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Family Cancer Syndromes

Cancer is a common disease, so it's no surprise that many families have at least a few members who have had cancer.

Sometimes, certain types of cancer seem to run in some families. In some cases, this might be because family members share certain behaviors or exposures that increase cancer risk, such as smoking. Cancer risk might also be affected by other factors, like obesity, that tend to run in some families.

But in some cases the cancer is caused by an abnormal gene that is being passed along from generation to generation. Although this is often referred to as *inherited* cancer, what is inherited is the abnormal gene that can lead to cancer, not the cancer itself. Only about 5% to 10% of all cancers result directly from gene defects (called *mutations*) inherited from a parent. This information is about those cancers.

Genes, mutations, and cancer

Cancer is a disease in which cells grow out of control. This happens because of changes in some of the genes inside cells. Genes are pieces of DNA that control how cells make the proteins the body needs to function, as well as how cells are kept in balance. Your genes affect things such as hair color, eye color, and height. They can also affect your chance of getting certain diseases, such as cancer.

Nearly every cell in your body has all of the genes you were born with. Although all cells have the same genes, different cells (or types of cells) may use different genes. For example, muscle cells use different genes than skin cells use. The genes that the cell doesn't need are turned off and not used. The genes that the cell is using are activated or turned on.

An abnormal change in a gene is called a **mutation**. Mutations in a gene can affect how

it functions. For example, a mutation might stop a gene from working. Or it might keep a gene turned on all the time (even when it's not needed). Either way, these can cause problems inside the cell.

Gene mutations can be either inherited or acquired.

- An **inherited gene mutation** is present in the egg or sperm cell that formed the child. When the egg is fertilized by the sperm, it creates one cell that then divides many times and eventually becomes a baby. Since all the cells come from this first cell, this kind of mutation is in every cell (including eggs or sperm) and so can be passed on to the next generation.
- An **acquired (somatic) mutation** does not come from a parent, but is acquired some time later. It starts in one cell, and then is passed on to any new cells that are created from that cell. This kind of mutation is not present in egg or sperm cells, so it is not passed on to the next generation. Acquired mutations are much more common than inherited mutations. Most cancers are caused by acquired mutations.

Many family cancer syndromes are caused by inherited mutations in *tumor suppressor genes*. These are genes that normally keep cells under control by slowing down how often they divide (to make new cells), repairing DNA mistakes, or telling cells to die at the right time.

You have 2 copies of most genes – one from each parent. When someone inherits an abnormal copy of a gene, their cells already start out with one mutation. Often this is not a problem, as the other gene copy is still working. But if the other gene copy stops working (because of an acquired mutation, for example), the gene's function can be lost altogether. When the gene that stops working is a tumor suppressor gene, cells can grow out of control, which can lead to cancer.

A person born with an inherited mutation in a copy of a tumor suppressor gene would only have to acquire a mutation in the other copy of that gene for it not to work. This is more likely to happen than acquiring mutations in both copies of a gene, so this person would have a higher risk of cancer than someone born without a gene mutation.

For more information about gene changes that can lead to cancer, see [Genes and Cancer](#)¹.

How do you recognize a family cancer syndrome?

It's important to keep in mind that cancer is common. In fact, about 1 in 3 people in the

United States will develop cancer during their lifetime, so it's not uncommon to have many cancers in a family.

When many cases of cancer occur in a family, it is most often due to chance or because family members have been exposed to a common risk factor, such as smoking.

Sometimes there might be an interaction between certain genes and exposures. For example, some people inherit gene changes that make it harder for their bodies to get rid of toxins in tobacco smoke. These people might be more likely to get cancer if they smoke than someone who does not have these gene changes.

Less often, cancers in a family are strongly linked to an inherited gene mutation that is part of a **family cancer syndrome**.

