

LABORATORY TESTS RELATED TO BREAST CANCER

**The terms “women” and “female” refer to all people assigned the female sex at birth. The terms “male” and “men” refer to all people assigned the male sex at birth.*

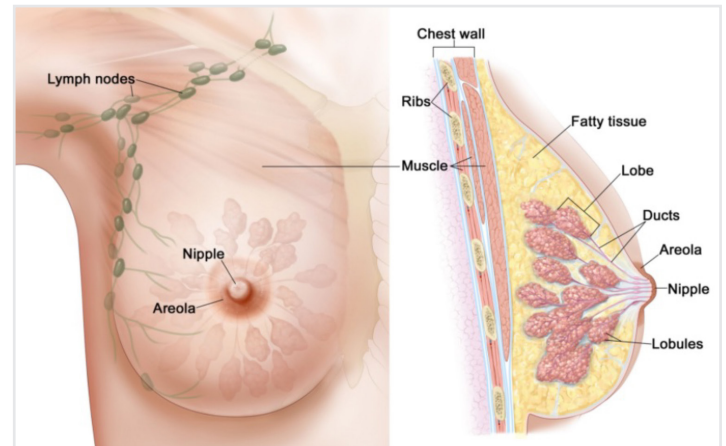
THE FEMALE AND MALE BREAST

The breast refers to tissue on the front of the chest, above the chest wall muscles. Breasts are made of connective tissue, fat, glands, and lymphatic vessels. Both male and female breasts have mammary glands (glands that can produce milk) and a nipple-areolar complex.

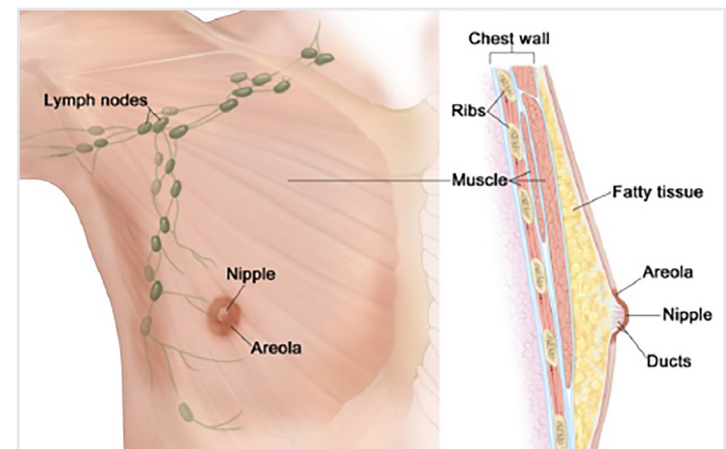
BREAST CANCER

Breast cancer is a malignant growth that begins in the breast. Most breast cancers are called carcinomas, and begin in the milk glands, (technically called terminal duct-lobular units) Some common signs and symptoms of breast cancer for both females and males include a lump or mass in the breast, nipple discharge that is not breast milk, breast or nipple pain, swelling of the breast, nipple turning inward and skin dimpling.

ANATOMY OF FEMALE BREAST



ANATOMY OF MALE BREAST



BREAST CANCER IN MEN

Male breast cancer is rare and seen most commonly in those with a genetic predisposition (BRCA1 and BRCA2). It is very similar to breast cancer in women, although most tumors are Estrogen Receptor positive and HER2 positive and triple negative breast cancers are very rare. The signs and symptoms for male breast cancer are the same as for females.

BREAST CANCER GENES (BRCA)

Breast Cancer genes (BRCA1 and BRCA2) suppress breast, ovarian and other types of cells from growing in an uncontrolled way. Every person has BRCA1 and BRCA2 genes and inherits a copy of each gene from each parent. The BRCA1 gene is located on chromosome 17 and the BRCA2 gene is on chromosome 13. An inherited genetic mutation from either parent in one or both of these genes can increase the risk of developing certain cancers. A mutated BRCA1 gene increases the risk of getting breast, ovarian, pancreatic, cervical, uterine and colon cancer. BRCA2 gene mutations increase the risk of getting breast, ovarian, pancreatic, gallbladder, bile duct and melanoma cancers. In men, BRCA1 and/or BRCA2 mutations increase the risk of getting testicular and prostate cancer.

