Pancreatic Neuroendocrine Tumors Early Detection, Diagnosis, and Staging

Know the signs and symptoms of pancreatic neuroendocrine tumors. Find out how it's tested for, diagnosed, and staged.

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Pancreatic Neuroendocrine Tumor Be Found Early?
- Signs and Symptoms of Pancreatic Neuroendocrine Tumor
- Tests for Pancreatic Neuroendocrine Tumor

Stages and Outlook (Prognosis)

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

- Pancreatic Neuroendocrine Tumor Stages

Can Pancreatic Neuroendocrine Tumor Be Found Early?

definitely will get pancreatic NET.

Testing for pancreatic neuroendocrine tumor in people at high risk

For people in families at high risk of pancreatic NET, such as MEN1 syndrome, tests for detecting cancer early may help. Although definitive screening guidelines for people with the MEN1 gene or their family members are not available, doctors have been able to find early, treatable pancreatic NETs in some members of high-risk families with these tests. Some tests that might be considered include:

- An endoscopic ultrasound of the pancreas every few years.
- A MRI of the pancreas every few years.
- Checking blood levels of certain hormones such as insulin, prolactin, gastrin, and calcium every few years. (Sometimes, changes in hormones can occur 10 years before the tumor is found by clinical symptoms.)
- An Octreoscan on a regular basis.

Hyperlinks

1. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
2. www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html
3. www.cancer.org/cancer/risk-prevention/genetics.html

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Signs and Symptoms of Pancreatic Neuroendocrine Tumor

Having one or more of the symptoms below does not mean you have a pancreatic neuroendocrine tumor (NET). In fact, many of these symptoms are more likely to be caused by other conditions. Still, if you have any of these symptoms, it's important to have them checked by a doctor so that the cause can be found and treated, if needed.

Pancreatic NETs often release excess hormones into the bloodstream. Different types of tumors make different hormones, which can lead to different symptoms.

Gastrinomas

These tumors make gastrin, a hormone that tells the stomach to make more acid. Too much gastrin causes a condition known as *Zollinger-Ellison syndrome*, in which the stomach makes too much acid. This leads to stomach ulcers, which can cause **pain, nausea,** and **loss of appetite.** Severe ulcers can bleed. Even if the bleeding is mild, it can lead to anemia (too few red blood cells), which can cause symptoms like **feeling tired** and **being short of breath.** If the bleeding is more severe, it can make **stool black and tarry.** Severe bleeding can itself be life-threatening.

If the stomach acid reaches the small intestine, it can damage the cells of the intestinal lining and break down digestive enzymes before they have a chance to digest food. This can cause **diarrhea** and **weight loss.**

Glucagonomas

These tumors make glucagon, a hormone that increases glucose (sugar) levels in the blood. Most of the symptoms that can be caused by a glucagonoma are mild and are more often caused by something else.

Excess glucagon can raise blood sugar, sometimes leading to diabetes. This can cause symptoms such as **feeling thirsty and hungry,** and **having to urinate often.**

People with these tumors can also have problems with **diarrhea, weight loss,** and **malnutrition.** The nutrition problems can lead to symptoms like **irritation of the tongue and the corners of the mouth.**

The symptom that brings most people with glucagonomas to their doctor is a rash called *necrolytic migratory erythema.* This is **a red rash with swelling and blisters that often travels from place to place on the skin.**

Insulinomas

These tumors make insulin, which lowers blood glucose levels. Too much insulin leads to low blood sugar, which can cause symptoms like **weakness, confusion, sweating,** and **rapid heartbeat.** When blood sugar gets very low, it can lead to a person **passing out or even going into a coma and having seizures.**

Somatostatinomas

These tumors make somatostatin, which helps regulate other hormones. Symptoms of this type of tumor can include **belly pain, nausea, poor appetite, weight loss, diarrhea, symptoms of diabetes (feeling thirsty and hungry, and having to urinate often),** and **jaundice (yellowing of the skin and eyes)**.

The early symptoms of a somatostatinoma tend to be mild and are more often caused by other things, so these tumors tend to be diagnosed at an advanced stage. Often, they are not found until they spread to the liver, when they cause problems like jaundice and pain.

