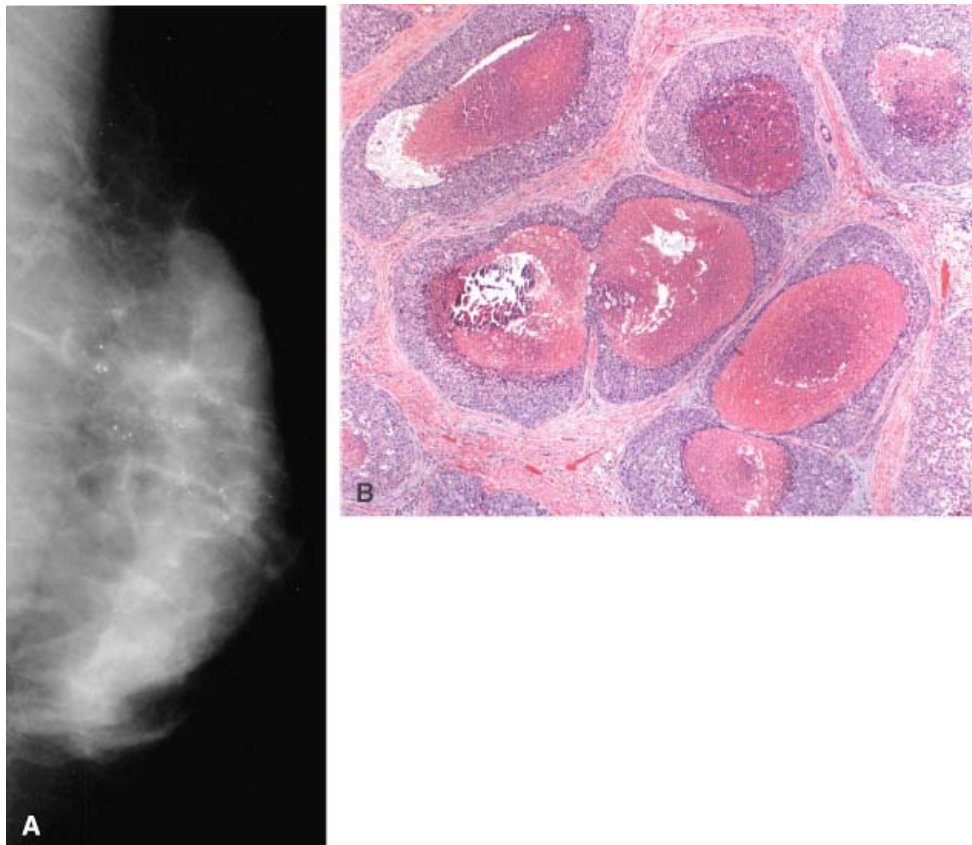
BRCA1-associated breast cancers are more commonly poorly differentiated, have a syncytial growth pattern with pushing margins, have a lymphocytic response, and do not express hormone receptors or overexpress *HER2/neu* (an epidermal growth factor receptor that is commonly overexpressed in breast cancer, to be discussed later), as compared to sporadic breast carcinomas. *BRCA2*-associated breast carcinomas do not have a distinct morphologic appearance.

CLASSIFICATION OF BREAST CARCINOMA

Carcinomas are divided into in situ carcinomas and invasive carcinomas. Carcinoma in situ refers to a neoplastic population of cells limited to ducts and lobules by the basement membrane. In some cases, the cells can extend to the overlying skin without crossing the basement membrane and appear clinically as Paget disease. However, carcinoma in situ does not invade into lymphatics and blood vessels and cannot metastasize

Carcinoma in situ was originally classified as ductal or lobular on the basis of the resemblance of the involved spaces to ducts and lobules

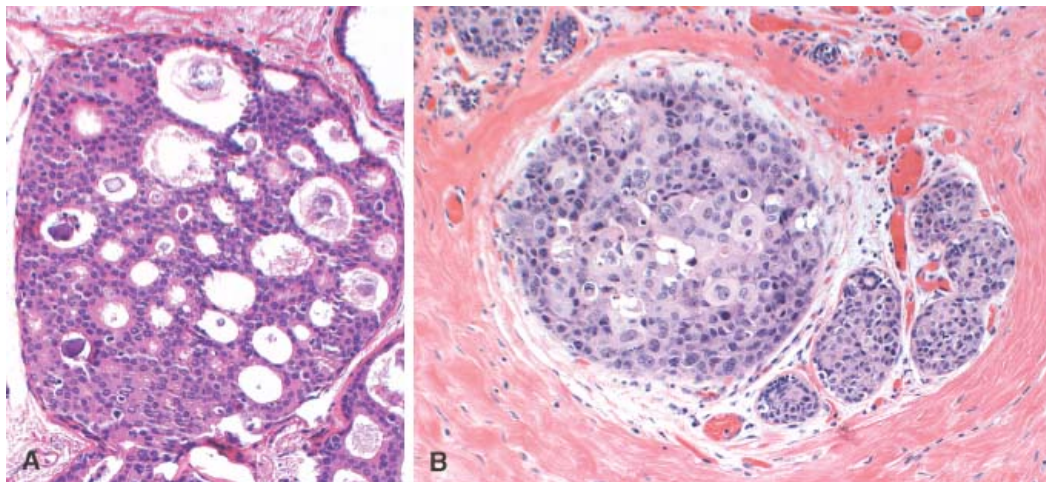
Ductal Carcinoma in Situ (DCIS; Intraductal Carcinoma)



