CONDITION

Zollinger-ellison syndrome

Zollinger-Ellison syndrome is caused by a gastrin-producing tumor that makes the stomach release too much acid.

WHAT IT IS
Gastrin-producing tumor causing excessive stomach acid

BODY SYSTEM
Digestive system and hormone-producing organs

MAIN SYMPTOMS
Abdominal pain, diarrhea, heartburn, recurrent peptic ulcers

WHAT CAUSES IT
Gastrinoma, sometimes inherited through MEN1

HOW IT IS DIAGNOSED
Fasting gastrin, stomach acid testing, and tumor imaging

MAIN TREATMENT
Acid suppression, tumor surgery, and cancer-directed therapies

CAN IT BE CURED?
Sometimes - complete tumor removal may cure

IS IT AN EMERGENCY?
Sometimes - vomiting blood, black stools, or sudden severe pain

LONG-TERM OUTLOOK
Often manageable; tumor spread shapes long-term outlook

Overview

Zollinger-Ellison syndrome, also called Z-E syndrome or ZES, is a rare condition caused by a tumor called a gastrinoma . This tumor releases too much gastrin, a hormone that tells your stomach to produce acid.

The extra acid can damage the stomach and the first part of the small intestine. It may cause repeated peptic ulcers, severe reflux, abdominal pain, or diarrhea. Acid-suppressing medicines often control these problems effectively.

Gastrinomas are a type of neuroendocrine tumor, meaning they begin in cells that release hormones. They are most often found in the small intestine near the pancreas or within the pancreas. Some remain localized, while others spread to nearby lymph nodes or organs such as the liver.

ZES matters because controlling the acid is only one part of care. The tumor must also be located, assessed for spread, and monitored over time.

Symptoms

Symptoms come mainly from excessive stomach acid. They may resemble more common conditions such as acid reflux or an ordinary peptic ulcer.

Possible symptoms include:

Diarrhea can occur because large amounts of acid enter the small intestine. The acid irritates its lining and interferes with the enzymes needed to digest fat.

Some people have mild or unclear symptoms, particularly while taking proton pump inhibitors like omeprazole or lansoprazole . These medicines strongly reduce stomach acid and may partly hide the condition.

Vomiting blood, passing black stools, fainting, or developing sudden severe abdominal pain may signal ulcer bleeding or a hole in the digestive tract. These require emergency care.

- Burning or aching pain in the upper abdomen
- Frequent or difficult-to-control heartburn
- Watery or greasy diarrhea
- Nausea or vomiting
- Reduced appetite or unintended weight loss
- Ulcers that return after treatment
- Bleeding from an ulcer

Causes and risk factors

ZES is caused by one or more gastrinomas. It is not caused by eating spicy food, emotional stress, or producing an ordinary amount of stomach acid.

Many gastrinomas occur without a known inherited cause. These are called sporadic tumors.

Some are linked to multiple endocrine neoplasia type 1 , usually shortened to MEN1. MEN1 is an inherited condition caused by a change in the MEN1 gene. It can lead to tumors in several hormone-producing organs, especially the parathyroid glands, pituitary gland, pancreas, and nearby small intestine.

If ZES is related to MEN1, there may be several small gastrinomas rather than one tumor. Other family members may carry the same gene change. MEN1 is inherited in an autosomal dominant pattern, meaning a parent with the gene change has a chance of passing it to each child.

A personal or family history of MEN1, overactive parathyroid glands, high blood calcium, pituitary tumors, or pancreatic neuroendocrine tumors may lead to genetic evaluation.

Diagnosis

Diagnosing ZES usually begins with blood tests. A fasting serum gastrin test measures the amount of gastrin in your blood after you have not eaten for a set period.

A high gastrin result does not confirm ZES by itself. Proton pump inhibitors can raise gastrin, as can several other stomach and medical conditions. Doctors therefore interpret the result alongside a measure of stomach acidity, often the stomach's pH. In ZES, gastrin is elevated even though the stomach remains strongly acidic.

A secretin stimulation test may be used when the diagnosis remains uncertain. Secretin is a natural digestive hormone. During the test, a manufactured form is given through a vein and gastrin levels are checked. An unusual rise in gastrin supports ZES.

Do not stop a proton pump inhibitor on your own before testing. Suddenly removing acid suppression can allow a rapid return of severe acid production. If treatment needs to be adjusted for testing, this requires a planned and closely supervised approach.

After biochemical tests support the diagnosis, imaging is used to find the tumor and see whether it has spread. Tests may include:

If tissue is obtained during surgery or a biopsy, a pathologist can confirm that it is a neuroendocrine tumor and assess how quickly its cells appear to be growing.

Blood calcium, parathyroid hormone, and other hormone tests may be needed if MEN1 is suspected. Genetic counseling can help you understand what genetic testing may mean for you and your relatives.

- CT or MRI scans
- Somatostatin receptor PET/CT, which looks for receptors common on these tumors
- Endoscopic ultrasound, using an ultrasound probe passed into the digestive tract
- Upper endoscopy to examine ulcers and acid-related damage

Treatment and management

Treatment has two main goals: controlling stomach acid and managing the gastrinoma.

Proton pump inhibitors are the main acid-suppressing treatment. They reduce acid production and allow ulcers and inflammation to heal. People with ZES may need more intensive acid suppression than people with ordinary reflux, but the medicine and amount are selected individually.

Symptoms often improve once acid is controlled. Treatment may need to continue long term if the tumor cannot be completely removed. Changing or stopping the medicine without medical guidance can allow symptoms and complications to return.

