BREAST DISEASES

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BREAST DISEASES

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PREFACE

The management of patients with breast diseases, particularly those who are at risk for or who have developed breast cancer, continues to be a major public health problem—one that demands the involvement and expertise of physicians and scientists in a wide variety of disciplines. It was with this fact in mind that we compiled the first edition of *Breast Diseases.* Our intention was to cover the range of issues subsumed under this heading by assembling experts in the field to provide the important material in a comprehensive, balanced, and easy-to-read work. In reviewing the history of the field, we were struck by the succession of theories that were strongly held despite a paucity of supporting data. We wished, in contrast, to provide the reader with the pertinent information in order to allow for independent review and analysis. The guiding principles behind the first edition, then, were to provide information that was current, to emphasize data regarding breast diseases that are scientifically valid, and to avoid dogma. We have been gratified by the success of the first edition and have taken this to mean that, at least in part, we achieved our goals.

The second edition of *Breast Diseases* was prompted both by the rapid pace of research in breast cancer and by our desire to provide the most current information to the reader. In this edition, we have attempted to maintain the same guiding principles as in the first edition. We have added new sections and expanded old sections in response to new developments. A number of new specialists have been added to the list of contributors. In particular, this edition provides new information on the diagnosis and management of benign breast conditions, the evaluation and management of mammographic abnormalities, the management of in situ cancers, the influence of exogenous hormone administration on the risk of developing breast cancer and the risk of recurrence following treatment, new treatment modalities, and advances in molecular biology and other laboratory sciences that are likely to shed light on the topic of breast cancer. In addition, we have added a new feature—a Management Summary—at the end of each clinically related section. The purpose of these summaries is to provide a succinctly worded conclusion regarding the clinical guidelines that we believe can be derived from the currently available information. The summaries are the responsibility of the editors, and it is our hope that they will make the detailed information that is provided more accessible, particularly for the non-specialist.

We hope that this second edition of *Breast Diseases* will be of use both to the wide range of physicians who are concerned with diseases of the breast and to their patients.

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occur at any point along the milk streak from the axilla to the groin. Rarely, accessory true mammary glands develop. These are most often located in the axilla (polymastia). During pregnancy and lactation, an accessory breast may swell; occasionally, if there is an associated nipple, it may function.

Hypoplasia is the underdevelopment of the breast, congenital absence of a breast is termed *amastia*. When breast tissue is lacking but a nipple is present, the condition is termed *amazia*. A wide range of breast abnormalities have been described and may be classified as follows:[5,6]

- Unilateral hypoplasia, contralateral normal
- Bilateral hypoplasia with asymmetry
- Unilateral hyperplasia, contralateral normal
- Bilateral hyperplasia with asymmetry
- Unilateral hypoplasia, contralateral hyperplasia
- Unilateral hypoplasia of breast, thorax, and pectoral muscles (Poland's syndrome)

Most of these abnormalities are not severe. The severest deformity, amastia or marked breast hypoplasia, is associated with hypoplasia of the pectoral muscle in 90% of cases,[7] but the reverse does not apply. Ninety-two percent of women with pectoral muscle abnormalities have a normal breast.[8] Congenital abnormalities of the pectoral muscle are usually manifested by the lack of the lower third of the muscle and an associated deformity of the ipsilateral rib cage. The association between absence of the pectoral muscle, chest wall deformity, and breast abnormalities was first recognized by Poland in 1841. The original description, however, did not note the concomitant abnormalities of the hand (synbrachydactyly, with hypoplasia of the middle phalanges and central skin webbing),[9] and considerable controversy has evolved concerning the validity of the eponym for this congenital syndrome.[10,11]

Acquired Abnormalities

The most common—and avoidable—cause of amazia is iatrogenic. Injudicious biopsy of a precociously developing breast results in excision of most of the breast bud and subsequent marked deformity during puberty. The use of radiation therapy in prepubertal females to treat either hemangioma of the breast or intrathoracic disease may also result in amazia. Traumatic injury of the developing breast, such as that resulting from a severe cutaneous burn, with subsequent contracture, may also result in deformity.