VIPomas

These tumors make a substance called *vasoactive intestinal peptide* (VIP). Too much VIP can lead to problems with **diarrhea.** This may be mild at first, but gets worse over time. By the time they are diagnosed, most people have severe, watery diarrhea.

Other symptoms can include **nausea, vomiting, muscle cramps, feeling weak or tired,** and **flushing (redness and warmth in the face or neck).**

People with these tumors also tend to have low levels of acid in their stomachs, which can lead to **problems digesting food.**

Carcinoid tumors

These tumors often make serotonin or its precursor, 5-HTP. Carcinoid tumors often don't cause symptoms until they spread outside the pancreas. When these tumors do spread, it is most often to the liver. There, the cancer cells can release hormones directly into the blood. This can cause the carcinoid syndrome, with symptoms including **flushing (redness and warmth in the face or neck), diarrhea, wheezing,** and a **rapid heart rate.** These symptoms often occur in episodes, between which the person may feel fine.

Over a long time, the hormone-like substances released by these tumors can damage heart valves, causing **shortness of breath, weakness,** and a **heart murmur (an abnormal heart sound).**

Non-functioning neuroendocrine tumors

These tumors don't make excess hormones, so they don't cause symptoms in early stages and often grow quite large before they are found. Most of these start to cause problems as they get larger or spread outside the pancreas. Symptoms can be litoms until theybnorma

sometimes leading to **jaundice (yellowing of the skin and eyes)** and **abnormal blood tests.**

These cancers can also spread to other organs and tissues. The symptoms depend on where the cancer is growing. For example, cancer spread to the lungs can cause **shortness of breath or a cough.** Spread to bones can cause **pain** in those areas.

References

National Cancer Institute. Physician Data Query (PDQ). Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment – Patient Version. 2018. Accessed at https://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq on October 1, 2018.

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Tests for Pancreatic Neuroendocrine Tumor

- Medical history and physical exam
- Imaging tests
- Radionuclide scans
- Blood tests
- Biopsy

Medical history and physical exam

In taking your medical history, the doctor will ask you questions about your general health, lifestyle habits, symptoms, and risk factors. The doctor will also probably ask about symptoms related to excess hormone production such as diarrhea, abdominal (belly) pain, or rash.

Your doctor will also examine you to look for signs of pancreatic NET or other health problems. The exam will probably focus mostly on your belly. Pancreatic NETs can sometimes cause the liver or gallbladder to swell, which the doctor might be able to feel during the exam.

If the results of the exam are abnormal, your doctor will probably order tests, such as imaging, labs, or other procedures, to help find the problem. You might also be referred to a gastroenterologist (a doctor who treats digestive system diseases) for further tests and treatment.

Imaging tests

Computed tomography (CT) scan

A CT scan[1] uses x-rays taken from different angles, which are combined by a computer to make detailed pictures of the organs. An iodine-based dye may be injected into your vein before the scan to show details better. This test is most often used to look at the belly (abdomen) to see the pancreas clearly and if the pancreatic NET has spread to nearby lymph nodes or other organs such as the liver. It can also be used to guide a biopsy needle into an area of concern.

Magnetic resonance imaging (MRI)

Like CT scans, MRI scans[2] show detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. A dye called **gadolinium** may be injected into a vein before the scan to show details better. An MRI scan

sometimes can see cancer that has spread to the liver better than a CT scan.

Ultrasound

Ultrasound[3] tests use sound waves to create images of organs such as the pancreas.

Abdominal ultrasound: For this test, a wand-shaped probe is moved over the skin of the abdomen. It gives off sound waves and picks up the echoes as they bounce off organs. If it's not clear what might be causing a person's abdominal symptoms, this might be the first test done because it is easy to do and it doesn't expose a person to radiation.

Endoscopic ultrasound (EUS): This test uses an endoscope with a small ultrasound probe on the end. The scope is then passed through your mouth or nose, down through the stomach, and into the first part of the small intestine. It is then pointed toward the pancreas, which is next to the small intestine. The probe on the tip of the endoscope can get very close to the pancreas, so this is a very good way to look at it. If a tumor is seen, a small, hollow needle can be passed down the endoscope to get biopsy samples of it.

Cholangiopancreatography tests

These imaging tests look at the pancreatic ducts and bile ducts to see if they are blocked, narrowed, or dilated. These tests can help show if someone might have a pancreatic neuroendocrine tumor that is blocking a duct. They can also be used to help plan surgery. These tests can be done in different ways, each of which has pros and cons.

