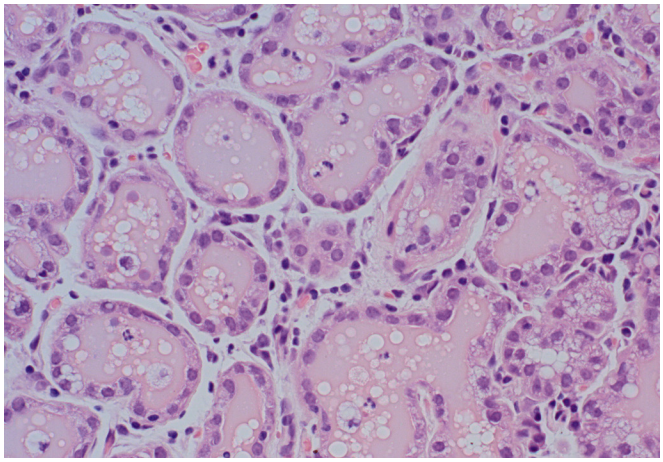
CHAPTER 23

The Breast

PBD9 Chapter 23 and PBD8 Chapter 23: The Breast

BP9 Chapter 18 and BP8 Chapter 19: Female Genital System and Breast



1 A 21-year-old woman delivered a normal term infant a week ago and is now nursing the infant. She now notes a lump in her right axilla that has increased in size over the past week. On physical examination there is a rubbery, mobile, 1.5-cm mass beneath the skin at the right anterior axillary line. The mass is excised and the microscopic appearance is shown in the figure. Which of the following hormones most likely produced the greatest effect upon this tissue?

A Cortisol
B Growth hormone
C Oxytocin
D Prolactin
E Testosterone

2 A 24-year-old woman is breastfeeding 3 weeks after giving birth to a normal term infant. She notices fissures in the skin around her left nipple. Over the next 3 days, a 5-cm region near the nipple becomes erythematous and tender. Purulent exudate from a small abscess drains through a fissure. Which of the following organisms is most likely to be cultured from the exudate?

A *Candida albicans*
B *Lactobacillus acidophilus*
C *Listeria monocytogenes*
D *Staphylococcus aureus*
E Viridans streptococci

3 A 30-year-old woman sustained a traumatic blow to her right breast. Initially, there was a 3-cm contusion beneath the skin that resolved within 3 weeks, but she then felt a firm, painless lump that persisted below the site of the bruise 1 month later. What is the most likely diagnosis for this lump?

A Abscess
B Fat necrosis
C Fibroadenoma
D Inflammatory carcinoma
E Sclerosing adenosis

4 A study of mammographic findings on women of reproductive years is performed. The study identifies mammograms showing 1- to 5-cm cysts with focal microcalcifications and surrounding densities. Subsequent fine-needle aspiration yielded turbid fluid with few cells. Which of the following microscopic changes is most likely to be present in these lesions?

A Apocrine metaplasia
B Ductal carcinoma in situ
C Fat necrosis
D Papillomatosis
E Sclerosing adenosis

5 A 27-year-old woman feels a lump in her right breast. She has normal menstrual cycles, she is G3, P3, and her last child was born 5 years ago. On examination a 2-cm, irregular, firm area is palpated beneath the lateral edge of the areola. This lumpy area is not painful and is movable. There are no lesions of the overlying skin and no axillary lymphadenopathy. A biopsy specimen shows microscopic evidence of an increased number of dilated ducts surrounded by fibrous connective tissue. Fluid-filled ducts with apocrine metaplasia also are present. What is the most likely diagnosis?

A Fibroadenoma
B Fibrocystic changes
C Infiltrating ductal carcinoma
D Mammary duct ectasia
E Traumatic fat necrosis

6 A 47-year-old woman has a routine health examination. There are no remarkable findings except for a barely palpable mass in the right breast. A mammogram shows an irregular, 1.5-cm area of density with scattered microcalcifications in the upper outer quadrant. A biopsy specimen from this area is obtained and microscopically shows ductal hyperplasia. Which of the following is the most appropriate option for follow-up of this patient?

A Cessation of smoking cigarettes
B Continued screening for breast cancer
C Performing a simple mastectomy
D Testing for the *BRCA1* oncogene
E Prescribing broad-spectrum antibiotic therapy

7 A 34-year-old woman has noticed a bloody discharge from the nipple of her left breast for the past 3 days. On physical examination, the skin of the breasts appears normal, and no masses are palpable. There is no axillary lymphadenopathy. She has regular menstrual cycles and is using oral contraceptives. Excisional biopsy is most likely to show which of the following lesions in her left breast?

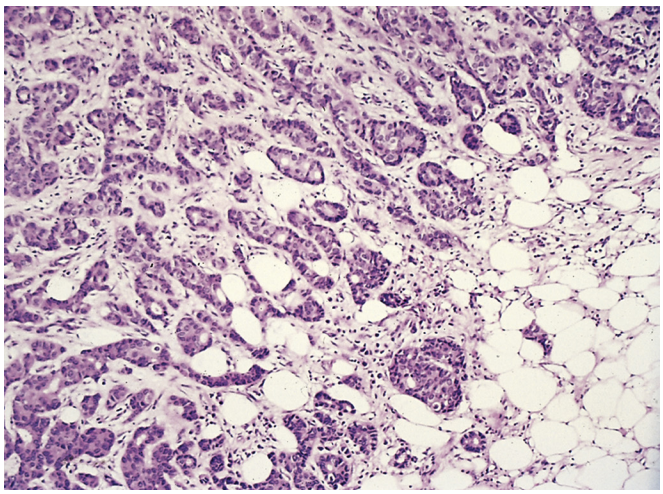
A Acute mastitis
B Fibroadenoma
C Intraductal papilloma
D Phyllodes tumor
E Sclerosing adenosis

8 A 57-year-old man has developed bilateral breast enlargement over the past 2 years. On physical examination, the enlargement is symmetric and is not painful to palpation. There are no masses. He is not obese and is not taking any medications. Which of the following underlying conditions best accounts for his findings?

