Zollinger-Ellison Syndrome

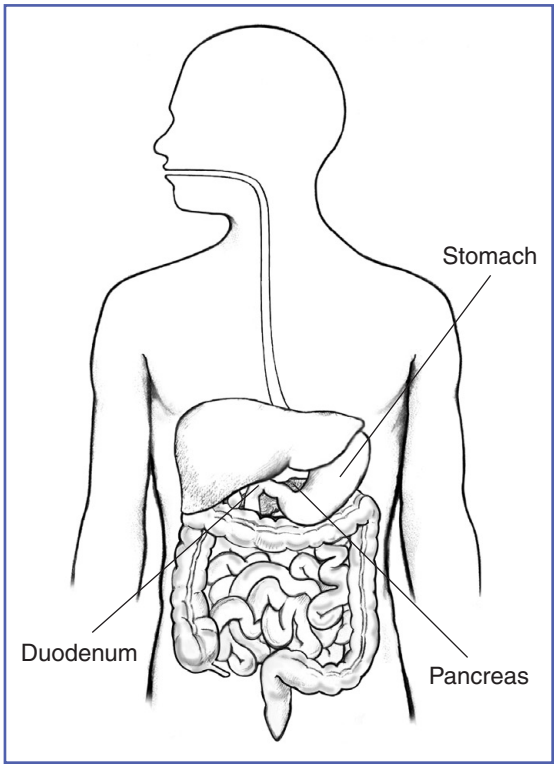
National Digestive Diseases Information Clearinghouse

National Institute of Diabetes and Digestive and Kidney Diseases

What is Zollinger-Ellison syndrome?

Zollinger-Ellison syndrome is a rare disorder that occurs when one or more tumors form in the pancreas and duodenum. The tumors, called gastrinomas, release large amounts of gastrin that cause the stomach to produce large amounts of acid. Normally, the body releases small amounts of gastrin after eating, which triggers the stomach to make gastric acid that helps break down food and liquid in the stomach. The extra acid causes peptic ulcers to form in the duodenum and elsewhere in the upper intestine.

The tumors seen with Zollinger-Ellison syndrome are sometimes cancerous and may spread to other areas of the body.



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- The stomach stores swallowed food and liquid. The muscle action of the lower part of the stomach mixes the food and liquid with digestive juice. Partially digested food and liquid slowly move into the duodenum and are further broken down.
- The duodenum is the first part of the small intestine—the tube-shaped organ between the stomach and the large intestine—where digestion of the food and liquid continues.
- The pancreas is an organ that makes the hormone insulin and enzymes for digestion. A hormone is a natural chemical produced in one part of the body and released into the blood to trigger or regulate particular functions of the body. Insulin helps cells throughout the body remove glucose, also called sugar, from blood and use it for energy. The pancreas is located behind the stomach and close to the duodenum.

What causes Zollinger-Ellison syndrome?

Experts do not know the exact cause of Zollinger-Ellison syndrome. About 25 to 30 percent of gastrinomas are caused by an inherited genetic disorder called multiple endocrine neoplasia type 1 (MEN1).[1] MEN1 causes hormone-releasing tumors in the endocrine glands and the duodenum. Symptoms of MEN1 include increased hormone levels in the blood, kidney stones, diabetes, muscle weakness, weakened bones, and fractures.

Read more about MEN1 in *Multiple Endocrine Neoplasia Type 1* at *www.endocrine.niddk.nih.gov.*

How common is Zollinger-Ellison syndrome?

Zollinger-Ellison syndrome is rare and only occurs in about one in every 1 million people.[1] Although anyone can get Zollinger-Ellison syndrome, the disease is more common among men 30 to 50 years old. A child who has a parent with MEN1 is also at increased risk for Zollinger-Ellison syndrome.[2]

What are the signs and symptoms of Zollinger-Ellison syndrome?

Zollinger-Ellison syndrome signs and symptoms are similar to those of peptic ulcers. A dull or burning pain felt anywhere between the navel and midchest is the most common symptom of a peptic ulcer. This discomfort usually

- occurs when the stomach is empty—between meals or during the night—and may be briefly relieved by eating food
- lasts for minutes to hours
- comes and goes for several days, weeks, or months

Other symptoms include

- diarrhea
- bloating
- burping
- nausea
- vomiting
- weight loss
- poor appetite

Some people with Zollinger-Ellison syndrome have only diarrhea, with no other symptoms. Others develop gastroesophageal reflux (GER), which occurs when stomach contents flow back up into the esophagus—a muscular tube that carries food and liquids to the stomach. In addition to nausea and vomiting, reflux symptoms include a painful, burning feeling in the midchest. Read more about GER in *Gastroesophageal Reflux (GER) and Gastroesophageal Reflux Disease (GERD) in Adults* at *www.digestive.niddk.nih.gov.*

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[1]Metz DC. Diagnosis of the Zollinger-Ellison syndrome. *Clinical Gastroenterology and Hepatology.* 2012;10(2):126–130.