Endoscopic retrograde cholangiopancreatography (ERCP): For this test, an endoscope (a thin, flexible tube with a tiny video camera on the end) is passed down the throat, through the esophagus and stomach, and into the first part of the small intestine. This is usually done while you are sedated (given medicine to make you sleepy).

The doctor can see the ampulla of Vater (where the common bile duct empties into the small intestine) through the endoscope. The doctor guides a catheter (a very small tube) through the tip of the endoscope and into the common bile duct. A small amount of dye is then injected into the common bile duct, and x-rays are taken. This dye outlines the bile and pancreatic ducts. The x-rays can show narrowing or blockage in these ducts that might be caused by a pancreatic neuroendocrine tumor. The doctor doing this test can also put a small brush through the tube to remove cells for a biopsy

(see below).

point, the doctor can either use endoscopic ultrasound (EUS) to pass a needle into the tumor or endoscopic retrograde cholangiopancreatography (ERCP) to remove cells from the bile or pancreatic ducts. These tests are described in more detail above.

Surgical biopsy: In rare cases, an endoscopic biopsy or a CT-guided needle biopsy will not be able to get enough tissue to identify the type of tumor. In such cases, surgery may be needed to remove a tissue sample. Surgical biopsies are done much less often now than in the past since PNETs are mostly diagnosed using imaging (CT or MRI scans), somatostatin receptor-based imaging, EUS biopsy, and checking for excessive levels of hormones.

Some people might not need a biopsy

Rarely, the doctor might not do a biopsy on someone who has a neuroendocrine tumor in the pancreas if imaging tests, blood tests, and somatostatin receptor-based imaging show the tumor is very likely to be cancer and if it looks like surgery can remove all of it. Instead, the doctor will proceed directly with surgery, at which time the tumor cells can be looked at in the lab to confirm the diagnosis. During surgery, if the doctor finds that the cancer has spread too far to be removed completely, only a sample of the cancer may be removed to confirm the diagnosis, and the rest of the planned operation may be stopped.

See Testing Biopsy and Cytology Specimens for Cancer[4] to learn more about different types of biopsies, how the biopsy samples are tested in the lab, and what the results will tell you.

Hyperlinks

1. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html
2. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html
3. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ultrasound-for-cancer.html
4. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html

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Pancreatic Neuroendocrine Tumor Stages

serious the cancer is and how best to treat[1] it. Doctors also use a cancer's stage when talking about survival statistics.

The stages of pancreatic NET range from I (1) through IV (4). As a rule, the lower the stage, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. Although each person’s cancer experience is unique, cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

How is the stage determined?

The staging system most often used for pancreatic NETs is the American Joint Committee on Cancer (AJCC) **TNM** system, which is based on 3 key pieces of information:

- The size and extent of the main **tumor (T):** How large is the tumor? Has it grown into nearby structures or organs?
- The spread to nearby lymph **nodes (N):** Has the cancer spread to nearby lymph nodes?
  The spread (**metastasis**) to distant sites **(M):** nodes?

Stages of pancreatic neuroendocrine tumors

AJCC Stage	Stage grouping	Stage description*
I	**T1 N0 M0**	The tumor is less than 2 centimeters (cm) across and is still just in the pancreas (T1). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0).
II	**T2 N0 M0**	The tumor is at least 2 cm across but no more than 4 cm across, and it is still just in the pancreas (T2). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0).
	OR	
	T3 N0 M0	The tumor is more than 4 cm across and is still just in the pancreas, OR the tumor has grown into the duodenum (the first part of the small intestine) or the common bile duct (T3). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0).
III	**T4 N0 M0**	The tumor has grown into nearby organs (such as the stomach, spleen, colon, or adrenal gland) or it has grown into nearby large blood vessels (T4). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0).
	OR	
	Any T N1 M0	The tumor can be any size and might or might not have grown outside of the pancreas (any T). It has spread to nearby lymph nodes (N1), but not to distant parts of the body (M0).
IV	**Any T Any N M1**	The tumor can be any size and might or might not have grown outside of the pancreas (any T). It might or might not have spread to nearby lymph nodes (any N). The cancer has spread to distant parts of the body (M1).