A ACTH-secreting pituitary adenoma
B Choriocarcinoma of the testis
C Chronic glomerulonephritis
D Diabetes mellitus
E Micronodular cirrhosis
F Rheumatoid arthritis

9 A 58-year-old woman sees her naturopathic health care provider for a routine health examination. There are no remarkable findings on physical examination. A screening mammogram shows a 0.5-cm irregular area of increased density with scattered microcalcifications in the upper outer quadrant of the left breast. Excisional biopsy shows atypical lobular hyperplasia. She has been on postmenopausal estrogen-progesterone therapy for the past 10 years. She has smoked 1 pack of cigarettes per day for the past 35 years. Which of the following is the most significant risk factor for the development of lobular carcinoma in patients with such lesions?

A Atypical cytologic changes
B History of smoking
C Hormone replacement therapy
D Postmenopausal age
E Underlying *BRCA1* gene mutation

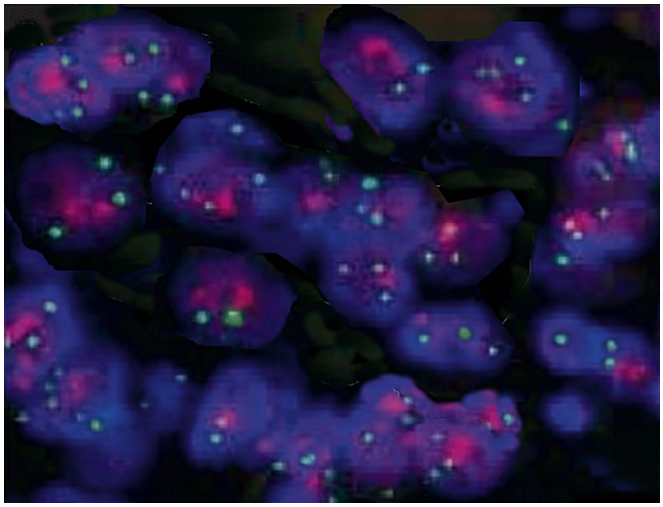


10 A 25-year-old Jewish woman sees her physician after finding a lump in her right breast. On physical examination, a 2-cm, firm, nonmovable mass is palpated in the upper outer quadrant. No overlying skin lesions and no axillary lymphadenopathy are present. The figure shows an excisional biopsy specimen. The family history indicates that the patient's mother, maternal aunt, and maternal grandmother have had similar lesions. Her 18-year-old sister has asked a physician to determine whether she is genetically at risk of developing a similar disease. A mutated gene encoding for which of the following is most likely to be found in her sister?

A *BRCA1*
B Estrogen receptor *(ER)*
C *HER2/neu*
D *TP53*
E Progesterone receptor *(PR)*
F *RB1*

11 A clinical study is performed on postmenopausal women living in Paris, France, who are between the ages of 45 and 70 years. All have been diagnosed with infiltrating ductal carcinoma positive for estrogen receptor (ER) and progesterone receptor (PR), but negative for *HER2* expression, which has been confirmed by biopsy and microscopic examination of tissue. None has the *BRCA1* or *BRCA2* mutation. Which of the following is most likely to indicate the highest relative risk of developing the carcinomas seen in this group of women?

A Age at menarche older than 16 years
B Age at menopause younger than 45 years
C First-degree relative with breast cancer
D Multiparity
E Prior diagnosis of mastitis

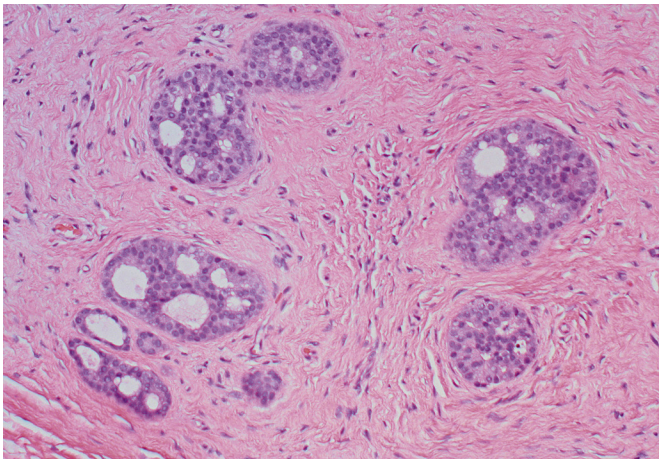


12 A 54-year-old woman feels a lump in her left breast. On examination there is a firm, irregular mass in the lower outer quadrant. A mammogram shows a 2-cm density with focal microcalcifications. Excisional biopsy shows intraductal and invasive carcinoma. Immunohistochemical staining is negative for estrogen receptor (ER). FISH analysis (green = *HER2*; red = chromosome 17 centromere) shows the findings in the figure. When combined with doxorubicin, which of the following drugs is most likely to be useful in treating this patient?

A Hydroxyurea
B Letrozole
C Raloxifene
D Tamoxifen
E Trastuzumab

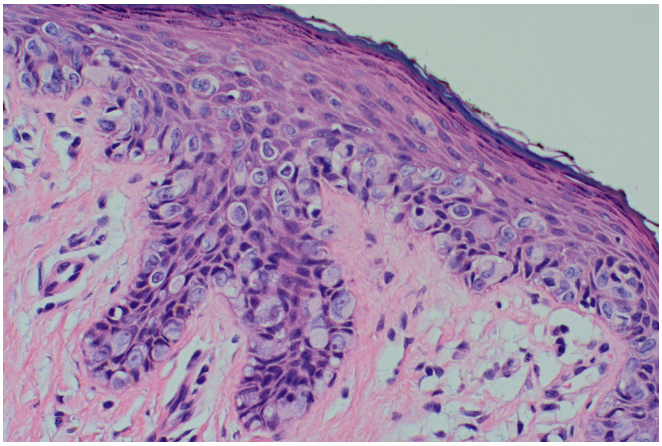
13 A 66-year-old nulliparous woman received hormone replacement therapy for 7 years following menopause at age 53 years. Her BMI is 33. She now undergoes screening mammography, and an irregular mass is identified in the right breast. An excisional biopsy yields a 1.5-cm mass that microscopically has invasive cells that are positive for estrogen receptor but negative for *HER2,* with low proliferation markers and mutated *PIK3CA* gene. Following surgical removal of the mass, which of the following clinical courses will most likely occur over the next year?