[2]Del Valle J. Zollinger-Ellison syndrome. In: Yamada T, ed. *Textbook of Gastroenterology.* 5th ed. Hoboken, NJ: Blackwell Publishing; 2009: 982–1002.

Seek Help for Emergency Symptoms

A person who has any of the following emergency symptoms should call or see a health care provider right away:

- chest pain
- sharp, sudden, persistent, and severe stomach pain
- red blood in stool or black stools
- red blood in vomit or vomit that looks like coffee grounds

These symptoms could be signs of a serious problem, such as

- internal bleeding—when gastric acid or a peptic ulcer breaks a blood vessel
- perforation—when a peptic ulcer forms a hole in the duodenal wall
- obstruction—when a peptic ulcer blocks the path of food trying to leave the stomach

How is Zollinger-Ellison syndrome diagnosed?

A health care provider diagnoses Zollinger-Ellison syndrome based on the following:

- medical history
- physical exam
- signs and symptoms
- blood tests
- upper gastrointestinal (GI) endoscopy
- imaging tests to look for gastrinomas
- measurement of stomach acid

Medical History

Taking a medical and family history is one of the first things a health care provider may do to help diagnose Zollinger-Ellison syndrome. The health care provider may ask about family cases of MEN1 in particular.

Physical Exam

A physical exam may help diagnose Zollinger-Ellison syndrome. During a physical exam, a health care provider usually

- examines a person's body
- uses a stethoscope to listen to bodily sounds
- taps on specific areas of the person's body

Signs and Symptoms

A health care provider may suspect Zollinger-Ellison syndrome if

- diarrhea accompanies peptic ulcer symptoms or if peptic ulcer treatment fails.
- a person has peptic ulcers without the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen or a bacterial *Helicobacter pylori (H. pylori)* infection. NSAID use and *H. pylori* infection may cause peptic ulcers.
- a person has severe ulcers that bleed or cause holes in the duodenum or stomach.
- a health care provider diagnoses a person or the person's family member with MEN1 or a person has symptoms of MEN1.

Blood Tests

The health care provider may use blood tests to check for an elevated gastrin level. A technician or nurse draws a blood sample during an office visit or at a commercial facility and sends the sample to a lab for analysis. A health care provider will ask the person to fast for several hours prior to the test and may ask the person to stop acid-reducing medications for a period of time before the test. A gastrin level that is 10 times higher than normal suggests Zollinger-Ellison syndrome.[2]

A health care provider may also check for an elevated gastrin level after an infusion of secretin. Secretin is a hormone that causes gastrinomas to release more gastrin. A technician or nurse places an intravenous (IV) needle in a vein in the arm to give an infusion of secretin. A health care provider may suspect Zollinger-Ellison syndrome if blood drawn after the infusion shows an elevated gastrin level.

Upper Gastrointestinal Endoscopy

The health care provider uses an upper GI endoscopy to check the esophagus, stomach, and duodenum for ulcers and esophagitis—a general term used to describe irritation and swelling of the esophagus. This procedure involves using an endoscope—a small, flexible tube with a light—to see the upper GI tract, which includes the esophagus, stomach, and duodenum. A gastroenterologist—a doctor who specializes in digestive diseases—performs the test at a hospital or an outpatient center. The gastroenterologist carefully feeds the endoscope down the esophagus and into the stomach and duodenum. A small camera mounted on the endoscope transmits a video image to a monitor, allowing close examination of the intestinal lining. A person may receive a liquid anesthetic that is gargled or sprayed on the back of the throat. A technician or nurse inserts an IV needle in a vein in the arm if anesthesia is given.

Imaging Tests

To help find gastrinomas, a health care provider may order one or more of the following imaging tests:

- **Computerized tomography (CT) scan.** A CT scan is an x ray that produces pictures of the body. A CT scan may include the injection of a special dye, called contrast medium. CT scans use a combination of x rays and computer technology to create images. CT scans require the person to lie on a table that slides into a tunnel-shaped device where an x-ray technician takes x rays. A computer puts the different views together to create a model of the pancreas, stomach, and duodenum. The x-ray technician performs the procedure in an outpatient center or a hospital, and a radiologist—a doctor who specializes in medical imaging—interprets the images. The person does not need anesthesia. CT scans can show tumors and ulcers.
- **Magnetic resonance imaging (MRI).** MRI is a test that takes pictures of the body's internal organs and soft tissues without using x rays. A specially trained technician performs the procedure in an outpatient center or a hospital, and a radiologist interprets the images. The person does not need anesthesia, though people with a fear of confined spaces may receive light sedation, taken by mouth. An MRI may include the injection of contrast medium. With

most MRI machines, the person will lie on a table that slides into a tunnel-shaped device that may be open ended or closed at one end. Some machines allow the person to lie in a more open space. During an MRI, the person, although usually awake, remains perfectly still while the technician takes the images, which usually takes only a few minutes. The technician will take a sequence of images from different angles to create a detailed picture of the upper GI tract. During sequencing, the person will hear loud mechanical knocking and humming noises.