TYPES OF BREAST CANCER

The type of breast cancer refers to the affected cells in the breast or the location of the cancer. There are numerous types of breast cancer and certain types are more common than others.

INVASIVE BREAST CANCER - INVASIVE LOBULAR CARCINOMA, INVASIVE DUCTAL CARCINOMA

Invasive breast cancer is cancer that has spread beyond the duct-lobular units into the surrounding breast tissue stroma. The most common types of invasive breast cancer are invasive ductal carcinoma (80%) and invasive lobular carcinoma (15%). Both tumors develop from the duct-lobular unit and the names describe their different appearance under the microscope and differences in biology. The signs and symptoms of invasive breast cancer include redness of the skin on the breast or nipple, a small lump or mass in the breast, a blood stained or clear liquid discharge from the nipple and change in shape or position of the nipple.

ESTROGEN-RECEPTOR POSITIVE BREAST CANCER

Estrogen receptor is an important protein that drives the growth of many breast cancers using the hormone, estrogen (approximately 70% in Caucasians and Asians, and 55% in Africans).

HER2-POSITIVE BREAST CANCER

Human epidermal growth factor receptor 2 (HER2) is another protein that drives the growth of many breast cancers (approximately 15% in Caucasians, 20% in Asians, and 25% in Africans). HER2 positive breast cancers typically grow and spread more aggressively compared to other types of breast cancers.

TRIPLE-NEGATIVE BREAST CANCER (TNBC)

Triple-negative breast cancer is a type of cancer where the cancer cells do not have estrogen receptors, progesterone receptors, or HER2. TNBC grows and spreads quickly. Women who are younger than 40, have the BRCA1 mutation or who are African, Black or Hispanic are more commonly diagnosed with TNBC. Triple-Negative breast cancer contributes to about 15% of all breast cancer cases.

INFLAMMATORY BREAST CANCER (IBC)

Inflammatory breast cancer is a rare type of cancer where the cancer cells fill and block the lymphatic vessels in the skin. IBC is usually a type of invasive ductal carcinoma and it develops quickly. The signs and symptoms include discoloration of the breast, enlargement of the breast, enlarged lymph nodes under the arm and dimpling of the skin on the breast. Between 1-5% of all breast cases are inflammatory breast cancers.

DUCTAL CARCINOMA IN SITU (DCIS)

DCIS is a non-invasive cancer that develops in the milk glands. Typically, there are no signs or symptoms for DCIS but signs could potentially (rarely) include a breast lump and bloody nipple discharge. It is most commonly diagnosed on a screening mammogram as the presence of suspicious calcifications (small deposits of calcium). The risk factors for DCIS include increasing age, genetic mutations such as BRCA1 and BRCA 2, personal history of benign breast disease and having your first menstrual cycle before age 12.

PAGET'S DISEASE OF THE BREAST

Paget's disease of the breast is rare and contributes to about 1 to 5% of all breast cancers. It is ductal carcinoma in situ that has spread up the nipple ducts and out onto the nipple skin. In half the cases it is associated with an invasive breast cancer too, not just in situ cancer. The signs and symptoms include tingling or burning sensation on the nipple, hardened skin on the nipple, a flattened or inverted nipple, itching and thickening skin on the breast.

ANGIOSARCOMA

Angiosarcoma is a very rare cancer that begins in the stromal cells lining the blood vessels. Primary angiosarcoma occurs in the breast tissue in women who have never been diagnosed with breast cancer while secondary angiosarcoma occur in the breast skin as a result of radiation treatment in women who have been previously diagnosed with breast cancer (post-radiation associated cutaneous angiosarcoma). Angiosarcomas are malignant and can spread beyond the breast. The signs and symptoms of angiosarcoma include splotchy purple colored skin and a lump in the breast.