A Detection of cancer in the left breast
B Need for chemotherapy
C Very low likelihood of recurrence
D Need for treatment with trastuzumab
E Occurrence of widespread metastases



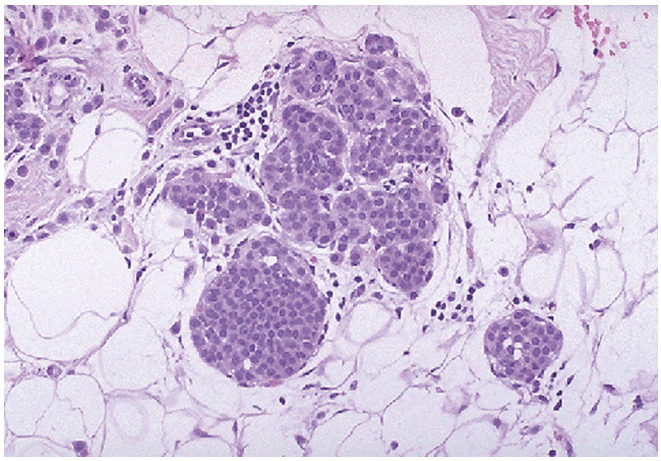
14 A 63-year-old woman has a screening mammogram that shows an irregular density with microcalcifications. On physical examination, there are no lesions of the overlying skin, and there is no axillary lymphadenopathy. An excisional biopsy specimen shows no mass on sectioning. Microscopic examination shows the findings in the figure. What is the most likely diagnosis?

A Colloid carcinoma
B Ductal carcinoma in situ
C Infiltrating ductal carcinoma
D Infiltrating lobular carcinoma
E Medullary carcinoma
F Papillary carcinoma



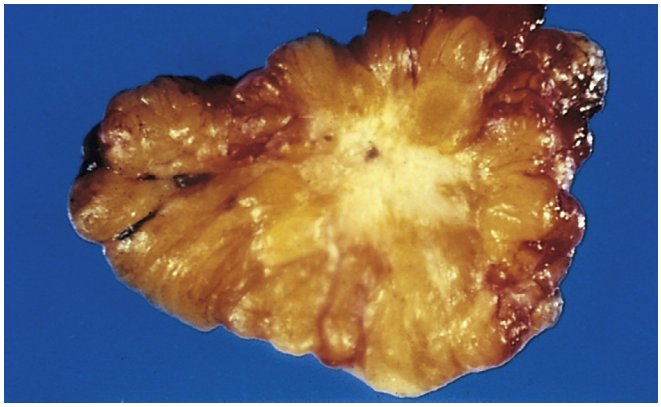
15 A 48-year-old woman has noticed a red, scaly area of skin on her left breast that has grown slightly larger over the past 4 months. On physical examination, there is a 1-cm area of eczematous skin adjacent to the areola. The figure shows the microscopic appearance of the skin biopsy specimen. What is the most likely diagnosis?

A Apocrine metaplasia
B Fat necrosis
C Inflammatory carcinoma
D Lobular carcinoma in situ
E Paget disease of the breast



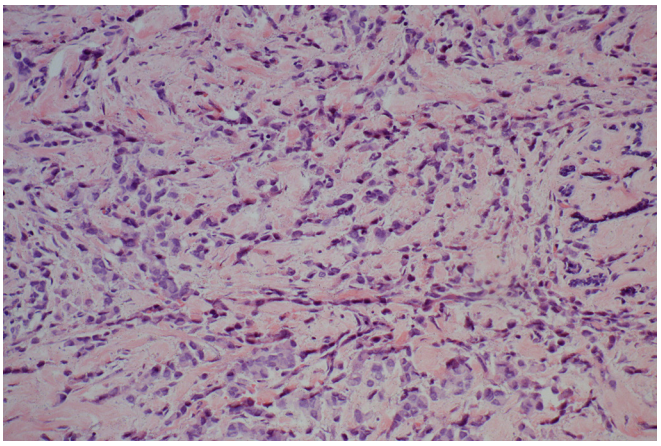
16 A 54-year-old woman noticed a lump in her right breast. On examination, she has an ill-defined, 1-cm mass in the upper outer quadrant. The mass is cystic on ultrasound. An excision is done, and microscopically the mass shows predominantly fibrocystic changes, but the lesion shown in the figure also is present. Fine-needle aspirates of both breasts reveal additional foci of similar cells. Which of the following breast lesions is most likely to produce these findings?

A Infiltrating ductal carcinoma
B Lobular carcinoma in situ
C Malignant phyllodes tumor
D Medullary carcinoma
E Mucinous (colloid) carcinoma



17 A 49-year-old woman felt a lump in her left breast 1 week ago. On examination, a firm, irregular mass is palpable in the upper outer quadrant of her left breast. There are no overlying skin lesions. The gross appearance of the excisional biopsy specimen is shown in the figure. Which of the following additional findings is she most likely to have on physical examination?

A Axillary lymphadenopathy
B Bloody discharge from the nipple
C Chest wall tenderness
D Cushingoid facies
E Mass in the opposite breast



18 A 57-year-old woman has felt a lump in her left breast for 4 months. She has had new onset headaches associated with nausea for the past month. Her physician palpates a firm but irregular 2-cm mass in her left breast. CT imaging of her brain shows leptomeningeal enhancement. A lumpectomy with axillary node sampling is performed. Immunohistochemical staining of these cells shows absence of E-cadherin and HER2, but presence of estrogen receptor (ER) and progesterone receptor (PR). An H and E stained section is shown in the figure. No nodal metastases are present. Which of the following is the most likely diagnosis?