- **Endoscopic ultrasound.** This procedure involves using a special endoscope called an endoechoscope to perform ultrasound of the pancreas. The endoechoscope has a built-in miniature ultrasound probe that bounces safe, painless sound waves off organs to create an image of their structure. A gastroenterologist performs the procedure in an outpatient center or a hospital, and a radiologist interprets the images. The gastroenterologist carefully feeds the endoechoscope down the esophagus, through the stomach and duodenum, until it is near the pancreas. A person may receive a liquid anesthetic that is gargled or sprayed on the back of the throat. A sedative helps the person stay relaxed and comfortable. The images can show gastrinomas in the pancreas.
- **Angiogram.** An angiogram is a special kind of x ray in which an interventional radiologist—a specially trained radiologist—threads a thin, flexible tube called a catheter through the large arteries, often from the groin, to the artery of interest. The radiologist injects contrast medium through the catheter so the images show up more clearly on the x ray. The interventional radiologist performs the procedure and interprets the images in a hospital or an outpatient center. A person does not need anesthesia, though a light sedative may help reduce a person's anxiety during the procedure. This test can show gastrinomas in the pancreas.
- **Somatostatin receptor scintigraphy.** An x-ray technician performs this test, also called OctreoScan, at a hospital or an outpatient center, and a radiologist interprets the images. A person does not need anesthesia. A radioactive compound called a radiotracer, when injected into the bloodstream, selectively labels tumor cells. The labeled cells light up when scanned with a device called a gamma camera. The test can show gastrinomas in the duodenum, pancreas, and other parts of the body.

Small gastrinomas may be hard to see; therefore, health care providers may order several types of imaging tests to find gastrinomas.

Stomach-acid Measurement

Using a sample of stomach juices for analysis, a health care provider may measure the amount of stomach acid a person produces. During the exam, a health care provider puts in a nasogastric tube—a tiny tube inserted through the nose and throat that reaches into the stomach. A person may receive a liquid anesthetic that is gargled or sprayed on the back of the throat. Once the tube is placed, a health care provider takes samples of the stomach acid. High acid levels in the stomach indicate Zollinger-Ellison syndrome.

How is Zollinger-Ellison syndrome treated?

A health care provider treats Zollinger-Ellison syndrome with medications to reduce gastric acid secretion and with surgery to remove gastrinomas. A health care provider sometimes uses chemotherapy—medications to shrink tumors—when tumors are too widespread to remove with surgery.

Medications

A class of medications called proton pump inhibitors (PPIs) includes

- esomeprazole (Nexium)
- lansoprazole (Prevacid)
- pantoprazole (Protonix)
- omeprazole (Prilosec or Zegerid)
- dexlansoprazole (Dexilant)

PPIs stop the mechanism that pumps acid into the stomach, helping to relieve peptic ulcer pain and promote healing. A health care provider may prescribe people who have Zollinger-Ellison syndrome higher-than-normal doses of PPIs to control the acid production. Studies show that PPIs may increase the risk of hip, wrist, and spine fractures when a person takes them long term or in high doses, so it's important for people to discuss risks versus benefits with their health care provider.

Surgery

Surgical removal of gastrinomas is the only cure for Zollinger-Ellison syndrome. Some gastrinomas spread to other parts of the body, especially the liver and bones. Finding and removing all gastrinomas before they spread is often challenging because many of the tumors are small.

Chemotherapy

Health care providers sometimes use chemotherapy drugs to treat gastrinomas that cannot be surgically removed, including

- streptozotocin (Zanosar)
- 5-fluorouracil (Adrucil)
- doxorubicin (Doxil)

Eating, Diet, and Nutrition

Researchers have not found that eating, diet, and nutrition play a role in causing or preventing Zollinger-Ellison syndrome.

Points to Remember

- Zollinger-Ellison syndrome is a rare disorder that occurs when one or more tumors form in the pancreas and duodenum.
- Experts do not know the exact cause of Zollinger-Ellison syndrome.
- About 25 to 30 percent of gastrinomas are caused by an inherited genetic disorder called multiple endocrine neoplasia type 1 (MEN1).
- Although anyone can get Zollinger-Ellison syndrome, the disease is more common among men 30 to 50 years old.
- Zollinger-Ellison syndrome signs and symptoms are similar to those of peptic ulcers.
- Some people with Zollinger-Ellison syndrome have only diarrhea, with no other symptoms. Others develop gastroesophageal reflux (GER).
- A health care provider diagnoses Zollinger-Ellison syndrome based on the following:
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- A health care provider treats Zollinger-Ellison syndrome with medications to reduce gastric acid secretion and with surgery to remove gastrinomas. A health care provider sometimes uses chemotherapy—medications to shrink tumors—when tumors are too widespread to remove with surgery.

Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports basic and clinical research into many digestive disorders, including Zollinger-Ellison syndrome.

Clinical trials are research studies involving people. Clinical trials look at safe and effective new ways to prevent, detect, or treat disease. Researchers also use clinical trials to look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, why they matter, and how to participate, visit the NIH Clinical Research Trials and You website at *www.nih.gov/health/clinicaltrials.* For information about current studies, visit *www.ClinicalTrials.gov.*

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