Zollinger-Ellison Syndrome

National Digestive Diseases Information Clearinghouse

U.S. Department of Health and Human Services

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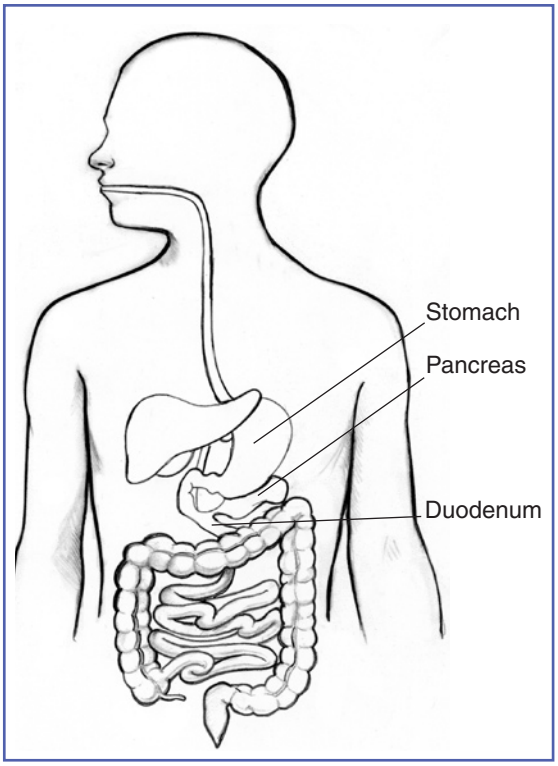
What is Zollinger-Ellison syndrome (ZES)?

ZES is a rare disorder characterized by one or more tumors in the pancreas, duodenum, or both. The tumors cause the stomach to make too much acid, leading to peptic ulcers in the duodenum. The tumors are sometimes cancerous and spread to other areas of the body.

What are the stomach, duodenum, and pancreas?

The stomach, duodenum, and pancreas are digestive organs. The stomach produces gastric acid and other digestive juices that break down food. Partially digested food moves into the duodenum and is further broken down. The duodenum is the first part of the small intestine—the tube-shaped organ between the stomach and the large intestine. The pancreas is a large gland that produces digestive juices that flow into the duodenum. The pancreas also makes hormones that are released into the bloodstream. Hormones are powerful chemicals produced by glands that control the function of cells and organs.



Tumors called gastrinomas that grow in the pancreas and duodenum cause Zollinger-Ellison syndrome.

What causes ZES?

ZES is caused by tumors called gastrinomas, which release the hormone gastrin.

Normally, cells in the stomach produce and control gastrin so only the right amount is released. Gastrin travels through the bloodstream to signal other cells in the stomach to release gastric acid to help break down food. Gastrinomas release abnormal amounts of gastrin, resulting in excess gastric acid in the stomach and duodenum. The excess acid eventually causes sores called peptic ulcers to form in the lining of the duodenum.

Scientists are unsure what causes the majority of gastrinomas, which appear sporadically. About 25 percent of gastrinoma cases are caused by an inherited genetic disorder called multiple endocrine neoplasia type 1 (MEN1).[1] MEN1 can cause a variety of hormone-releasing tumors such as prolactinomas and insulinomas. Prolactinomas form in the pituitary gland in the brain and cause excess prolactin—a hormone that influences milk production, fertility, and bone strength. Insulinomas form in the pancreas and cause excess insulin—a hormone that helps control blood glucose, also called blood sugar. Signs and symptoms of MEN1 include increased hormone levels in the blood, kidney stones, diabetes, muscle weakness, and weakened bones and fractures.

Who gets ZES?

Anyone can get ZES, but the disease is more common among men 30 to 50 years old. People with MEN1 have a 20 to 61 percent chance of developing ZES.[2] Children who have a parent with MEN1 have a 50 percent chance of inheriting the *MEN1* gene and are, therefore, also at increased risk of ZES.

What are the symptoms of ZES?

ZES symptoms are similar to those of peptic ulcers and include

- burning abdominal pain
- nausea and vomiting
- weight loss
- diarrhea
- severe gastroesophageal reflux—a condition where gastric acid and food from the stomach backs up into the esophagus

How is ZES diagnosed?

A doctor diagnoses ZES by

- assessing symptoms
- measuring stomach acid and the amount of gastrin circulating in the blood
- conducting imaging tests to look for gastrinomas

A doctor may suspect ZES if diarrhea accompanies peptic ulcer symptoms or if treatment for peptic ulcers fails. Most peptic

[1]Norton JA, Fraker DL, Alexander HR, et al. Surgery to cure the Zollinger-Ellison syndrome. *New England Journal of Medicine*. 1999;341(9):635–644.

[2]Jensen RT. Management of the Zollinger-Ellison syndrome in patients with multiple endocrine neoplasia type 1. *Journal of Internal Medicine*. 1998;243(6):477–488.

ulcers are caused by bacteria called *Helicobacter pylori (H. pylori)* or the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen. Peptic ulcers in the absence of *H. pylori* infection or NSAIDs usage or severe peptic ulcers that bleed or cause perforation of the duodenum are possible indicators of ZES. A MEN1 diagnosis in the patient or the patient's family or the presence of MEN1 signs and symptoms strongly suggests ZES.