A Lobular carcinoma
B Medullary carcinoma
C Metaplastic carcinoma
D Metastatic glioblastoma
E Phyllodes tumor

19 A 39-year-old woman has noticed an enlarging mass in her left breast for the past 2 years. The physician palpates a 4-cm firm mass. Following biopsy, a simple mastectomy is performed with axillary lymph node sampling. On gross sectioning, the mass has a soft, tan, fleshy surface. Histologically, the mass is composed of large cells with vesicular nuclei and prominent nucleoli. There is a marked lymphocytic infiltrate within the tumor, and the tumor has a discrete, noninfiltrative border. No axillary node metastases are present. The tumor cells are triple negative, for HER2, estrogen receptor (ER), and progesterone receptor (PR). What is the most likely diagnosis?

A Colloid carcinoma
B Infiltrating ductal carcinoma
C Infiltrating lobular carcinoma
D Medullary carcinoma
E Papillary carcinoma
F Phyllodes tumor

20 An epidemiologic study is conducted with male subjects who have been diagnosed with breast carcinoma. Their demographic data, medical histories, family histories, and laboratory data are examined to identify factors that increase the risk of cancer. Which of the following factors is most likely to be associated with the greatest number of male breast carcinomas?

A Age older than 70 years
B Asian ancestry
C *ATM* gene mutation
D Chronic alcoholism
E Gynecomastia

21 A study of women with breast carcinoma is done to determine the presence and amount of estrogen receptor (ER) and progesterone receptor (PR) in the carcinoma cells. Large amounts of ER and PR are found in the carcinoma cells of some patients. These receptors are not present in the cells of other patients. The patients with positivity for ER and PR are likely to exhibit which of the following traits?

A Greater immunogenicity
B Greater likelihood of metastases
C Greater risk of familial breast cancer
D Higher response to therapy
E Higher tumor stage
F Higher tumor grade

22 A 26-year-old woman has felt a breast lump for the past month and is worried because she has a family history of early onset and bilateral breast cancers. On physical examination, there is a firm, 2-cm mass in the upper outer quadrant of her left breast. A biopsy is done, and the specimen microscopically shows carcinoma. Genetic analysis shows that she is a carrier of the *BRCA1* gene mutation, as are her mother and sister. Which of the following histologic types of breast carcinoma has the highest incidence in families such as hers?

A Lobular carcinoma
B Medullary carcinoma
C Metaplastic carcinoma
D Papillary carcinoma
E Tubular carcinoma

23 A 79-year-old, previously healthy woman feels a lump in her right breast. The physician palpates a 2-cm firm mass in the upper outer quadrant. Nontender right axillary lymphadenopathy is present. A lumpectomy with axillary lymph node dissection is performed. Microscopic examination shows that the mass is an infiltrating ductal carcinoma. Two of 10 axillary nodes contain metastases. Flow cytometry on the carcinoma cells shows a small aneuploid peak and high S-phase. Immunohistochemical tests show that the tumor cells are positive for estrogen and progesterone receptor (ER/PR), negative for *HER2/neu* expression, and positive for cathepsin D expression. What is the most important prognostic factor for this patient?

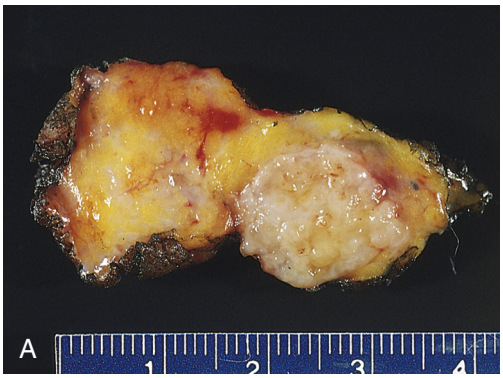
A Age at diagnosis
B DNA content in the carcinoma
C Estrogen receptor positivity
D Expression of stromal proteases in the carcinoma
E Histologic subtype of carcinoma
F Lack of *HER2/neu* expression in the carcinoma
G Presence of lymph node metastases

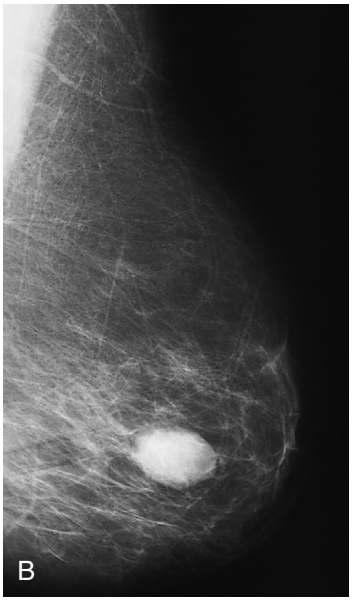
24 A study of gene expression profiling involving breast biopsies showing invasive carcinoma of no specific type (NST) is performed. A subset of these cases, comprising about 15% of all cases, has the following characteristics: estrogen receptor (ER) and progesterone receptor (PR) negative, *HER2/neu* negative, basal keratin positive, flow cytometry showing aneuploidy and high proliferation rate, and association with *BRCA1* mutations. Which of the following therapies is most likely to be effective in women with this subset of NST breast cancer?

A Chemotherapy
B Radiation
C Surgery alone
D Tamoxifen
E Trastuzumab

25 A 51-year-old woman has noticed an area of swelling with tenderness in her right breast that has worsened over the past 2 months. On physical examination, the 7-cm area of erythematous skin is tender with a rough, firm surface resembling an orange peel. There is swelling of the right breast, nipple retraction, and right axillary nontender lymphadenopathy. Excisional biopsy of skin and breast is most likely to show which of the following lesions?

A Acute mastitis
B Atypical epithelial hyperplasia
C Fat necrosis
D Infiltrating ductal carcinoma
E Sclerosing adenosis





26 A 26-year-old woman has noticed a lump in her right breast for the past year. A 2-cm, firm, circumscribed, movable mass is palpated in the lower outer quadrant. The figure shows the excised mass (*A*) and the mammogram (*B*). What is the most likely diagnosis?

