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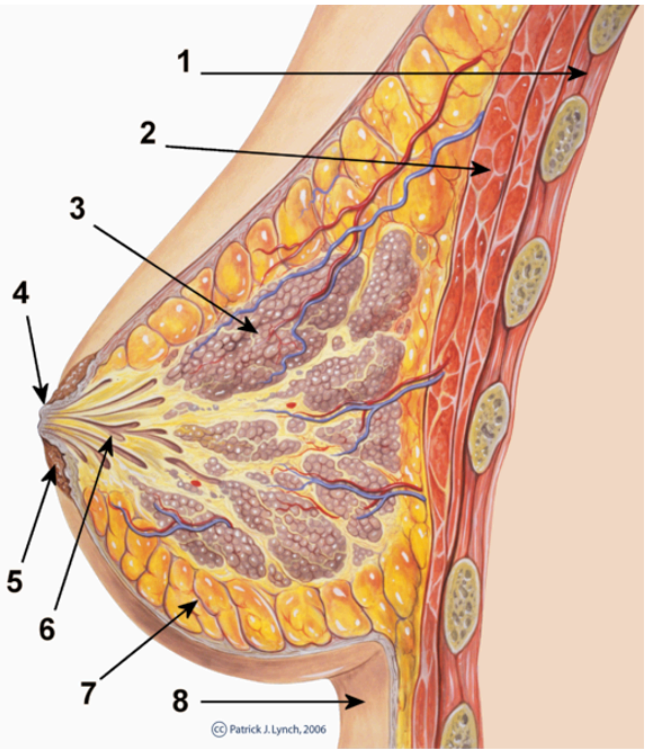
Breast Structures and Breast Cancer



1. Chest wall
2. Pectoralis muscle
3. Lobules
4. Nipple
5. Areola
6. Lactiferous duct
7. Fatty tissue
8. Skin

Female Breast Anatomy *File:Breast anatomy normal scheme.png; Patrick J. Lynch; https://commons.wikimedia.org/wiki/File:Breast_anatomy_normal_scheme.png; This file is licensed under the Creative Commons Attribution 3.0 Unported license.*

Breast Structures and Their Responses to Hormones

Before discussing breast cancer, we must understand several breast structures. Much of the breast consists of the **mammary glands** which consist of 15-20 **glandular lobules**. Each lobule drains into a **lactiferous duct** that in turns drains into an opening at the **nipple**. The lobules contain many **alveoli**, which are hollow cavities about a millimeter in size. The alveoli are lined with **cuboidal epithelial cells** that can develop and mature to make milk. These cuboidal cells are surrounded by **myoepithelial cells** that function to contract and push the milk out and towards the ducts. The myoepithelial cells are found between the basement membrane and cuboidal epithelium. In fact, myoepithelial cells are found in multiple glandular tissues where they also function to contract and help expel glandular secretions.

The structure of the breast changes during the menstrual cycle. Estrogen stimulates the growth of the ductile tissues and progesterone stimulates the maturation of secretory cells of the glandular lobes and ductal cells. Early in the menstrual cycle, the ducts are like thin cords with little to no patent (open) lumen. As estrogen increases around mid-

cycle, the secretory cells of the duct system increase in size, the lumen appears, and watery glandular secretions (not milk) can accumulate. This causes a feeling of breast “fullness” or swelling that can be tender.

Pregnancy also has a profound influence on breast structures. During pregnancy, placental estrogen and progesterone continue to increase glandular and ductile cell growth and development. Mammary gland lobes expand in size considerably. Prolactin begins to increase from the pituitary in the first trimester. Prolactin can stimulate the production of milk by cuboidal alveolar cells (also called lobule secretory cells), but placental hormones inhibit complete milk production. This is why breast milk does not fully develop until after the woman gives birth.

Breast Cancer

Breast cancer is the most common type of cancer seen in women. It is second only to lung cancer in female morbidity due to cancer. Most breast cancers arise from epithelial cells of the mammary gland ducts. When the cancer arises from these duct cells, it is called **ductal carcinoma**. While less common, it is also possible to see cancer develop from the lobules which is called **lobular carcinoma**.

Cancer of the breast may manifest as a mass, a puckering of the skin, texture changes of the skin, nipple retractions, or abnormal nipple discharge. Many cases of breast cancer are discovered by self-examinations where such changes are noticed. As a screening tool, self-examination is useful but may not detect changes as early as clinical mammography. **Mammography** is an x-ray picture of the breast that can detect a mass as small as 1 mm in size.

This internet site further describes the signs and symptoms of breast cancer:

https://books.byui.edu/-WEtE

Most breast cancer patients are women who have no significant identifiable risk factor. That being said, obesity, physical inactivity, caffeine consumption, alcohol consumption, smoking, and long-term use of hormone replacement therapy are all modifiable risk factors that are associated with breast cancer. About 12% of all breast cancer is considered hereditary. Mutations in the breast cancer 1 (BRCA1) and breast cancer 2 (BRCA2) genes account for the majority of hereditary breast cancers. These are tumor suppressor genes that normally suppress cell growth. A female who inherits a mutated BRCA 1 or 2 has an increased lifetime risk for breast cancer of 40-50%, or more. Also, the risk for ovarian cancer is nearly as high with one of these mutated genes. A woman who knows she has a mutated BRCA gene may choose to follow a strict surveillance and screening regimen. Some women may choose to undergo prophylactic surgery called bilateral mastectomy (removal of both breasts) and bilateral oophorectomy (removal of both ovaries). While these radical surgeries certainly lower the risk of getting cancer, they come with significant physical and psychological side effects.

Treatments for breast cancer include radiation, chemotherapy, drugs (including hormone manipulation), and surgery. In extreme cases a **radical mastectomy** may be performed that involves removal of the whole breast, underlying muscle, and axillary lymph nodes.

There are several drug classes used to treat breast cancer. Hormonal manipulation therapies include the use of the non-steroidal drug, tamoxifen. Tamoxifen belongs to a class of drugs called **selective estrogen receptor modulators (SERMs)**. Tamoxifen can bind intracellular estrogen receptors and activate or inhibit their action depending on the type of estrogen receptor expressed by that tissue. In breast tissue, tamoxifen antagonizes the estrogen receptors, but has the opposite effect in bone and cardiovascular tissue. Since breast cancer tissue is more sensitive to estrogen due to overexpression of estrogen receptors, tamoxifen is an effective treatment to selectively target the breast cancer and shrink the mass without causing the unwanted side effect of osteoporosis or decreased heart function.

Some breast cancers express another growth-promoting receptor on their plasma membranes called **human epidermal growth factor receptor type II (HER2)**. This receptor is a tyrosine kinase. It is not well known what ligands naturally regulate this receptor, but it is known that when cancer cells express this receptor, they can be stimulated to grow aggressively. The drug Trastuzumab (Herceptin) is a derived monoclonal antibody that can bind to and block the HER2 receptors. It helps shrink tumor tissue and slow cancer progression.

Another class of drugs that may be considered for breast cancer treatment are aromatase inhibitors. They may be useful in lowering the amount of circulating estrogen available to stimulate breast tissue and tumor growth.