Multiple ulcers in the duodenum—seen during upper gastrointestinal (GI) endoscopy—may cause a doctor to suspect ZES. Upper GI endoscopy is used to see inside the upper GI tract. During the procedure, an endoscope—a thin, flexible, lighted tube with a small camera on the tip—is inserted through the mouth, esophagus, and stomach and into the duodenum. The endoscope sends images taken inside the upper GI tract to a video monitor where they can be viewed. Upper GI endoscopy, however, rarely reveals gastrinomas, which grow in tissue layers beneath the visible surface.

A procedure called somatostatin receptor scintigraphy (SRS)—sometimes called OctreoScan—is used to find gastrinomas in the duodenum, pancreas, and other parts of the body. SRS uses a radioactive compound called a radiotracer that, when injected into the bloodstream, selectively labels tumor cells. The labeled cells light up when scanned with a device called a gamma camera.

Other imaging procedures used to find gastrinomas include the following:

- **Angiography** is sometimes used to find tumors in the pancreas. A special tube called a catheter is guided through the bloodstream to blood vessels in the pancreas. Contrast material is injected through the catheter. On x ray, the contrast material highlights blood vessels, which are more dense inside tumors.
- **Endoscopic ultrasonography** is sometimes used to look for tumors in the pancreas. A special endoscope called an endoechoscope is used to perform ultrasound inside the duodenum. Ultrasound uses sound waves to look beyond the surface of tissues.
- **A computerized tomography (CT) scan** takes hundreds of cross-sectional x-ray images in a few seconds. A computer assembles the images to produce three-dimensional views of internal organs and tissues. While not good at finding tumors in the pancreas or duodenum, this technique is more useful in finding gastrinomas that have spread to the liver.

How is ZES treated?

ZES is treated with medications to relieve ulcer symptoms and surgery, if appropriate, to remove tumors. Chemotherapy is sometimes used when tumors are too widespread to remove with surgery.

A class of drugs called proton pump inhibitors effectively reduces gastric acid secretion in the stomach and includes

- esomeprazole (Nexium)
- lansoprazole (Prevacid)
- pantoprazole (Protonix)
- omeprazole (Prilosec)

Reducing stomach acid allows peptic ulcers to heal and relieves ZES symptoms.

Surgical removal of gastrinomas is the only cure for ZES. Some gastrinomas behave like cancers and spread to other parts of the body, especially the liver and bones. Finding and removing all gastrinomas is often challenging.

Gastrinomas that cannot be surgically removed are sometimes treated with chemotherapy drugs, including

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

What is the likely outcome for people with ZES?

The outcome for people with ZES largely depends on the nature and extent of the gastrinomas. About 25 percent of gastrinoma cases are considered cancerous, with an estimated 10-year survival rate of around 30 percent.[3] The remaining cases are considered slow-growing, with an estimated 10-year survival rate of around 95 percent.[3] If peptic ulcer symptoms are well controlled, however, most patients—even those with tumors that spread—will feel well until the late stages of the disease.

Points to Remember

- Zollinger-Ellison syndrome (ZES) is a rare disorder characterized by tumors called gastrinomas in the pancreas, duodenum, or both.
- Gastrinomas result in excess gastric acid, which can lead to ulcers in the duodenum.
- Anyone can get ZES, but the disease is more common among men 30 to 50 years old or in people who have an inherited condition called multiple endocrine neoplasia type 1 (MEN1).
- ZES symptoms are similar to those of peptic ulcers.
- A doctor diagnoses ZES by assessing symptoms, measuring stomach acid and the amount of gastrin circulating in the blood, and conducting imaging tests to look for gastrinomas.
- ZES is treated with medications to relieve ulcer symptoms and surgery, if appropriate, to remove tumors. ZES is sometimes treated with chemotherapy.
- The outcome for people with ZES largely depends on the nature and extent of the gastrinomas. About 25 percent of gastrinomas are considered cancerous. If peptic ulcer symptoms are well controlled, however, most patients—even those with tumors that spread—will feel well until the late stages of the disease.

[3]Del Valle J, Scheiman JM. Zollinger-Ellison syndrome. In: Yamada T, ed. *Textbook of Gastroenterology*. Vol. 1. Philadelphia: Lippincott Williams & Wilkins; 2003: 1377–1394.

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 ZES. The NIDDK is working on better approaches to the diagnosis and management of ZES, including better ways of diagnosing MEN1 and finding gastrinomas.

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit *www.ClinicalTrials.gov*.

For More Information

A fact sheet about MEN1 is available from the National Endocrine and Metabolic Diseases Information Service (NEMDIS), part of the NIDDK. The fact sheet is available online at *www.endocrine.niddk.nih.gov/pubs/men1/men1.htm* or by contacting the NEMDIS at 1–888–828–0904.

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You may also find additional information about this topic by

- searching the NIDDK Reference Collection at *www.catalog.niddk.nih.gov/resources*
- visiting MedlinePlus at *www.medlineplus.gov*

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This fact sheet is also available at *www.digestive.niddk.nih.gov*.

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