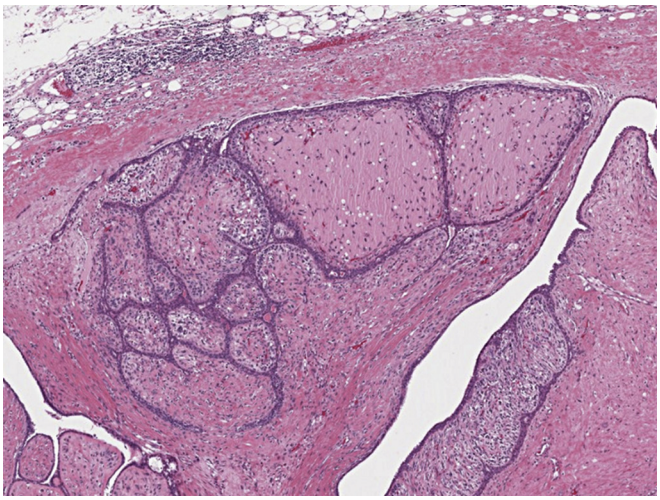
A Fat necrosis
B Fibroadenoma
C Fibrocystic changes
D Infiltrating ductal carcinoma
E Mastitis
F Phyllodes tumor

27 A 27-year-old woman in the third trimester of her third pregnancy discovers a lump in her left breast. On physical examination, a 2-cm, discrete, freely movable mass beneath the nipple is palpable. After the birth of a term infant, the mass appears to decrease in size. The infant is breastfed without difficulty. What is the most likely diagnosis?

A Fibroadenoma
B Intraductal papilloma
C Lobular carcinoma in situ
D Medullary carcinoma
E Phyllodes tumor

28 A 24-year-old woman notes a lump in her right breast for the past month. She is concerned because her sister was diagnosed with a poorly differentiated "triple negative" breast cancer at age 31. Ultrasonography of the breast shows a solid mass. Fine needle aspiration is attempted but no diagnostic cells are obtained. Mammography is performed and there is a single 1-cm density with small clustered calcifications in the right breast but no lesions of the opposite breast. Which of the following is the best course of action for this patient?

A Biopsy to obtain tissue from the lesion
B Continued monthly breast self-examination
C Genetic testing for *BRCA1* mutations
D Hormonal therapy with tamoxifen
E Radiologic imaging to detect metastases



29 A 48-year-old woman has felt a poorly defined lump in her right breast for the past year. On examination, she has a nontender, firm, 6-cm mass in the upper inner quadrant of her right breast. There are no lesions of the overlying skin and no axillary lymphadenopathy. A biopsy is performed, and microscopic examination of the specimen shows the findings in the figure. The mass is excised with a wide margin, but recurs 1 year later. After further excision, the lesion does not recur. What is the most likely diagnosis?

A Fibroadenoma
B Fibrocystic changes
C Lobular carcinoma
D Phyllodes tumor
E Tubular carcinoma

ANSWERS

1 D This is accessory breast tissue with lactational change. Prolactin secretion from the adenohypophysis increases in postpartum women to support milk production in breast lobules. Oxytocin released from the posterior pituitary stimulates myoepithelial cells to contract during nursing. The remaining hormones listed do not have a direct effect upon breast tissue. The presence of the breast tissue in the axilla represents accessory breast tissue, and can explain the origins of breast cancer in women following simple mastectomy.

PBD9 1045 BP9 705 PBD8 1067 BP8 739

2 D Staphylococcal acute mastitis typically produces localized abscesses, whereas streptococcal infections tend to spread throughout the breast, because streptococci often produce streptolysins. Acute mastitis can be associated with the first few months of breastfeeding. *Candida* may cause some local skin irritation, but is likely to become invasive only in immunosuppressed patients. *Lactobacillus acidophilus* is the organism used to produce fermented nonhuman milk. Listeriosis can be spread by contaminated food, including milk products, not by human milk.

PBD9 1046 BP9 707 PBD8 1069 BP8 742

3 B Fat necrosis is typically caused by trauma to the breast. The damaged, necrotic fat is phagocytosed by macrophages, which become lipid laden. The lesion resolves as a collagenous scar within weeks to months. The firm scar can mammographically and grossly resemble a carcinoma. An abscess may form a palpable but painful mass lesion, and often from *Staphylococcus aureus* infection when localized. A fibroadenoma is a neoplasm, and tumors are not induced by trauma. Inflammatory carcinoma refers to dermal lymphatic invasion by an underlying breast carcinoma, giving a rough red-to-orange appearance to the skin. Sclerosing adenosis is a feature of fibrocystic changes, a common cause of nontraumatic breast lumps.

PBD9 1047 BP9 707 PBD8 1070 BP8 742

4 A Nonproliferative cysts are quite common in the breast. When they are fluid-filled, they are unlikely to contain proliferative elements. The cells lining these cysts may be flattened cuboidal to atrophic, but often have abundant pink cytoplasm resembling apocrine change. Microcalcifications may be seen in both benign and malignant breast lesions, but in the case of cysts they represent calcified secretions. If excised, the intact cysts may have a blue to brown color. Ductal carci-

nomas are likely to be solid lesions. Fat necrosis may contain many macrophages, but also connective tissue, producing a firm lesion. Papillomatosis is a proliferative feature in fibrocystic changes that tends to form a solid lesion. Sclerosing adenosis produces a firm, fibrous lesion.

