

CHRONIC PANCREATITIS

GENETIC TESTING



What is chronic pancreatitis?

Chronic pancreatitis is ongoing inflammation of the pancreas. Your pancreas lies behind your stomach and in front of your spine. It is made up of two types of glands. One type of gland makes a digestive juice containing a protein (enzyme) that helps break down certain foods so their nutrients can be absorbed into your bloodstream. The other type of gland makes insulin and glucagon, hormones that control the amount of sugar (glucose) in your blood.

Over time, chronic pancreatitis can damage the pancreas and may lead to health problems such as¹:

- Chronic, severe upper abdominal pain
- Nausea and vomiting
- Incomplete digestion of food
- Diabetes
- Pancreatic cancer (rare)

The most common cause of chronic pancreatitis is alcohol abuse (alcohol-induced pancreatitis).² About 20% of cases of chronic pancreatitis have no known cause and are called sporadic or idiopathic chronic pancreatitis.^{2,3} Less than 5% of the time, chronic pancreatitis affects more than 1 member of a family.² These cases are known as **hereditary chronic pancreatitis (HCP)**.

People who have HCP tend to develop symptoms at a young age (late childhood or early teens).^{1,2} Early symptoms of HCP include sudden, recurrent attacks of upper abdominal pain with nausea and vomiting.¹ Long-term damage to the pancreas and the health problems resulting from that damage may take decades to develop in people with HCP.^{1,2}

Treatment of chronic pancreatitis may include¹:

- Medications to relieve pain
- Taking enzyme pills to aid digestion
- Eating a low-fat diet and taking nutritional supplements
- Surgery to open blockages in channels (ducts) that lead from the pancreas to the intestine

- Treatment of diabetes and other health problems resulting from chronic pancreatitis

What role do genes play in the development of chronic pancreatitis?

Some cases of hereditary and sporadic chronic pancreatitis have been linked with abnormal changes in certain genes. Genes are found in every cell in your body. They carry the instructions for making proteins that control how each of your cells work. Genes can undergo abnormal changes (called mutations) that may cause cells to stop working the way they should. Gene mutations may result in health problems that may be passed from parent to child (inherited).

PRSS1, *SPINK1* and *CFTR* are genes that are linked with chronic pancreatitis when a mutation is present.

- The *PRSS1* gene instructs pancreas cells to make an enzyme called trypsinogen. This enzyme is released into the small intestine where it is changed into trypsin, which breaks down protein from food. A *PRSS1* mutation may result in trypsinogen being changed into trypsin inside the pancreas, which can lead to damage that causes pancreatitis.^{1,3}
- The *SPINK1* gene instructs pancreas cells to make a substance that binds to trypsin and limits (inhibits) its activity in the pancreas. A *SPINK1* mutation may result in reduced ability of the inhibitor to bind to trypsin, so trypsin that becomes activated inside the pancreas cannot be kept from causing damage that can lead to pancreatitis.³
- The *CFTR* gene tells cells to make a protein that controls the movement of chloride and water in and out of the cells, such as those in the pancreas that make digestive enzymes. Mutations in the *CFTR* gene can cause cystic fibrosis (CF). People born with 2 *CFTR* mutations are affected with CF, and most have reduced pancreatic function.⁴ People born with just 1 *CFTR* mutation are not affected with CF, but they may be at increased risk for idiopathic chronic pancreatitis.³

How is chronic pancreatitis diagnosed?

Chronic pancreatitis may be diagnosed with:

- Blood tests that can show how well the pancreas is working.
- Imaging tests (such as ultrasound, X-rays, or CT scan) that, in the later stages of the disease, can show

changes in the pancreas resulting from ongoing inflammation.

A genetic test called full gene sequencing can be done to confirm a diagnosis of hereditary or sporadic chronic pancreatitis. This blood test reads the instructions (DNA) that make up the *PRSS1*, *SPINK1*, and *CFTR* genes. The test can find mutations in those genes that are linked with chronic pancreatitis.

When might full gene sequencing for chronic pancreatitis be recommended?

Full gene sequencing to detect mutations linked with chronic hereditary pancreatitis may be recommended in the following cases¹:

- A child who has an unexplained attack of pancreatitis
- Unexplained, recurring attacks of acute (sudden, short-lived) pancreatitis in a person who has a family history of acute recurrent pancreatitis or chronic pancreatitis
- Unexplained chronic pancreatitis in a person who has a family history of acute recurrent pancreatitis or chronic pancreatitis
- Unexplained chronic pancreatitis in a person who has no family history of pancreatitis and does not have any other condition that could cause pancreatitis

What possible results can be reported, and what might they mean?

- **Negative:** After scanning the *PRSS1*, *SPINK1*, and *CFTR* genes, no detectable mutations are found. Full gene sequencing does not detect all possible mutations in the *PRSS1*, *SPINK1*, and *CFTR* genes. For this reason, a negative result cannot completely rule out a mutation in 1 of these genes or in another gene as the cause of pancreatitis.

- **Positive:** After scanning the *PRSS1*, *SPINK1*, and *CFTR* genes, 1 or more mutations are found. Along with the person's signs and symptoms, a positive genetic test result may confirm a diagnosis of chronic pancreatitis.
- **Variant of unknown significance:** After scanning the *PRSS1*, *SPINK1*, and *CFTR* genes, a mutation was found that has not been reported before. It is unclear if this mutation is the cause of the person's symptoms.

Test results should be combined with clinical findings and reviewed by your doctor or a genetics health professional for the best interpretation.

Full gene sequencing test results should be combined with clinical findings and reviewed by a health professional who specializes in medical genetics.

Where can I find more information?

If you have questions or want more information about genetic testing for chronic pancreatitis, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at www.nsgc.org.

- National Pancreas Foundation (NPF)
Telephone: 866-726-2737
Home page: www.pancreasfoundation.org
- Comprehensive Center for Chronic Pancreatitis (University of Arizona Medical Center)
Telephone: (520) 626-9911
Home page: www.pancreatitiscenter.org

Note: This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

References

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4. Moskowitz SM, Chmiel JF, Stern DL, Cheng E, Cutting GR. CFTR-related disorders. In: Pagon RA, Bird TD, Dolan CR, et al, eds. *GeneReviews*™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-. <http://www.ncbi.nlm.nih.gov/books/NBK1250/>. Updated February 19, 2008. Accessed October 25, 2012.



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