PHYLLODES TUMOR

Phyllodes Tumors are rare tumors that begin in the stromal cells and also include ducts or glands within the tumor mass. Most are benign and do not spread beyond the breast, but malignant phyllodes tumors can spread beyond the breast. The signs and symptoms of phyllodes tumor is typically a lump in the breast.

STAGES OF BREAST CANCER

The stages of breast cancer determine how far the cancer has spread and what parts of the body it has spread to. Your treatment plan and prognosis (course of the disease) will depend on the staging portion of your diagnosis. Below is a short description of each stage:

STAGE 0: The breast cancer is in situ – it has not spread beyond the duct-lobular units (milk ducts)

STAGE I: The breast cancer has spread beyond the duct-lobular units into the stroma of the breast tissue

STAGE IA: The invasive breast cancer has not spread outside of the breast and no lymph nodes are affected. The tumor size is up to 2 cm.

STAGE IB: The breast cancer has spread to the lymph nodes and the growth is larger than 0.2 mm but less than 2mm. There may be no tumor in the breast or the tumor is less than 2cm.

STAGE II: The breast cancer has spread to a larger area of the breast and has spread to some lymph nodes

STAGE IIA: One of the following conditions applies:

- There is no tumor in the breast but the cancer has spread to the axillary (underarm) lymph nodes or

- The tumor is smaller than 2cm and has spread to the axillary lymph nodes orAges 30 to 39: 45 to 270 µg/dL or 1.22 to 7.29 µmol/L
- The cancer has not spread outside the breast and the tumor is between 2cm-5cm

STAGE IIB: One of the following conditions applies:

- The tumor is larger is larger than 5 cm and the cancer has not spread to the axillary lymph nodes orAges 20 to 29: 65 to 380 µg/dL or 1.75 to 10.26 µmol/L
- The tumor is between 2cm -5 cm and has spread to the axillary lymph nodes

STAGE III: The breast cancer has spread to more lymph nodes and the size of the tumor has increased

STAGE IIIA: one of the following conditions applies:

- The cancer is present in 4-9 axillary lymph nodes and there is no tumor in the breast or the tumor may be of any size orThe tumor is smaller than 2cm and has spread to the axillary lymph nodes orAges 30 to 39: 45 to 270 µg/dL or 1.22 to 7.29 µmol/L
- The tumor is larger than 5cm and the cancer has spread to the lymph nodes or
- The tumor is larger than 5 cm and the cancer has spread to 1-3 axillary lymph nodes

STAGE IIIB:

- The tumor has spread to the chest wall or the skin of the breast and causes inflammation or an ulcer and
- The cancer has spread to about 9 axillary lymph nodes or lymph nodes near the breast bone.

STAGE IIIC:

- The tumor may be any size or may not be present and may have spread to the chest wall or the skin of the breast andII or the skin of the breast and causes inflammation or an ulcer and
- The cancer cells have spread to the lymph nodes around the collarbone or
- The cancer has spread to the axillary lymph nodes and lymph nodes near the breast bone

STAGE IV: The breast cancer has spread to nearby lymph nodes and other organs beyond the breast (metastatic) such as the lungs or the liver.

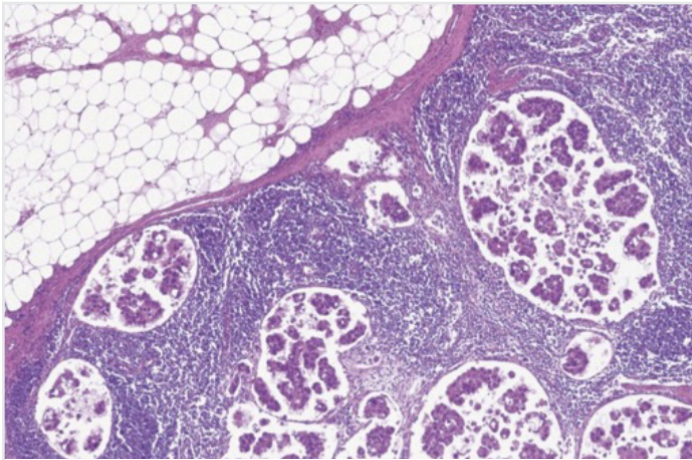
TUMOR GRADES

Tumor grades determine the appearance and growth rate of cancer cells compared to health cells in the breast.