Certain things make it more likely that cancers in a family are caused by a family cancer syndrome, such as:

- Many cases of the same type of cancer (especially if it is an uncommon or rare type of cancer)
- Cancers occurring at younger ages than usual (like colon cancer in a 20-year-old)
- More than one type of cancer in a single person (like a woman with both breast and ovarian cancer)
- Cancers occurring in both of a pair of organs (like both eyes, both kidneys, or both breasts)
- More than one [childhood cancer](#)² in siblings (like sarcoma in both a brother and a sister)
- Cancer occurring in the sex not usually affected (like breast cancer in a man)
- Cancer occurring in many generations (like in a grandfather, father, and son)

When trying to determine if cancer might run in your family, first gather some information. For each case of cancer, look at:

- Who has the cancer? How are you related? Which side of the family are they on (mother's or father's)?
- What type of cancer is it? Is it rare?
- How old was this relative when they were diagnosed?
- Did this person get more than one type of cancer?
- Did they have any known risk factors for their type of cancer (such as smoking for lung cancer)?

Cancer in a close relative, like a parent or sibling (brother or sister), is more cause for concern than cancer in a more distant relative. Even if the cancer was from a gene mutation, the chance of it passing on to you gets lower with more distant relatives.

It's also important to look at each side of the family separately. Having 2 relatives with cancer is more concerning if they are on the same side of the family. For example, it's more concerning if both relatives are your mother's brothers than if one was your father's brother and the other was your mother's brother.

The type of cancer matters, too. It is more concerning if many relatives have the same type of cancer than if they have several different kinds of cancer. Still, in some family cancer syndromes, a few types of cancer seem to go together. For example, breast cancer and ovarian cancer run together in families with hereditary breast and ovarian cancer syndrome (HBOC). Colon and endometrial cancers tend to go together in Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC).

By the same token, more than one case of the same rare cancer is more worrisome than cases of a more common cancer. For some rare cancers, the risk of a family cancer syndrome is relatively high with even one case.

The age of the person when the cancer was diagnosed is also important. For example, colon cancer usually is rare in people younger than 30. Having close relatives under 30 with colon cancer could be a sign of an inherited cancer syndrome. On the other hand, prostate cancer is very common in elderly men, so if both your father and his brother were found to have prostate cancer when they were in their 80s, it is less likely to be due to an inherited gene change.

Certain kinds of benign (not cancer) tumors and medical conditions are sometimes also part of a family cancer syndrome. For example, people with the multiple endocrine neoplasia, type II syndrome (MEN II) have a high risk of a certain kind of thyroid cancer. They also may develop benign tumors of the parathyroid glands and can also get tumors in the adrenal glands called pheochromocytomas, which are usually benign.

When many relatives have the same type of cancer, it's important to note if the cancer could be related to a risk factor like smoking. For example, lung cancer is commonly caused by smoking, so several cases of lung cancer in a family of people who are heavy smokers are more likely to be due to smoking than to an inherited gene change.

Examples of family cancer syndromes

There are many family cancer syndromes. Some of these are discussed briefly here as examples, but this is not a full list. For more information about a particular type of cancer and its genetic components, diagnosis, and treatment, please see our content on that specific type of cancer.

Hereditary Breast and Ovarian Cancer (HBOC) syndrome

In some families, many women develop breast cancer and/or ovarian cancer. Often these cancers are found in women who are younger than the usual age these cancers are found, and some women might have more than one cancer (such as breast cancer in both breasts, or both breast and ovarian cancer). This is known as Hereditary Breast and Ovarian Cancer syndrome (HBOC).

Most often, HBOC is caused by an inherited mutation in either the *BRCA1* or *BRCA2* gene. (Some families have HBOC based on cancer history, but don't have mutations in either of these genes. Scientists believe that there might also be other genes that can cause HBOC.)

The risk of breast and ovarian cancer is very high in women with mutations in either *BRCA1* or *BRCA2*, but it tends to be higher with *BRCA1* mutations. Along with breast and ovarian cancer, this syndrome can also lead to fallopian tube cancer, primary peritoneal cancer, [male breast cancer](#)³, [pancreatic cancer](#)⁴, and [prostate cancer](#)⁵, as well as some others. Male breast cancer, pancreatic cancer, and prostate cancer can be seen with mutations in either gene, but are more common in people with *BRCA2* mutations. In the US, mutations in the *BRCA* genes are more common in people of Ashkenazi Jewish descent than in the general population.

Women with a strong family history of breast cancer and/or ovarian cancer may choose to undergo genetic counseling to help estimate their risk for having a mutation in one of the *BRCA* genes. The genetics professional can estimate the risk based on a patient's history of cancer and the history of cancer in their family. If they have a high risk, they might choose to be tested (see [Understanding Genetic Testing for Cancer](#)⁶). If a mutation is present, the woman has a high risk of developing breast cancer and ovarian cancer (as well as some other cancers). She can then consider steps to find cancer early and even lower her risk of getting cancer.