NORMAL BREAST DEVELOPMENT DURING PUBERTY

Puberty in girls begins at the age of 10 to 12 years as a result of the influence of hypothalamic gonadotropin-releasing hormones secreted into the hypothalamic–pituitary portal venous system. The basophilic cells of the anterior pituitary release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Follicle-stimulating hormone causes the primordial ovarian follicles to mature into graafian follicles, which secrete estrogens, primarily in the form of 17β-estradiol. These hormones induce the growth and maturation of the breasts and genital organs.[12] During the first 1 to 2 years after menarche, there is unbalanced hypothalamic–adenohypophyseal function because the maturation of the primordial ovarian follicles does not result in ovulation or a luteal phase. Therefore, ovarian estrogen synthesis predominates over luteal progesterone synthesis. The physiologic effect of estrogens on the maturing breast is to stimulate longitudinal ductal growth of ductal epithelium. Terminal ductules also form buds that precede further breast lobules. Simultaneously, periductal connective tissues increase in volume and elasticity, with enhanced vascularity and fat deposition. These initial changes are induced by estrogens synthesized in immature ovarian follicles, which are anovulatory; subsequently, mature follicles ovulate and the corpus luteum releases progesterone. The relative role of these hormones is not clear. In experimental studies, estrogens alone induce a pronounced ductular increase, whereas progesterone alone does not. The two hormones together produce full ductular–lobular–alveolar development of mammary tissues.[12] There is marked individual variation in development of the breast, making it impossible to categorize histologic changes on the basis of age.[3,4] Breast development by age has been described by external morphologic changes. The evolution of the breast from childhood to maturity has been divided into five phases by Tanner,[13] as shown in Table 1-1.

MORPHOLOGY

The Adult Breast

The adult breast lies between the second and sixth ribs in the vertical axis, and between the sternal edge and the midaxillary line in the horizontal axis (Fig. 1-1). The average

Table 1–1
Phases of Breast Development

Phase I (age: puberty): Preadolescent elevation of the nipple with no palpable glandular tissue or areolar pigmentation.
Phase II (age: 11.1 ± 1.1 yr): Presence of glandular tissue in the subareolar region. The nipple and breast project as a single mound from the chest wall.
Phase III (age: 12.2 ± 1.09 yr): Increase in the amount of readily palpable glandular tissue with enlargement of the breast and increased diameter and pigmentation of the areola. The contour of the breast and nipple remains in a single plane.
Phase IV (age: 13.1 ± 1.15 yr): Enlargement of the areola and increased areola pigmentation. The nipple and areola form a secondary mound above the level of the breast.
Phase V (age: 15.3 ± 1.7 yr): Final adolescent development of a smooth contour with no projection of the areola and nipple.