* The following additional categories are not listed in the table above:

- **TX:** The main tumor cannot be assessed due to lack of information.
- **T0:** There is no evidence of a main tumor.
- **NX:** Nearby lymph nodes cannot be assessed due to lack of information.

Other prognostic factors

Although not formally part of the TNM system, other factors can also be important in determining a person's prognosis (outlook).

Tumor grade

The grade describes how quickly the cancer is likely to grow and spread. For pancreatic NETs, an important part of grading is measuring how many of the cells are in the process of dividing into new cells. This is determined by:

- The **mitotic count**, which is the number of cells seen under a microscope that are in the process of splitting into two new cells (mitosis).
- The **Ki-67 index**, which is a measure of the portion of cells that are almost ready to start splitting.

Based on these tests, NETs are divided into 2 main groups:

- **Well-differentiated tumors** (which include low-grade [G1] and intermediate-grade [G2] tumors) have 20 or fewer mitoses and a Ki-67 index of 20% or lower.
- **Poorly differentiated tumors** (high-grade [G3] tumors) have more than 20 mitoses or a Ki-67 index of more than 20%. These are also called **neuroendocrine carcinomas (NECs)**, and they often grow and spread quickly.

Tumor functionality

The outlook for pancreatic NETs can be affected by whether the tumor is functioning (making hormones) or non-functioning[4]. For functioning tumors, the type of hormone can also be important. For example, insulinomas (NETs that make insulin) tend to have a lower risk of spreading than other types of NETs.

Hyperlinks

1. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/treating/pnets-by-extent.html

2. www.cancer.org/cancer/diagnosis-staging/staging.html
3. www.cancer.org/cancer/types/pancreatic-cancer/detection-diagnosis-staging/staging.html
4. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/about/what-is-pnet.html

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Survival Rates for Pancreatic Neuroendocrine Tumor

means that people who have that cancer are, on average, about 90% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

Where do these numbers come from?

The American Cancer Society relies on information from the Surveillance, Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for pancreatic NET in the United States, based on how far the cancer has spread. The SEER database, however, does not group cancers by AJCC TNM stages (stage 1, stage 2, stage 3, etc.). Instead, it groups cancers into localized, regional, and distant stages:

- **Localized:** There is no sign the cancer has grown outside of the pancreas.
- **Regional:** The cancer has grown outside the pancreas into nearby tissues or has spread to nearby lymph nodes.
- **Distant:** The cancer has spread to distant parts of the body such as the lungs, liver or bones.

5-year relative survival rates for pancreatic NET

(These numbers are based on people diagnosed with pancreatic NET between 2012 and 2018.)

SEER* Stage	5-year Relative Survival Rate
Localized	95%
Regional	72%
Distant	23%
All SEER stages combined	53%

*SEER= Surveillance, Epidemiology, and End Results

Understanding the numbers

- **These numbers apply only to the stage of the cancer when it is first diagnosed.** They do not apply later on if the cancer grows, spreads, or comes back after treatment.
  These numbers don't take everything into account. Survival rates are grouped based on how far the cancer has spread, but your age, overa

When you're told you have a pancreatic neuroendocrine tumor

- What kind of pancreatic neuroendocrine tumor[1] do I have?
- Has my cancer spread beyond where it started?
- What is the stage of my cancer and what does that mean?
- Is my cancer resectable (removable by surgery)?
- Are my symptoms because the cancer is making too many hormones?
- Will I need any other tests before we can decide on treatment?
- Will I need to see other doctors or health care professionals?
- If I'm concerned about the costs and insurance coverage for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- How much experience do you have treating this type of cancer?
- What are my treatment options[2]?
- What do you recommend and why?
- What is the goal of the treatment?
- Should I get a second opinion[3]? How do I do that? Can you recommend a doctor or cancer center?
- How is treatment likely to help me?
- What risks or side effects might I expect? Are there things I can do to reduce these side effects?
  Should I think about taking part in a _____

2. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/treating.html
3. www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html
4. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html
5. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
6. www.cancer.org/support-programs-and-services/road-to-recovery.html
7. www.cancer.org/cancer/managing-cancer/side-effects.html
8. www.cancer.org/cancer/managing-cancer/side-effects/changes-in-mood-or-thinking.html
9. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/after-treatment.html
10. www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html

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