GRADE 1: The breast cancer cells look similar to normal cells, form the shapes of normal milk ducts, and are slow growing.

GRADE 2: The breast cancer cells do not look like similar cells and are growing a little faster than normal cells.

GRADE 3: The breast cancer cells are very abnormal and they grow and spread quickly.



UNDER THE MICROSCOPE

Metastatic breast cancer cells (islands with cleared out spaces around them) within the lymph node (dark blue cells) in a patient with advanced breast cancer.

LAB TESTS RELATED TO BREAST CANCER

**Please note that reference ranges are set by individual laboratories for their specific populations so reference ranges might differ slightly.*

SCREENING TESTS

BBRCA1/BRCA2 Testing: These tests measures the presence of genetic mutations on BRCA 1 or BRCA 2 genes in the blood. This test is important because it helps determine the risk of developing breast cancer. A positive

test result means that there is a genetic mutation in your BRCA1 or BRCA 2 gene which means there is a higher risk of developing breast or ovarian cancer.

DIAGNOSIS

BIOPSY: For this test, a small sample of breast tissue is removed from the breast. This test is important because the sample of tissue is examined in the laboratory to check for malignant cells in the breast. A normal breast biopsy would not show any cancer cells.

COMPLETE BLOOD COUNT (CBC): This test determines your overall health status by looking at your overall blood count levels, including your red and white blood cell count, your platelets, and lymphocytes. This test is important because it can indicate if you are having a condition or disease, such as an infection, anemia, inflammation, or cancer.

HER2 BY FLUORESCENCE IN SITU HYBRIDIZATION (FISH): This test checks for the presence of extra copies of the HER2 gene which produces the HER2 protein. This test is important because the level of HER2 protein indicates how fast the cancer cells will grow.

IMMUNOHISTOCHEMISTRY TESTS (IHC): This test measures the amount of HER2 protein, estrogen receptors and progesterone receptors that are present in a sample of breast tissue. This test is important because it helps determine the type of breast cancer that you may have and the type of treatment needed. If the results are positive for estrogen receptors or progesterone receptors, it means that you are ER-positive or PR-positive. These results mean that hormone therapy would be effective for cancer treatment. HER2 results are reported as follows:

Score	Result
0, 1+	HER2-negative
2+	Unclear, further testing needed (FISH)
3+	HER2-positive

ADDITIONAL SCREENING TESTS

BREAST MAGNETIC RESONANCE IMAGING (MRI): This test uses strong magnets and radio waves to take detailed images of the breast. This test is important because it identifies abnormalities in the breast such as breast cancer. Breast MRIs are recommended for women who are at high risk of breast cancer. For women with average risk, there is a higher possibility of false positive results.

BREAST SELF-EXAM: This test is an examination of your breasts to assess any changes in the breast tissue and armpit. Doing a self-exam once a month is helpful in increasing familiarity with breasts and helps increase awareness of changes early.

CLINICAL BREAST EXAM: This test is a physical examination of the breast by a medical professional to check for any lumps, changes to the texture of the skin and other abnormalities. This test is important because it is used together with mammograms to screen for breast cancer.

ESTRADIOL: This test measures the levels of estradiol levels, which is one type of estrogen. The test is important because it is used to monitor antiestrogen therapies that are used to treat cancer. A typical reference range* for menstruating women is between 15-350 pg/mL. However, the levels can vary widely through the menstrual cycle. During the follicular phase, the typical reference range* is between 19-140 pg/ml; just prior to ovulation, the typical reference range* is between 110-410 pg/ml; during the end of the cycle, the luteal phase, the typical reference range* is between 19-160 pg/ml. During pregnancy, the estradiol levels will continue to increase until the fetus is mature.