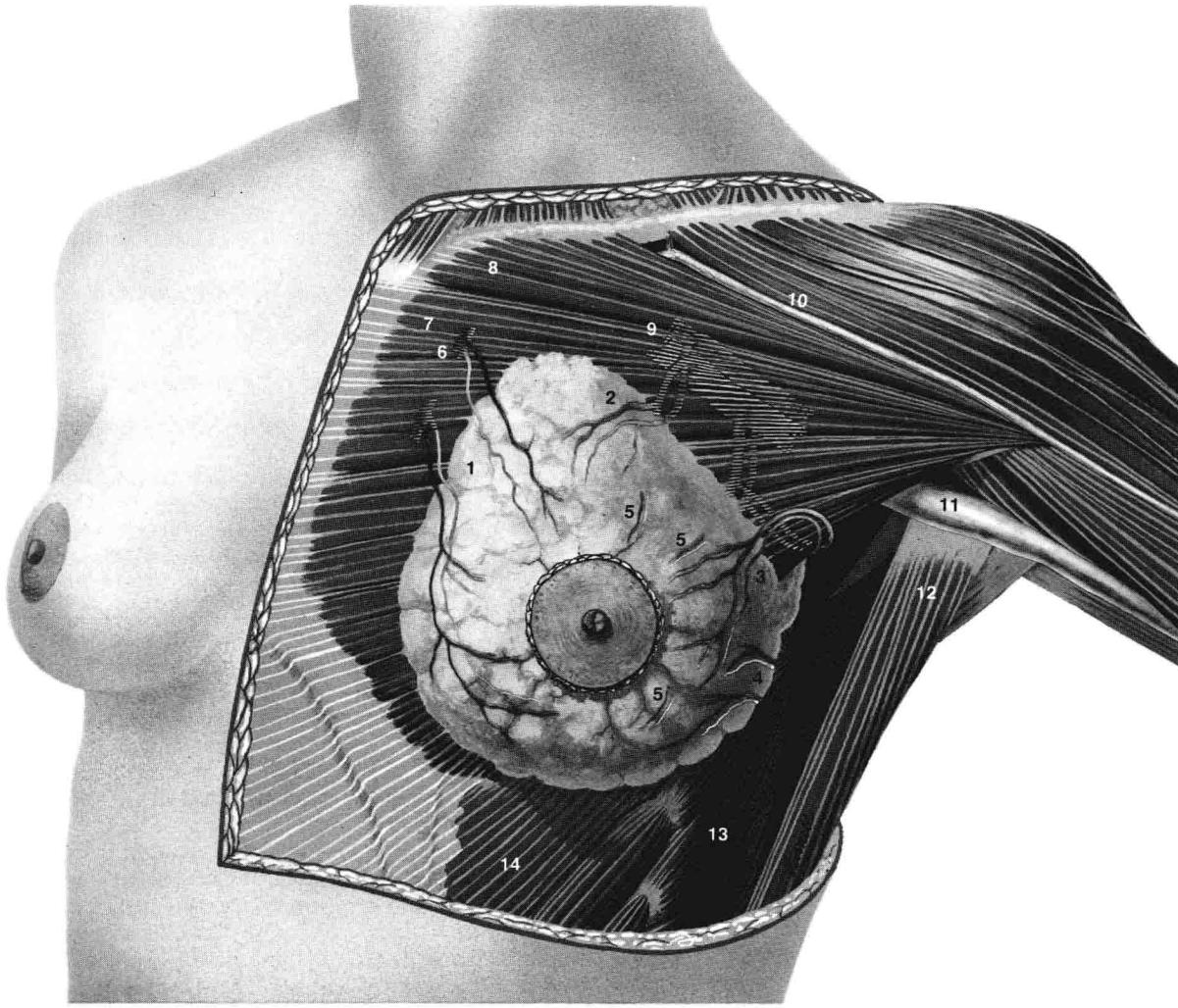

FIGURE 1–1. Normal anatomy of the breast and pectoralis major muscle.

1. *Perforating branches from internal mammary artery and vein*
2. *Pectoral branches from thoracoacromial artery and vein*
3. *External mammary branch from lateral thoracic artery and vein*
4. *Branches from subscapular and thoracodorsal arteries and veins*
5. *Lateral branches of third, fourth, and fifth intercostal arteries and veins*
6. *Internal mammary artery and veins*
7. *Sternocostal head of pectoralis major muscle*
8. *Clavicular head of pectoralis major muscle*
9. *Axillary artery and vein*
10. *Cephalic vein*
11. *Axillary sheath*
12. *Latissimus dorsi muscle*
13. *Serratus anterior muscle*
14. *External abdominal oblique muscle*

breast measures 10 to 12 cm in diameter and its average thickness centrally is 5 to 7 cm. Breast tissue also projects into the axilla as the axillary tail of Spence. The contour of the breast varies but is usually domelike, with a conical configuration in the nulliparous woman and pendulous in the parous woman. The breast comprises three major structures: skin, subcutaneous tissue, and breast tissue, with the last comprising both parenchyma and stroma. The parenchyma is divided into 15 to 20 segments that converge at the nipple in a radial arrangement. The collecting ducts draining each segment are 2 mm in diameter with subareolar lactiferous sinuses 5 to 8 mm in diameter. Between 5 and 10 major collecting milk ducts open at the nipple.

The nomenclature of the duct system is varied. The branching system may be named in a logical fashion, starting with the collecting ducts in the nipple and extending to the ducts draining each alveolus, as shown in Table 1-2.