PBD9 1048 BP9 705–706 PBD8 1071 BP8 739–740

5 B Nonproliferative (fibrocystic) changes account for the largest category of breast lumps. These lesions are probably related to cyclic breast changes that occur during the menstrual cycle. In about 30% of cases of breast lumps, no specific pathologic diagnosis can be made. Fibrocystic changes include ductal proliferation, ductal dilation (sometimes with apocrine metaplasia), and fibrosis. A fibroadenoma is a discrete mass formed by a proliferation of fibrous stroma with compressed ductules. Carcinomas have proliferations of atypical neoplastic cells that fill ducts and can invade stroma. Inspissated duct secretions may produce duct ectasia with a surrounding lymphoplasmacytic infiltrate. Trauma with subsequent fat necrosis may produce a localized, firm lesion that mimics carcinoma, but microscopically shows macrophages and neutrophils surrounding necrotic adipocytes, and healing leaves a fibrous scar.

PBD9 1048 BP9 705–706 PBD8 1071 BP8 739–741

6 B Fibrocystic changes without epithelial hyperplasia do not suggest a significantly increased risk of breast cancer. Moderate to florid hyperplasia increases the risk twofold, and atypical ductal or lobular hyperplasias increase the risk fivefold. The risk in this patient is not great enough to suggest radical or simple mastectomy at this time, but follow-up is needed. Breast cancers are not associated with tobacco use. The *BRCA1* gene accounts for a small percentage of breast cancers, primarily in families in which cancer onset occurs at a young age, and genetic testing of all persons at risk for breast cancer is not warranted. These proliferative changes are not the result of infection.

PBD9 1048–1049 BP9 705–706 PBD8 1071–1073 BP8 739–741

7 C Intraductal papillomas are usually solitary and smaller than 1 cm. They are located in large lactiferous sinuses or large ducts, and have a tendency to bleed, though they are benign. Abscesses complicating mastitis organize with a fibrous wall. Fibroadenomas contain ducts with stroma and are not highly vascular; these lesions are not located in ducts. Phyllodes tumors also arise from intralobular stroma and can be malignant, but they do not invade ducts to cause bleeding. Sclerosing adenosis, a lesion occurring with fibrocystic changes, has abundant collagen, not vascularity.

PBD9 1049–1050 BP9 708 PBD8 1072–1073 BP8 743

8 E Micronodular cirrhosis is most often a consequence of chronic alcoholism and impairs hepatic estrogen metabolism, which can lead to bilateral gynecomastia. ACTH-secreting pituitary adenomas cause truncal obesity because of Cushing syndrome. Choriocarcinomas of the testis produce human chorionic gonadotropin and may cause some breast enlargement. Choriocarcinomas are highly malignant neoplasms that would not remain indolent for 2 years. Chronic renal failure is unlikely to have this consequence. Diabetes mellitus slightly increases the risk for breast cancer in women. Rheumatoid nodules can appear in various locations along with rheumatoid arthritis, but they rarely occur in the breast and are unlikely to be bilateral.

PBD9 1049–1050 BP9 714 PBD8 1093 BP8 750

9 A Atypical lobular hyperplasia and atypical ductal hyperplasia increase the risk of breast cancer fivefold; the risk affects both breasts and is higher in premenopausal women or women who have a family history of breast cancer. Smoking and exogenous estrogen therapy are not well-established risk factors for breast cancer. The *BRCA1* mutation accounts for about 10% to 20% of familial breast carcinomas and only a few percent of all breast cancers.

PBD9 1050–1051 BP9 706 PBD8 1073 BP8 740–741

10 A The biopsy specimen shows an invasive breast cancer. Given the young age of the patient and the strong family history of breast cancer, it is reasonable to assume that she has inherited an altered gene that predisposes to breast cancer. There are two known breast cancer susceptibility genes: *BRCA1* and *BRCA2.* Both are cancer suppressor genes. Specific mutations of *BRCA1* are common in some ethnic groups, such as Ashkenazi Jews. Estrogen receptors are expressed in 50% to 75% of breast cancers. Their presence bodes well for therapy with hormone receptor antagonists. There is no known relationship between the structure of the estrogen receptor gene and susceptibility to breast cancer. Likewise, presence of progesterone receptors in the cancer cells indicates potential response to hormonal therapy, not risk for breast cancer. *HER2/neu* is a growth factor receptor gene that is amplified in certain breast cancers and is a marker of poor prognosis, not susceptibility. There is alteration of *TP53* in many cancers, typically acquired and not familial, including breast carcinomas, but it does not have predictive value for risk. Inheritance of *RB1* mutations increases the risk for retinoblastoma and osteosarcomas, but not breast carcinomas.

PBD9 1051–1055 BP9 708–709 PBD8 1077–1078 BP8 744

11 C The relative risk of breast cancer increases with various factors, but family history is one of the strongest. A history of bilateral breast disease and earlier age of onset of cancer increase the risk. The earlier age of onset increases the risk of identifying a *BRCA1* or *BRCA2* mutation. A longer reproductive life, with early menarche (<11 years old) and late menopause (>55 years old), and nulliparity increase the risk of breast cancer, probably because of increased estrogen exposure. "Soft" risk factors include exogenous estrogens and obesity. Mastitis does not affect the risk of breast cancer.

PBD9 1052–1053 BP9 708–709 PBD8 1076–1077 BP8 743–745

12 E The expression of *HER2/neu*, an epidermal growth factor receptor, suggests that biotherapy with trastuzumab may have some effectiveness. Drug names with the suffix *-mab* are monoclonal antibodies that target a specific

biochemical component of cells. This form of biotherapy is useful because normal breast cells do not express *HER2/neu*. Doxorubicin is a standard chemotherapeutic agent that is part of various multiagent protocols. Hydroxyurea is a cycle-acting agent that is not useful in breast cancer. Letrozole is an aromatase inhibitor that is useful for treating ER-positive breast cancers. Raloxifene is a selective estrogen receptor modulator (SERM) that reduces risk for breast cancer and reduces osteoporosis. Tamoxifen is an antiestrogenic compound that has effectiveness in the treatment of breast cancers positive for ER/PR.

PBD9 1055–1057 BP9 709–713 PBD8 1090 BP8 745, 747, 749

13 C This luminal A form comprises over half of all invasive breast cancers, and it tends to be low grade, and lack *BRCA1, BRCA2*, *TP53*, and *CHEK2* familial gene mutations. It is often responsive to antiestrogen hormonal therapy, although surgery alone can be curative. Even with metastases, the course is prolonged. This patient has multiple risks for breast cancer, including nulliparity, obesity, and hormone replacement therapy. Breast cancer at her age is less likely to be familial. Trastuzumab is useful for HER2-positive breast cancers.