DCIS consists of a malignant population of cells limited to ducts and lobules by the basement membrane. The myoepithelial cells are preserved, although they may be diminished in number. DCIS is a clonal proliferation and usually involves only a single ductal system

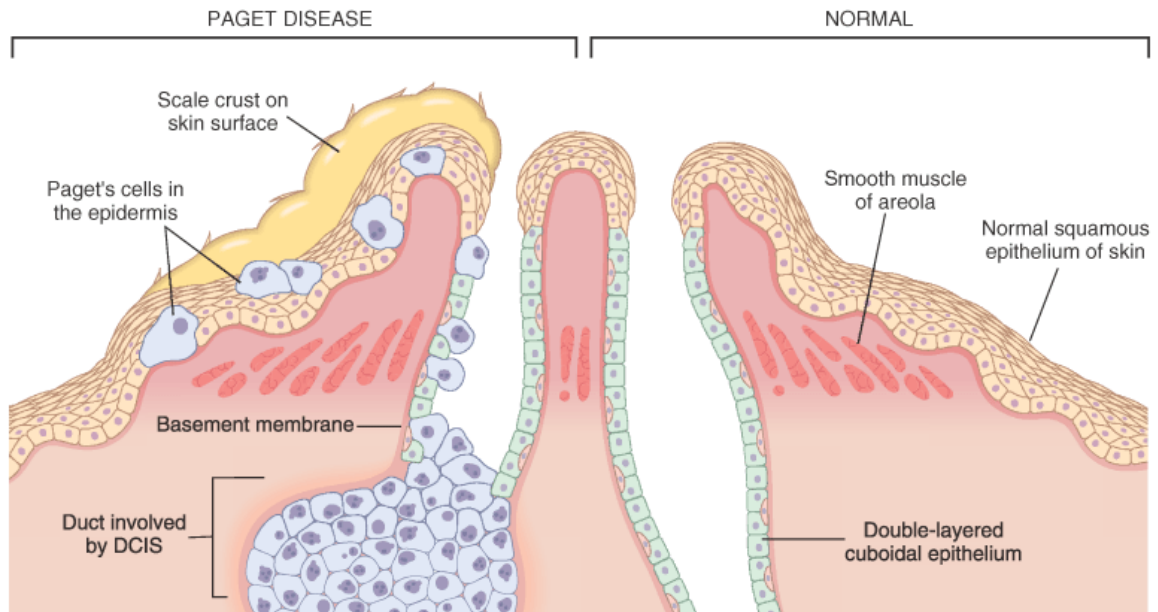
Comedocarcinoma is characterized by solid sheets of pleomorphic cells with high-grade nuclei and central necrosis . The necrotic cell membranes commonly calcify and are detected on mammography as clusters or linear and branching microcalcifications . Periductal concentric fibrosis and chronic inflammation are common,

Noncomedo DCIS consists of a monomorphic population of cells with nuclear grades ranging from low to high. In cribriform DCIS, intraepithelial spaces are evenly distributed and regular in shape (cookie cutter-like). Solid DCIS completely fills the involved spaces .



Paget disease of the nipple is a rare manifestation of breast cancer (1% to 2% of cases) and presents as a unilateral erythematous eruption with a scale crust. Pruritus is common, and the lesion might be mistaken for eczema. Malignant cells, referred to as Paget cells, extend from DCIS within the ductal system into nipple skin without crossing the basement membrane

A palpable mass is present in 50% to 60% of women with Paget disease, and almost all of these women will have an underlying invasive carcinoma.



Lobular Carcinoma in Situ (LCIS)

LCIS is always an incidental finding in a biopsy performed for another reason, as LCIS is not associated with calcifications or a stromal reaction that would form a density

LCIS is bilateral in 20% to 40% of women when both breasts are biopsied,

compared to 10% to 20% of cases of DCIS. LCIS is more common in young women, 80% to 90% of cases occurring prior to menopause.

The abnormal cells of atypical lobular hyperplasia (ALH), LCIS, and invasive lobular carcinoma are identical and consist of small cells that have oval or round nuclei with small nucleoli that do not adhere to one another. Signet-ring cells containing mucin are present commonly. LCIS rarely distorts the underlying architecture, and the involved acini remain recognizable as lobules.