Each duct drains a lobe made up of 20 to 40 lobules. Each lobule consists of 10 to 100 alveoli or tubulosaccular secretory units. The microanatomy has been described in detail by Parks.[14] The stroma and subcutaneous tissues of the breast contain fat, connective tissue, blood vessels, nerves, and lymphatics.

The skin of the breast is thin and contains hair follicles, sebaceous glands, and eccrine sweat glands. The nipple, which is located over the fourth intercostal space in the nonpendulous breast, contains abundant sensory nerve endings, including Ruffini-like bodies and end-bulbs of Krause. Also, there are sebaceous and apocrine sweat glands, but no hair follicles. The areola is circular and pigmented, measuring 15 to 60 mm in diameter. Morgagni's tubercles, located near the periphery of the areola, are elevations formed by the openings of the ducts of Montgomery's glands. Montgomery's glands are large, sebaceous glands capable of secreting milk; they represent an intermediate stage between sweat and mammary glands. Fascial tissues envelop the breast. The superficial pectoral fascia envelops the breast and is continuous with the superficial abdominal fascia of Camper. The undersurface of the breast lies on the deep pectoral fascia, covering the pectoralis major and anterior serratus muscles. Connecting these two fascial layers are fibrous bands (Cooper's suspensory ligaments) that represent the "natural" means of support of the breast.

Table 1–2
Nomenclature of the Breast Epithelial System

Major ducts	Collecting ducts Lactiferous sinuses Segmental ducts Subsegmental ducts
Terminal duct–lobular unit (TDLU)	Terminal ducts Extralobular Intralobular Lobules Alveoli

Blood Supply of the Breast

The principal blood supply to the breast is derived from the internal mammary and lateral thoracic arteries. Approximately 60% of the breast, mainly the medial and central parts, is supplied by the anterior perforating branches of the internal mammary artery. About 30% of the breast, mainly the upper, outer quadrant, is supplied by the lateral thoracic artery. The pectoral branch of the thoracoacromial artery: the lateral branches of the third, fourth, and fifth intercostal arteries; and the subscapular and thoracodorsal arteries all make minor contributions to the blood supply.

Lymphatic Drainage of the Breast

Lymph Vessels

The subepithelial or papillary plexus of the lymphatics of the breast are confluent with the subepithelial lymphatics over the surface of the body. These valveless lymphatic vessels communicate with subdermal lymphatic vessels and merge with Sappey's subareolar plexus. The subareolar plexus receives lymphatic vessels from the nipple and areola and communicates by way of vertical lymphatic vessels that are equivalent to those connecting the subepithelial and subdermal plexus elsewhere.[15] Lymph flows unidirectionally from the superficial to deep plexus and from the subareolar plexus through the lymphatic vessels of the lactiferous duct to the perilobular and deep subcutaneous plexus. The periductal lymphatic vessels lie just outside the myoepithelial layer of the duct wall.[16]

Flow from the deep subcutaneous and intramammary lymphatic vessels moves centrifugally toward the axillary and internal mammary lymph nodes. Injection studies with radiolabeled colloid[17] have demonstrated the physiology of lymph flow and have countered the old hypothesis of centripetal flow toward Sappey's subareolar plexus. It has been estimated that about 3% of the lymph from the breast flows to the internal mammary chain, whereas 97% flows to the axillary nodes.[18] Drainage of lymph to the internal mammary chain may be observed following injection of any quadrant of the breast.

Axillary Lymph Nodes

The topographical anatomy of the axillary lymph nodes has been studied as the major route of regional spread in primary mammary carcinoma. The anatomic arrangement of the axillary lymph nodes has been subject to many different classifications. The most detailed studies are those of Pickren, which show the pathologic anatomy of tumor spread.[19] Axillary lymph nodes may be grouped as the apical or subclavicular nodes, lying medial to the pectoralis minor muscle, and the axillary vein lymph nodes, grouped along the axillary vein from the pectoralis minor muscle to the lateral limit of the axilla; the interpectoral (Rotter's) nodes, lying between the pectoralis major and minor muscles along the lateral pectoral nerve; the scapular group, comprising