Although mutations in these genes most often are found in members of families with many cases of breast and/or <u>ovarian cancer</u><sup>1</sup>, they have also been found in men with breast cancer who did not have a strong family history.

Mutations in *CHEK2, PTEN* and PALB2 genes might also be responsible for some breast cancers in men.

## Klinefelter syndrome

Klinefelter syndrome is a congenital (present at birth) condition that affects about 1 in 1,000 men. Normally the cells in men's bodies have a single X chromosome along with a Y chromosome, while women's cells have two X chromosomes. Men with Klinefelter syndrome have cells with a Y chromosome plus at least two X chromosomes (but sometimes more).

Men with Klinefelter syndrome also have small testicles and are often infertile because they are unable to produce functioning sperm cells. Compared with other men, they have lower levels of androgens (male hormones) and more estrogens (female hormones). For this reason, they often develop gynecomastia<sup>2</sup> (benign male breast growth).

Men with Klinefelter syndrome are more likely to get breast cancer than other men. Having this condition can increase the risk anywhere between 20 - 60 times the risk of a man in the general population.

### **Radiation exposure**

A man whose chest area has been treated with <u>radiation</u><sup>3</sup> (such as for the treatment of a cancer in the chest, like <u>lymphoma</u><sup>4</sup>) has an increased risk of developing breast cancer.

# Alcohol

<u>Heavy drinking</u><sup>5</sup> (of alcoholic beverages) increases the risk of breast cancer in men. This may be because of its effects on the liver (see next paragraph).

## Liver disease

The liver plays an important role in balancing the levels of sex hormones. In cases of severe liver disease, such as cirrhosis, the liver is not working well and the hormone

levels are uneven, causing lower levels of androgens and higher levels of estrogen. Men with liver disease can also have a higher chance of developing benign male breast growth (gynecomastia) and also have an higher risk of developing breast cancer.

## **Estrogen treatment**

Estrogen-related drugs were once used in hormonal therapy for men with <u>prostate</u> <u>cancer</u><sup>6</sup>. This treatment may slightly increase breast cancer risk.

There is concern that transgender/transsexual individuals who take high doses of estrogen as part of gender-affirming hormonal treatment could also have a higher breast cancer risk. Still, research on breast cancer risk in transgender individuals is quite new, so it isn't clear what their breast cancer risk may be.

## Obesity

Studies have shown that women's breast cancer risk is increased by <u>obesity</u><sup>7</sup> (being extremely overweight) after menopause. Obesity is also a risk factor for male breast cancer as well. The reason is that fat cells in the body convert male hormones (androgens) into female hormones (estrogens). This means that obese men have higher levels of estrogens in their body.

# **Testicular conditions**

Certain conditions, such as having an undescended testicle, having mumps as an adult, or having one or both testicles surgically removed (orchiectomy) may increase male breast cancer risk.

# **Hyperlinks**

- 1. www.cancer.org/cancer/types/ovarian-cancer.html
- 2. <u>www.cancer.org/cancer/types/breast-cancer-in-men/about/what-is-breast-cancer-in-men.html</u>
- 3. <u>www.cancer.org/cancer/risk-prevention/radiation-exposure/x-rays-gamma-rays.html</u>
- 4. <u>www.cancer.org/cancer/types/lymphoma.html</u>

- 5. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-</u> <u>cancer.html</u>
- 6. <u>www.cancer.org/cancer/types/prostate-cancer.html</u>
- 7. www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-andcancer-risk.html

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Last Revised: April 27, 2018

# What Causes Breast Cancer in Men?

- Hormone levels
- Gene changes (mutations)

Although certain risk factors may increase a man's chances of developing breast cancer, the cause of most breast cancers in men is unknown.

## Hormone levels

Breast cells normally grow and divide in response to female hormones such as estrogen. The more cells divide, the more chances there are for mistakes to be made when they are copying their DNA. These DNA changes can eventually lead to cancer (see below).

Factors that unbalance the levels of female and male hormones in the body can therefore have an effect on breast cancer risk. Many of these were described in Risk Factors for Breast Cancer in Men.

## Gene changes (mutations)

Researchers are making great progress in understanding how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in our cells that makes up our *genes*, the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. However, DNA affects more than how we look.

Some <u>genes</u><sup>1</sup> contain instructions for controlling when our cells grow, divide, and die. Certain genes that speed up cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the appropriate time are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (defects) that turn on oncogenes or turn off tumor suppressor genes.

#### Acquired gene mutations

Most DNA mutations related to male breast cancer occur during life rather than having been inherited from a parent before birth. It's not clear what causes most of these mutations. Radiation to the breast area is a factor in a small number of cases. Some acquired mutations of oncogenes and/or tumor suppressor genes may be the result of cancer-causing chemicals in our environment or diet, but so far studies have not identified any chemicals that are responsible for these mutations in male breast cancers.

#### Inherited gene mutations

Certain inherited DNA changes can cause a high risk of developing certain cancers and are responsible for cancers that run in some families.

Some breast cancers are linked to inherited mutations of the *BRCA1* or *BRCA2* tumor suppressor genes. Normally, these genes make proteins that help cells recognize and/or repair DNA damage and prevent them from growing abnormally. But if a person has inherited a mutated gene from either parent, the chances of developing breast cancer are higher.

Men with inherited mutations in the *BRCA1* and *BRCA2* genes have a higher lifetime risk for breast cancer, and possibly some other cancers such as prostate and pancreatic cancer. There are also other hereditary cancer syndromes that can be associated with male breast cancer.

All men who have been diagnosed with breast cancer should consider <u>genetic testing</u><sup>2</sup> because they can be at risk for other cancers, such as prostate and pancreas cancer. Having one of these inherited gene changes might also affect their family members' chances of getting certain cancers.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html</u>
- 2. www.cancer.org/cancer/risk-prevention/genetics.html

#### References

them. But there are some things a man can do to lower his risk of breast cancer.

**Get to and stay at a healthy weight:** Both increased body weight and weight gain as an adult are linked with a higher risk of breast cancer in women. And since being <u>overweight or obese<sup>1</sup></u> is linked with an increased risk for several cancers, the American Cancer Society recommends you stay at a healthy weight throughout your life and avoid excess weight gain by balancing your food intake with physical activity.

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nutrition-physical-activity-cancer-prevention.html