PBD9 1055–1056 BP9 709–713 PBD8 1084–1085 BP8 745

14 B An intraductal carcinoma, or ductal carcinoma in situ (DCIS), may not produce a palpable mass. The figure shows ducts that contain large, atypical cells in a cribriform pattern. If grossly soft, white material is extruded from small ducts when pressure is applied, then there is necrosis of the neoplastic cells in the ducts (that leads to dystrophic calcification), and the term *comedocarcinoma* is applicable. Intraductal carcinomas represent about one fourth of all breast cancers. If not excised, such lesions become invasive. Intraductal carcinoma has several other histologic patterns, including noncomedo DCIS and Paget disease of the nipple, in which extension of the malignant cells to the skin of the nipple and areola produces the appearance of a seborrheic dermatitis. Colloid carcinomas occur about as frequently as medullary carcinomas, but they are often positive for estrogen receptor and progesterone receptor, and the prognosis is better than average. Infiltrating ductal carcinomas tend to produce irregular, firm, mass lesions because they are more invasive. Infiltrating lobular carcinomas can have a diffuse pattern without significant mass effect. Medullary carcinomas tend to be large masses; microscopically, they have nests of large cells with a surrounding lymphoid infiltrate. True papillary carcinomas are rare, although a papillary component may be present in other types of breast carcinoma.

PBD9 1057–1058 BP9 710 PBD8 1080–1081 BP8 745–748

15 E Paget cells are large cells that have clear, mucinous cytoplasm and infiltrate the skin overlying the breast. They are malignant and extend to the skin from an underlying breast carcinoma, which may be occult, so that Paget disease may be the first sign of malignancy. Apocrine metaplasia affects the cells lining the cystically dilated ducts in fibrocystic change. The macrophages in fat necrosis do not infiltrate the skin and do not have the atypical nuclei seen in the figure. *Inflammatory carcinoma* does not refer to a specific histologic type of breast cancer; rather, it describes the involvement of dermal lymphatics by infiltrating carcinoma, and there may be thickening and a reddish-orange appearance to the skin. In lobular carcinoma in situ, terminal ducts or acini within the breast are filled with neoplastic cells.

PBD9 1057, 1059 BP9 710 PBD8 1080–1081 BP8 745–746

16 B Among primary malignancies of the breast, lobular carcinoma in situ (LCIS) is most likely to be bilateral. LCIS may precede invasive lesions by several years. Lobular carcinoma may be mixed with ductal carcinoma, and it may be difficult to distinguish them histologically. The other neoplasms listed are less likely to be bilateral and more likely to produce a single mass effect.

PBD9 1059–1060 BP9 710–711 PBD8 1082–1083 BP8 745–747

17 A This irregular, infiltrative mass is an infiltrating (invasive) ductal carcinoma, the most common form of breast cancer. Breast carcinomas are most likely to metastasize to regional lymph nodes. By the time a breast cancer becomes palpable, lymph node metastases are present in more than 50% of patients. A bloody discharge from the nipple most often results from an intraductal papilloma. Pain in the chest wall could be bone metastases, but less likely local invasion, and there is a margin of adipose tissue around the mass in the specimen shown. Breast cancers are associated in rare cases with ectopic corticotropin secretion or Cushing syndrome. Lobular carcinomas are more often bilateral, but they are less common than infiltrating ductal carcinomas.

PBD9 1060–1064 BP9 708–711 PBD8 1083–1085 BP8 743–749

18 A In this lobular carcinoma, note the pleomorphic cells infiltrating single file through the stroma. The metastatic profile of this cancer includes the carcinomatous meningitis suggested by her leptomeningeal enhancement, as well as intra-abdominal metastases. E-cadherin is an adhesion molecule that serves as a tumor suppressor, and its loss characterizes another infiltrating carcinoma—signet ring carcinoma of the stomach. Medullary carcinomas are solid masses of cells with little desmoplasia, but prominent lymphoid infiltrates. Metaplastic carcinomas are rare in humans and have a component resembling another tissue, such as squamous carcinomas. In the setting of a malignant breast mass, any brain lesion is a suspected metastatic lesion; although glioblastoma is capable of extracranial metastases, this is rare, and there should be a bulky cerebral mass present. Phyllodes tumors can be malignant, with a stromal component, but these are typically bulky masses, and there is a microscopic leaflike pattern of cystic spaces lined by epithelium.

PBD9 1065 BP9 711–712 PBD8 1085–1087 BP8 747

19 D Medullary carcinomas account for about 1% to 5% of all breast carcinomas. They tend to occur in women at

younger ages than do most other breast cancers. Despite poor prognostic indicators (such as absence of HER2, ER, and PR), medullary carcinomas have a better prognosis than most other breast cancers. Perhaps the infiltrating lymphocytes are a helpful immune response. Colloid carcinomas occur about as frequently as medullary carcinomas, but they are often positive for ER, and the prognosis is better than average. Infiltrating ductal and infiltrating lobular carcinomas tend not to produce large, localized lesions because they are more invasive, and they lack a distinct lymphoid infiltrate. True papillary carcinomas are quite rare, although other types of breast carcinoma may have a papillary component. The phyllodes tumor is typically large, but it has stromal and glandular components.

PBD9 1065–1066 BP9 712 PBD8 1087 BP8 747–748

20 A Male breast cancers are rare, and they occur primarily among the elderly. Additional risk factors include first-degree relatives with breast cancer, decreased testicular function, exposure to exogenous estrogens, infertility, obesity, prior benign breast disease, exposure to ionizing radiation, and residency in Western countries. Of cases in men, 4% to 14% are attributed to germline *BRCA2* mutations, less frequently for *BRCA1*, and *ATM* mutations in less than 1%. Gynecomastia does not seem to be a risk factor.