MAMMOGRAPHY: This test is an x-ray picture of the breast called a mammogram. This test is important because it helps detect breast cancer early when there are no signs or symptoms. Annual mammograms are recommended for women above the age of 45 in the US, and 50 in most of Europe. It is less effective in pre-menopausal women, than post-menopausal women as the density of breast tissue affects its sensitivity and pre-menopausal women typically have very dense breasts.

CT SCAN: This test is a type of x-ray scan, usually of the whole body if there is any suggestion from a clinical examination or blood test that a cancer present in the breast has spread beyond the breast, for example, to lung, liver, or bones.

LAB TESTS RELATED TO BREAST CANCER MONITORING

CANCER ANTIGEN 15-3 (CA 15-3): This test measures the levels of the protein CA 15-3 in the blood. Increased levels of CA 15-3 in the blood indicate the presence of cancer tumors and the test may help monitor the response to treatment. The typical reference range* of CA15-3 is less than 30 U/mL. This is not used as screening, but may occasionally be used for monitoring disease progression.

BLOOD CELL COUNTS: These tests measure the white blood cell counts, red blood cell counts and platelet counts in the blood. This test is important during treatment because it helps to monitor effects of the chemotherapy.

ASK YOUR DOCTOR

- What screening test do you recommend for breast cancer?
- What is the course of action based on my lab results?
- What are all my treatment options?
- Why do you recommend this particular treatment option?
- How do we know the procedure was successful/what lab tests and which results indicate successful treatment?
- What are the markers we are monitoring? What are the levels we are hoping for? What happens if the markers are higher than we would like to see?
- What are the follow-up tests and what are we looking for?
- Are there additional tests that could be used to better understand my disease and prognosis?

MEET ANNE AND MICHELE

ANNE

“My career is based on data and technology. So being a woman of science, lab results are very important to me. I use it to validate the information that my doctors give me. Read all your lab results. It might be difficult to understand but it will be worth it.”



After finding a lump in her right breast, in January of 2019, Anne immediately scheduled a doctor’s appointment. What was presumed to be a one-hour appointment turned into four hours consisting of a mammogram, an ultrasound and a biopsy. A missed phone call and a “results available” notification signified the beginning of Anne’s battle with Stage 3 invasive ductal carcinoma cancer. Her background in laboratory work helped Anne understand and appreciate the importance of the lab and it helped her navigate the decision-making during her treatment. In order to treat her cancer, Anne had a double mastectomy operation and chemotherapy. Her experiences growing up in the slums of the Philippines have equipped her with resilience and inspiration to win the battle with cancer.



MICHELE

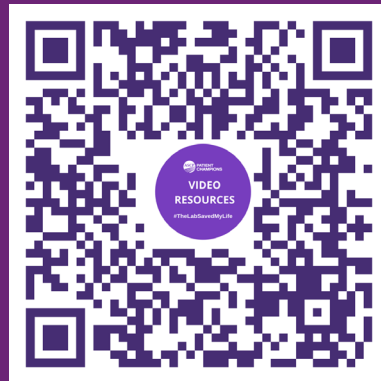
“Understanding what tests are ordered and what the lab work means is empowering. The knowledge you gain can be transformative. It was for me! Pathology is at the core of every diagnosis. Understanding what tests are ordered and what the lab work means is empowering.”

After only enjoying eight months of newly wedded bliss, Michele received a Stage 1 Invasive ductal carcinoma diagnosis. Within half an hour of sharing the news with her husband, he suffered a stroke and passed away a month later. The treatment journey for Michele was challenging as she lost her financial stability, home and health. Michele signed up for an experimental test to determine whether she was a good candidate for chemotherapy. After receiving the laboratory test results, she had surgery, began chemotherapy, radiation and adjunctive therapy to treat the Stage 1 Grade 2 aggressive tumor. Since her diagnosis, Michele has grown an appreciation for the lab and now has a better understanding of pathology reports. She is currently in remission and has become an avid patient advocate.

ADDITIONAL RESOURCES



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