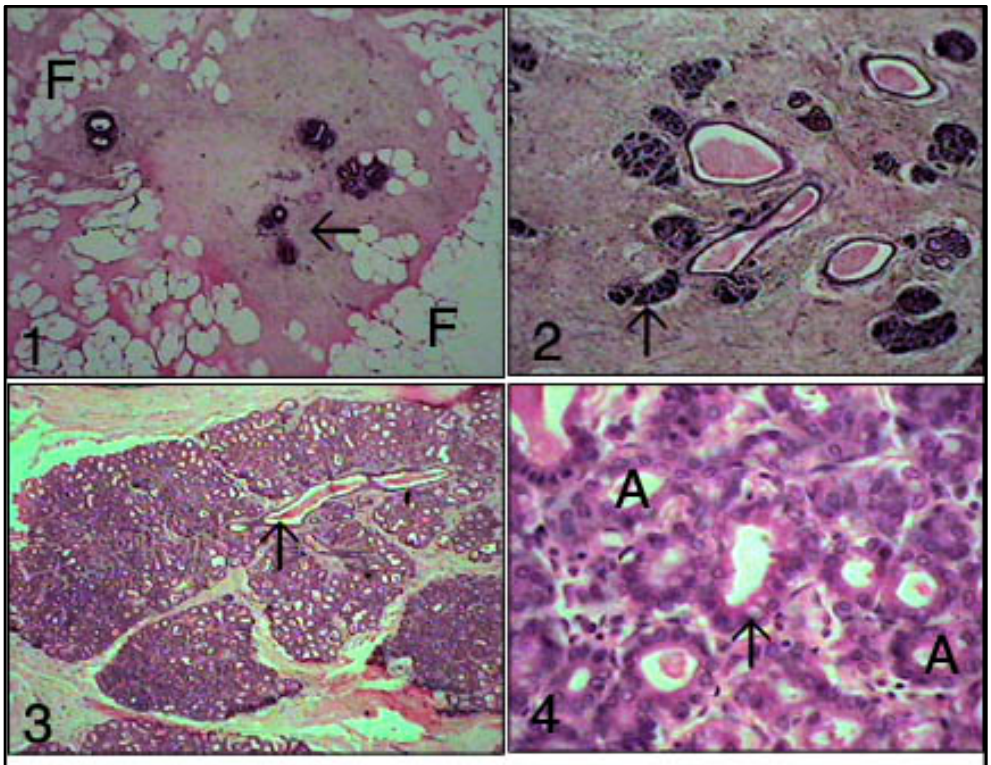
Breast Tissue



1. The resting breast consisits primarily of ductal components (arrow) embedded in dense connective tissue surrounded by abundant fat (F).
2. Breast during the first half of pregnancy. Terminal portions of the ductal system (arrow) grow rapidly.
3. Lactating breast. Note the extensive development of alveoli. An interlobular duct (arrow) receives several intralobular ducts which in turn drain surrounding alveoli.
4. Alveoli (A) from lactating breast. Lipid droplets (arrow) are observed within alveolar epithelium.

Breast tissue is present in both sexes but in men remain rudimentary throughout life. In women, the size, shape, and structure vary with age and functional status. Prior to puberty, the female breasts are undeveloped but enlarge rapidly at puberty due mainly to accumulation of adipose tissue. They reach their greatest development at late pregnancy and lactation. In women, the breasts are variably hemispherical and conical in shape, each surmounted by a cylindrical projection, the nipple. Surrounding the nipple is a slightly raised, circular area of hairless pigmented skin, the areola. The mammary glands are compound tubuloalveolar glands and are of cutaneous origin, representing modified apocrine sweat glands.

Structure of the Resting Gland

Each breast consists of 15 to 20 individual pyramid-shaped lobes that radiate from a nipple. The lobes are separated by septa of dense connective tissue. Each lobe represents an individual mammary gland and contains glandular tissue drained by its own ductal components, embedded in connective tissue. The proportions of glandular and nonglandular

tissue vary with functional status. In the resting gland, the principal glandular elements are the ducts, which are grouped together to form lobules. The smallest branches of the ductal system are lined by simple cuboidal epithelium, but the lining increases in height as the ducts unite and pass toward the nipple. Just beneath the areola, the ducts expand to form the lactiferous sinuses, which are lined by a two-layered stratified cuboidal epithelium. As the duct ascends through the nipple, it becomes lined by stratified squamous epithelium. Secretory units consist of clusters of alveoli surrounding a small duct. The alveolar wall consists of simple cuboidal epithelium resting on a basement membrane. Between the epithelial cells and the basement membrane are highly branched myoepithelial cells whose long, slender processes embrace the alveolus in a basket-like network. Alveoli are not prominent in the resting gland, and there is some question as to whether they are present at all. When present, they usually occur as small, budlike extensions of the terminal ducts. The intralobular connective tissue around the ductules and alveoli is loosely arranged and cellular, whereas that surrounding the larger ducts and lobes (interlobular connective tissue) is variably dense and contains much adipose tissue.