PBD9 1066 BP9 714 PBD8 1093–1094 BP8 750

21 D The estrogen receptor and progesterone receptor (ER and PR) status helps predict whether chemotherapy with antiestrogen compounds such as tamoxifen would be effective; however, the correlation is not perfect. ER and PR do not affect immunogenicity and are not targets for immunotherapy. In contrast, immunotherapy targeted to the overexpressed *HER2/neu* gene is being used. The overall prognosis may be predicted from several factors, including histologic type, histologic grade, presence of metastases, degree of aneuploidy, and tumor stage. A family history and the presence of specific mutations such as *BRCA1* or *BRCA2* correlate with familial risk of breast cancer.

PBD9 1066–1068 BP9 713 PBD8 1076 BP8 745

22 B Patients with the *BRCA1* gene mutation have a high incidence of carcinomas with medullary features that are poorly differentiated and triple negative (do not express the HER2/neu protein, and are negative for estrogen and progesterone receptors).

PBD9 1065 BP9 712 PBD8 1087 BP8 747

23 G Many factors affect the course of breast cancer. The involvement of axillary lymph nodes is the most important prognostic factor listed. If there is no spread to axillary nodes, the 10-year survival rate is almost 80%. It decreases to 35% to 40% with 1 to 3 positive nodes, and to 15% with more than 10 positive nodes. Increasing age is a risk for breast cancer, but age alone does not indicate a prognosis, and treatment of cancers in the elderly can be successful. An increased DNA content with aneuploidy and a high S-phase suggests a worse prognosis, but staging is still a more important determinant of prognosis. Estrogen receptor positivity suggests a better response to hormonal manipulation of the tumor, whereas expression of *HER2/neu* suggests responsiveness to biotherapy with the monoclonal antibody trastuzumab. Some histologic types of breast cancer have a better prognosis than others, but staging is a more important factor than histologic type. The expression of stromal proteases, such as cathepsin D, predicts metastases, but in this case "the horse is out of the barn," and metastasis has occurred.

PBD9 1066–1068 BP9 712–713 PBD8 1089–1090 BP8 748–749

24 A This is the basal-like subset of NST breast cancers that is triple negative for the usual immunohistochemical markers. Hence, lack of ER positivity predicts that antihormonal therapy with tamoxifen will not be of benefit, and lack of HER2/neu indicates that trastuzumab will be ineffective. The basal-like cancers are highly aggressive and tend to metastasize early, so containment with surgery or radiation is unlikely. However, some of them are cured by chemotherapy. This emphasizes the importance of gene expression profiling, so that treatment is individualized to each cancer patient for the best chance of success.

PBD9 1062 BP9 713 PBD8 1084–1085 BP8 745

25 D The gross appearance of the skin is consistent with invasion of dermal lymphatics by carcinoma—the so-called inflammatory carcinoma, which is not a histologic type of breast cancer, but a descriptive phrase based upon the gross appearance (peau d'orange) resembling an inflammatory process. Nipple retraction and nontender axillary lymphadenopathy also suggest invasive ductal carcinoma. Atypical ductal hyperplasia may increase the risk of carcinoma, but it is not capable of invasion and does not produce visible surface skin changes. Acute mastitis may produce pain and swelling, but it is more likely to occur in association with breastfeeding, and as an inflammatory process would be more likely to produce painful lymphadenopathy. Fat necrosis on palpation can mimic that of carcinoma, but the skin is not involved. Sclerosing adenosis is a feature of benign fibrocystic changes producing breast lumps, but it has no skin involvement.

PBD9 1066–1067 BP9 712 PBD8 1083, 1089 BP8 747

26 B Grossly and radiographically, this patient has a discrete mass that in a woman her age is most likely a fibroadenoma. Fat necrosis and infiltrating cancers are masses with irregular outlines. Fibrocystic changes are generally irregular lesions, not discrete masses. Mastitis has a more diffuse involvement, without mass effect. Phyllodes tumors are typically much larger and are far less common.

PBD9 1069 BP9 707–708 PBD8 1091–1092 BP8 742–743

27 A Fibroadenomas are common and may enlarge during pregnancy or late in each menstrual cycle. Most intraductal

papillomas are smaller than 1 cm and are not influenced by hormonal changes. Lobular carcinoma in situ is typically an ill-defined lesion without a mass effect. Medullary carcinomas tend to be large; they account for only about 1% of all breast carcinomas. Phyllodes tumors are uncommon and tend to be larger than 4 cm.

PBD9 1069 BP9 707–708 PBD8 1091–1092 BP8 742–743

28 A Her age would suggest the lesion is probably benign, and even fibroadenomas and fibrocystic changes can have calcifications. The fibrous component of a fibroadenoma or fibrocystic changes can make it difficult to aspirate cells from them. However, the family history and the mammographic appearance of small clustered calcifications are concerning for carcinoma. A delay in diagnosis and treatment of breast cancer decreases survival. Although *BRCA1* mutations are associated with HER2 and ER- and PR-negative breast cancers, the lesion must still be diagnosed. Based upon the histologic findings and molecular markers, a treatment plan can then be instituted that may include additional studies and pharmacologic therapies.

PBD9 1045–1046, 1069 BP9 705–708 PBD8 1068, 1091 BP8 739, 742

29 D Phyllodes tumors, although grossly and microscopically similar to fibroadenomas, occur at an older age, are larger, and are more cellular than fibroadenomas; they can recur locally following excision, but rarely metastasize. The figure shows cellular stroma protruding into spaces lined by a single layer of cuboidal epithelium. In contrast, fibrocystic changes can produce a breast lump, but usually not as large as 6 cm, and without firm areas of cellular stroma. A lobular carcinoma has malignant-appearing epithelial cells in clusters and rows and may not even produce a significant mass effect. Tubular carcinomas of the breast are uncommon, most are less than 1 cm in diameter, and most have small tubular structures in a noncellular stroma.

PBD9 1069–1070 BP9 707 PBD8 1092–1093 BP8 743