

Hereditary Pancreatic Cancer

Most people develop pancreatic cancer by chance or as a result of risk factors that occur over the course of a lifetime. Risk factors for pancreatic cancer include increasing age, smoking and tobacco use, family history, obesity/being overweight, chronic inflammation of the pancreas (pancreatitis), diabetes, and environmental exposures. Pancreatic cancer may occur more frequently in men versus women, and in those of African descents versus Caucasian and other backgrounds.

Approximately 10 percent of people who are diagnosed with pancreatic cancer develop it due to a hereditary pancreatic cancer syndrome. A hereditary pancreatic cancer syndrome is an inherited increased risk to develop pancreatic and possibly other cancers. Inherited conditions are passed to an individual through their blood relatives. People who have a hereditary pancreatic cancer gene mutation have a higher than average risk of developing pancreatic and possibly other cancers.

What Causes Hereditary Pancreatic Cancer?

Hereditary pancreatic cancer syndromes are caused by an inherited change, called a mutation, in a gene. Genes are the set of instructions that tell all of the cells in our bodies what to do. Genes determine physical characteristics, such as our hair and eye color, the shape of our nose, and our blood type. A mutation is a change in a gene that causes the gene to stop working. In the case of hereditary pancreatic cancer, a gene that normally helps to prevent cancer has stopped working. Therefore, certain types of cancer are more likely to develop and are also more likely to occur at a younger age than usual.

Hereditary cancer syndromes with increased pancreatic cancer risk include Hereditary Breast and Ovarian Cancer (HBOC) Syndrome due to *BRCA1/BRCA2* gene mutations; Lynch Syndrome due to mutations in *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM*; Peutz-Jeghers syndrome due to mutations in *STK11*; Li-Fraumeni Syndrome due to mutations in *TP53*; familial adenomatous polyposis due to *APC* mutations; and Melanoma-Pancreatic Cancer syndrome due to *CDKN2A* mutations. Mutations in additional genes, such as *PALB2* and *ATM*, may also increase the risk for pancreatic and other cancer types. In addition, individuals who have hereditary pancreatitis also have an increased risk to develop pancreatic cancer.

Each person inherits two copies of most genes, one copy from our mother and one copy from our father. Inheriting a mutation in one copy of a hereditary pancreatic cancer syndrome gene is enough to increase the risk for cancer. There is a 50 percent chance that a person with a hereditary pancreatic cancer syndrome gene mutation will pass it to each of his or her children. However, if a person does not inherit the hereditary pancreatic cancer syndrome gene mutation present in his or her family member(s), that person usually has an average chance of developing cancer.

Why Is It Important to Diagnose Hereditary Pancreatic Cancer in a Family?

People who have a hereditary pancreatic cancer syndrome have a greater than average chance to develop pancreatic and other cancers than the general population. For someone who already has been diagnosed with pancreatic cancer, the diagnosis of a hereditary pancreatic cancer syndrome may indicate a greater chance of developing another cancer.

Because a hereditary pancreatic cancer syndrome is inherited, the diagnosis also affects family members. If genetic testing identifies a mutation in a gene that causes a hereditary pancreatic cancer syndrome, family members can be tested for that same gene mutation.

It is very important for people with a hereditary cancer syndrome to consider specialized cancer screening exams. Cancer screening exams are medical tests performed to help identify cancers at their earliest, most treatable stages. They may also consider medical options that can lower their risk of developing cancer. Usually a team of specialists will tailor a cancer screening and risk reduction plan to each patient and his or her family members.

How Is Hereditary Pancreatic Cancer Diagnosed?

A genetics evaluation includes a review of a person's medical and family history. A family tree, called a pedigree, is often drawn during the evaluation. This information is used to determine the likelihood that the person has a hereditary pancreatic cancer syndrome. A genetic counselor usually conducts this evaluation.

Hereditary pancreatic cancer may be suspected when there are multiple family members diagnosed with pancreatic cancer; relatively early ages at cancer diagnosis; and additional family history of breast, ovarian, uterine, colon, stomach, small bowel, prostate, urinary tract, and/or melanoma skin cancers (on the same side of the family).

If you or your family members have any of the above features, you may consider the option of genetic counseling and testing. We encourage you to discuss this with your physician.

What Is Genetic Testing?

A person's blood or saliva sample can be tested to search for a genetic mutation that causes hereditary pancreatic cancer. This testing may be limited to the HBOC and/or Lynch Syndrome genes or may include other genes that cause hereditary pancreatic cancer. In general, there are three types of results:

- **Positive for a mutation.** If a mutation is found, then the diagnosis of a hereditary cancer syndrome is confirmed. Next, other family members may have a genetic test to learn whether or not they carry the same mutation and have the same hereditary cancer syndrome.
- **Negative for a mutation.** If no mutation is found the cancer in the family may not be hereditary. However, a negative genetic test result does not eliminate the possibility of a hereditary cancer syndrome in the family. This is because current genetic testing technology is not able to identify all mutations that cause hereditary cancer. It is also possible that the cancer in the family is being caused by a gene that was not included in the test.
- **Variant of unknown significance.** A variant is a gene change that does not provide clear information regarding cancer risks. More research is needed to determine whether a genetic variant increases cancer risk. Thus, a variant result should not be used to make medical decisions.

If you are concerned about the possibility of a hereditary cancer syndrome in your family, you are encouraged to discuss your personal and/or family history with your healthcare provider. Your physician may refer you to the Cancer Genetics Program at MD Anderson Cancer Center at Cooper for a genetic evaluation and discussion of your genetic testing options. If genetic testing is recommended and you choose to proceed, a blood or saliva sample will be taken during your visit. Please note that health insurance companies may cover most if not all of the cost of genetic testing on a case-by-case basis.

Where Can I Find More Information?

Cancer Net offers oncologist-approved cancer information from the American Society of Clinical Oncology. Visit www.cancer.net/cancer-types/familial-pancreatic-cancer.

National Cancer Institute website has valuable cancer related health information on more than 200 cancer types, clinical trials, cancer statistics, prevention, screening, risk factors, genetics, and support resources. Information is available in Spanish. Visit www.cancer.gov.

American Cancer Society (ACS) is a voluntary national health organization that supports research, provides information about cancer, and offers many programs and services to patients and their families. Information is available in Spanish. Visit www.cancer.org.

Genetic Alliance, Inc., supports individuals with genetic conditions and their families, educates the public, and advocates for consumer-informed public policies. This site provides information on genetic policy and research and a helpline for people with genetic questions. Visit www.geneticalliance.org.