Because breast cancer is rare in men, men with this cancer are often offered genetic counseling and testing for *BRCA* mutations. Although having a mutation is less likely to affect a man's future health than it is a woman's, it can affect his risk of some cancers, such as prostate and pancreatic cancer. It can also be helpful for a man's close relatives to know that he has a mutation and that they might be at risk.

If someone has a *BRCA* mutation, it means that their close relatives (parents, siblings, and children) have a 50% chance of having a mutation, too. They may wish to be tested for the mutation, or even without testing may wish to start screening for certain cancers early or take other precautions to lower their risk of cancer.

HBOC is not the only family cancer syndrome that can cause breast or ovarian cancer. For information about other genes and syndromes that raise the risk of these cancers, see [Breast Cancer](#)⁷ and [Ovarian Cancer](#)⁸.

Lynch syndrome (hereditary non-polyposis colorectal cancer)

The most common inherited syndrome that increases a person's risk for colon cancer is Lynch syndrome, also called hereditary non-polyposis colorectal cancer (HNPCC). People with this syndrome are at high risk of developing colorectal cancer. Most of these cancers develop before they are 50.

Lynch syndrome also leads to a high risk of [endometrial cancer](#)⁹ (cancer in the lining of the uterus), as well as cancers of the [ovary](#)¹⁰, [stomach](#)¹¹, [small intestine](#)¹², [pancreas](#)¹³, [kidney](#)¹⁴, [brain](#)¹⁵, ureters (tubes that carry urine from the kidneys to the bladder), and [bile duct](#)¹⁶.

Lynch syndrome can be caused by a mutation in any of several mismatch repair (MMR) genes, including *MLH1*, *MSH2*, *MSH6*, *PMS1*, and *PMS2*. These genes are normally involved in repairing damaged DNA. When one of these genes isn't working, cells can develop mistakes in their DNA, which might lead to other gene mutations and eventually cancer.

Doctors and genetics professionals can check if Lynch syndrome is likely based on your personal and family cancer history using certain criteria. These, known as the Amsterdam criteria and the revised Bethesda guidelines, are discussed in detail in [Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer](#).¹⁷ Mutations in the genes that cause Lynch syndrome can then be tested for with genetic testing.

For people who have colorectal or endometrial cancer, the tumor tissue can be tested for MMR gene changes, or for other changes that can be caused when one of these genes is faulty, which is known as microsatellite instability (or MSI). Having normal findings (no MMR gene changes or MSI) implies that a person probably does not have Lynch syndrome. But if one of these is present, the person may have Lynch syndrome, and is referred for genetic counseling and possible testing. For more information about genetic testing, see [Genetics and Cancer](#)¹⁸.

Someone who is known to carry a gene mutation linked to Lynch syndrome may start screening for colorectal cancer when they are younger (such as during their early 20s), or take other steps to try to prevent cancer from starting (discussed in more detail in Colorectal Cancer). Women with Lynch syndrome may start screening for endometrial cancer or take other steps to try to prevent this cancer. These are discussed in more detail in Endometrial Cancer.

If someone has Lynch syndrome, it means that their close relatives (parents, siblings, and children) have a 50% chance of having a mutation, too. They may wish to be tested, or even without testing they may wish to start screening early for certain cancers or take other precautions to help lower their risk of cancer.

Li-Fraumeni syndrome

Li-Fraumeni syndrome is a rare inherited syndrome that can lead to the development of a number of cancers, including sarcoma (such as [osteosarcoma](#)¹⁹ and [soft-tissue sarcomas](#)²⁰), [leukemia](#)²¹, [brain \(central nervous system\) cancers](#)²², cancer of the [adrenal cortex](#)²³ and [breast cancer](#)²⁴. These cancers often develop when people are relatively young.

People with Li-Fraumeni also can develop more than one cancer in their lifetime. They also seem to have a higher risk of getting cancer from radiation therapy, so doctors treating these patients might try to avoid giving them radiation when possible.

This syndrome is most often caused by inherited mutations in the *TP53* gene, which is a tumor suppressor gene. A normal *TP53* gene makes a protein that helps stop abnormal cells from growing.