Nipple and Areola

Keratinizing stratified squamous epithelium continuous with that of the skin overlying the breast covers the nipple. The dermis projects deeply into the epithelium, forming unusually tall dermal papillae. The skin of the nipple is pigmented and contains many sebaceous glands but is devoid of hair and sweat glands. Many lactiferous ducts, each of which drains a lobe and empties onto the tip of the nipple, traverse the nipple. The outer parts of the ducts also are lined by keratinizing stratified squamous epithelium. The dense collagenous connective tissue of the nipple contains bundles of elastic fibers, and much smooth muscle is present. The smooth muscle cells are arranged circularly and radially and, on contraction, produce erection of the nipple. The areola is the pigmented area of skin that encircles the base of the nipple. During pregnancy, the areola becomes larger and more deeply pigmented. It contains sweat, sebaceous, and areolar glands. The latter appear to be intermediate in structure between apocrine sweat glands and true mammary glands.

Pregnancy and Lactation

During pregnancy, mammary glands undergo extensive development in preparation for their role in lactation. During the first half of pregnancy, the terminal portions of the ductal system grow rapidly, branch, and develop terminal buds that expand to become alveoli. Proliferation of glandular tissue takes place at the expense of the fat and stromal connective tissue, which decrease in amount. The connective tissue becomes infiltrated with lymphocytes, plasma cells, and granular leukocytes. During late pregnancy, proliferation of glandular tissue subsides, but the alveoli expand and there is some formation of secretory materials. The first secretion, colostrum, is thin and watery. It is poor in lipid but contains a considerable amount of immunoglobulin that provides passive immunity to the newborn. True milk secretion begins a few days after parturition, but not all the breast tissue is functioning at the same time. In some areas, alveoli are distended with milk, the epithelial lining is flattened, and the lumen is distended; in other areas, the alveoli are resting and are lined by tall columnar epithelial cells. Secreting cells have abundant granular endoplasmic reticulum, moderate numbers of relatively large mitochondria, and supranuclear Golgi complexes. Milk proteins are elaborated by the granular endoplasmic reticulum and in association with the Golgi body form membrane-bound vesicles. These are carried to the apex of the cell, where the contents are released by

exocytosis. Lipid arises as cytoplasmic droplets that coalesce to form large spherical globules. The droplets and globules reach the apex of the cell and protrude into the lumen. Ultimately, they pinch off, surrounded by a thin film of cytoplasm and the detached portion of the plasmalemma. This method of release is a form of apocrine secretion, but only minute amounts of cytoplasm are lost. Immunoglobulins in milk are synthesized by plasma cells in the connective tissue surrounding the alveoli of the mammary glands. The secreted immunoglobulin is taken up by receptor-mediated endocytosis along the basolateral plasmalemma of mammary gland epithelial cells and transported in small vesicles to the cell apex, where it is discharged into the lumen by exocytosis. Passage of milk from alveoli into and through the initial ductal segments is due to the contraction of myoepithelial cells.

Average milk production by a woman breast-feeding a single infant is about 1200 ml/day. Milk consists of about 88% water, 6.5% carbohydrate, 3.3% lipid, and 1.5% protein. Lactose is the primary carbohydrate and casein the primary protein. In addition, immunoglobulins (IgE and IgA), electrolytes (Na^+, K^+, Cl^-), minerals (Ca^{++}, Fe^{++}, Mg^{++}), and other substances occur in milk. Women in the fourth and fifth months of lactation may secrete as much as 0.5 g of immunoglobulin per day in her milk. Such immunoglobulins are important in the resistance of enteric infections and provide the infant with considerable passive immunity. With weaning, lactation soon ceases, and the glandular tissue returns to its resting state. However, regression is never complete, and not all the alveoli completely disappear.

Hormonal Control

Before puberty, growth of the mammary gland parallels general body growth, but as the ovaries become functional, the mammary tissue comes under the influence of estrogen and progesterone. While some structural changes can be observed, the cyclic response of the breast is minor. During pregnancy, the glands are continuously stimulated by estrogen and progesterone from the corpus luteum and placenta. Generally, growth of the ductal system depends on estrogen, but for alveolar development, both progesterone and estrogen are required. To attain the full development in pregnancy, other hormones -somatotropin, prolactin, adrenal corticoids, and human chorionic somatomammotropin - appear to be necessary.

At the end of pregnancy (birth), the levels of circulating estrogen and progesterone fall abruptly. In the absence of their inhibition, there is an increased output of prolactin by cells of the adenohypophysis. Prolactin is a powerful lactogenic stimulus, and full lactation is established in a few days after birth. Maintenance of lactation requires continuous secretion of prolactin, which results from a neurohormonal reflex established by suckling. Periodic suckling also causes release of oxytocin from the neurohypophysis, which stimulates contraction of myoepithelial cells, resulting in release of milk from alveoli and into the ducts (milk letdown).