Li-Fraumeni syndrome can also be caused by mutations in a tumor suppressor gene called *CHEK2*, which also normally helps stop cells with DNA damage from growing.

If someone has Li-Fraumeni syndrome, their close relatives (especially children) have an increased chance of having a mutation, too. They may wish to be tested, or even without testing they may wish to start screening for certain cancers early or take other precautions to help lower their risk of cancer.

Genetic counseling and testing

People with a strong family history of cancer may want to learn their genetic makeup. This may help the person or other family members plan their health care for the future. Since inherited mutations affect all cells of a person's body, they can often be found by

genetic testing done on blood or saliva (spit) samples. Still, genetic testing is not helpful for everyone, so it's important to speak with a genetic counselor first to find out if testing might be right for you. For more information, see [Understanding Genetic Testing for Cancer](#)²⁵.

Other common family cancer syndromes

You can learn more about the family cancer syndromes listed above, along with other inherited syndromes and gene mutations that might affect a person's risk for cancer, by reading:

[Genetic Counseling and Testing for Breast Cancer Risk](#)²⁶: Hereditary Breast and Ovarian Cancer Syndrome (HBOC), *BRCA1* and *BRCA2* mutations, and other specific gene mutations

[Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer](#)²⁷: Lynch syndrome, familial adenomatous polyposis (FAP), and other specific gene mutations

[Genetic Counseling and Testing for People at High Risk of Melanoma](#)²⁸: Specific gene mutations

[Ovarian Cancer Risk Factors](#)²⁹: Hereditary Breast and Ovarian Cancer Syndrome (HBOC), Lynch syndrome, Peutz-Jeghers syndrome, MUTYH-associated polyposis, *BRCA1* and *BRCA2* mutations, and other specific gene mutations

Hyperlinks

1. www.cancer.org/cancer/cancer-causes/genetics/genes-and-cancer.html
2. www.cancer.org/cancer/cancer-in-children.html
3. www.cancer.org/cancer/breast-cancer-in-men.html
4. www.cancer.org/cancer/pancreatic-cancer.html
5. www.cancer.org/cancer/prostate-cancer.html
6. www.cancer.org/cancer/cancer-causes/genetics/understanding-genetic-testing-for-cancer.html
7. www.cancer.org/cancer/breast-cancer.html
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23. www.cancer.org/cancer/adrenal-cancer.html
24. www.cancer.org/cancer/breast-cancer.html
25. www.cancer.org/cancer/cancer-causes/genetics/understanding-genetic-testing-for-cancer.html
26. www.cancer.org/cancer/breast-cancer/risk-and-prevention/genetic-testing.html
27. www.cancer.org/cancer/colon-rectal-cancer/causes-risks-prevention/genetic-tests-screening-prevention.html
28. www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/genetic-counseling-and-testing-for-people-at-high-risk-of-melanoma.html
29. www.cancer.org/cancer/ovarian-cancer/causes-risks-prevention/risk-factors.html
30. <http://www.cancer.gov>
31. <http://www.nsgc.org>
32. <http://www.cancer.gov>
33. <http://www.nsgc.org>

Additional resources

Along with the American Cancer Society, other sources of information and support include:

National Cancer Institute Toll-free number: 1-800-4-CANCER (1-800-422-6237)
Website: www.cancer.gov (<http://www.cancer.gov>)³⁰

Provides accurate, up-to-date information on a variety of cancer-related topics such as finding support, financial assistance and other resources; coping with cancer; cancer genetics, etc (click the “Cancer Topics” tab on the home page). Also has an Online

Cancer Genetics Services Directory to identify professionals who provide services related to cancer genetics (cancer risk assessment, genetic counseling, genetic susceptibility testing, and others).

National Society of Genetic Counselors (NSGC) Telephone: 1-312-321-6834

Website: www.nsgc.org (<http://www.nsgc.org>)³¹

Offers a "Consumer Information" link with the following:

- "Making Sense of Your Genes" – a 24-page guide to genetic counseling (may be downloaded and printed)
- Directory of genetic counselors – may be searched by your area
- "Five Questions to Ask Before Considering Genetic Testing" (may be downloaded and printed)
- Guide on collecting family history – a helpful tool in determining possible genetic risks
- FAQs on genetic testing and genetic counselors

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

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