Surgery may offer a cure when a localized sporadic gastrinoma can be completely removed. Before recommending surgery, the care team considers the tumor's location, whether it has spread, and your overall health.

Surgical decisions can be more complex in MEN1 because tumors are often small, numerous, or difficult to locate. The possible benefits of an operation must be balanced against the extent and risks of surgery.

If the tumor has spread or cannot be removed, treatment may focus on controlling its growth and hormone effects. Depending on the tumor's features and location, options can include:

These treatments are not interchangeable. Tumor grade, growth rate, receptor imaging, previous treatment, and the organs involved help determine which options may be suitable.

Follow-up commonly includes symptom review, blood tests, and repeat imaging. People with MEN1 also need monitoring for tumors or hormone problems in other glands.

Medicines commonly used for this include rabeprazole . Which one suits you, if any, is a decision for you and your doctor.

- Somatostatin analogue medicines
- Peptide receptor radionuclide therapy, which delivers radiation to receptor-positive tumor cells
- Targeted medicines that interfere with tumor growth pathways
- Chemotherapy for selected tumors
- Procedures directed at tumors in the liver

Complications

Without enough acid suppression, ZES can cause deep or repeated peptic ulcers. Possible

complications include bleeding, a blockage that prevents food from leaving the stomach, or perforation-a hole through the stomach or intestinal wall.

Ongoing reflux can inflame the esophagus, the tube connecting the mouth to the stomach. Severe inflammation may cause narrowing and difficulty swallowing.

Persistent diarrhea may lead to dehydration, weight loss, or poor absorption of nutrients. These problems often improve when acid production is controlled.

The gastrinoma itself may spread, most commonly to nearby lymph nodes or the liver. Spread to the liver has an important effect on treatment choices and long-term outlook.

Prevention

There is no established way to prevent a sporadic gastrinoma.

MEN1 is inherited, so lifestyle changes cannot prevent the gene change. Genetic counseling and testing may identify relatives who carry it, allowing monitoring to begin before complications develop. This is early detection, not prevention.

If you have ZES, taking acid-suppressing treatment as directed helps prevent ulcers and other acid-related complications. It does not remove the underlying tumor.

Living with it and what to expect

ZES usually requires long-term care, even when symptoms are well controlled. Acid-related pain and diarrhea may improve substantially with treatment, while tumor monitoring continues for years.

After complete removal of a localized gastrinoma, some people remain free of the condition. Follow-up is still important because a tumor can occasionally persist or return.

When surgery cannot remove all the tumor, ZES may be managed as a chronic condition. Some neuroendocrine tumors grow slowly and can be controlled for long periods. Faster-growing tumors or those that have spread to the liver may need several forms of treatment over time.

Many people can continue their usual work, relationships, and activities while taking regular medicine and attending follow-up appointments. The amount of disruption is shaped by symptom control, tumor growth, treatment effects, and whether MEN1 causes other hormone problems.

Keep an up-to-date medicine list and tell healthcare professionals that you have ZES. This is especially important if you cannot take your acid-suppressing medicine because of vomiting,

surgery, or another illness.

When to get medical help

Arrange a routine medical appointment if you have persistent or recurring upper abdominal pain, diarrhea, heartburn, or ulcers, especially if symptoms continue despite treatment. These symptoms have many more common causes, but they may need investigation.

Contact your care team promptly if known ZES symptoms worsen, you cannot keep your acid-suppressing medicine down, or you develop increasing trouble swallowing. Ongoing vomiting, reduced urination, or marked weakness may indicate dehydration and requires urgent assessment.

Seek emergency care for:

These signs can indicate major bleeding, perforation, or another serious problem. Do not wait for a routine follow-up appointment.

- Vomiting blood or material resembling coffee grounds
- Black, tar-like stools or heavy rectal bleeding
- Fainting, confusion, or severe weakness with possible bleeding
- Sudden, severe abdominal pain, especially with a rigid abdomen
- Severe chest or abdominal pain with difficulty breathing

Common questions

Is Zollinger-Ellison syndrome cancer?

ZES is caused by a neuroendocrine tumor called a gastrinoma. Gastrinomas have the potential to be cancerous because they can invade nearby tissue or spread elsewhere. Some stay localized for years. Imaging, biopsy findings, tumor grade, and evidence of spread provide more information about an individual tumor.

Can Zollinger-Ellison syndrome be cured?

Sometimes. Complete surgical removal of a localized sporadic gastrinoma may cure it. A cure is less likely when there are several tumors, when MEN1 is involved, or when the tumor has spread. Acid production can often still be controlled even when the tumor cannot be removed completely.

Why does ZES cause diarrhea?

Too much acid passes from the stomach into the small intestine. It irritates the intestinal lining and can stop digestive enzymes from working properly. This interferes with digestion, particularly fat digestion, and can cause watery or greasy stools.

Do I need to stop my proton pump inhibitor before a gastrin test?

Do not stop it without a supervised plan. Proton pump inhibitors can raise gastrin and affect test results, but abruptly stopping them in ZES may expose the digestive tract to very high acid levels. Testing can be planned around this risk.

Is Zollinger-Ellison syndrome inherited?

Some cases are inherited as part of MEN1, but many occur without an inherited syndrome. Genetic counseling may be recommended if you have other MEN1-related tumors, abnormal calcium or parathyroid results, or a relevant family history.

Can ZES look like ordinary reflux or ulcers?

Yes. Heartburn and upper abdominal pain are common in many digestive conditions. Clues that may prompt testing include ulcers that repeatedly return, ulcers in unusual locations, severe acid symptoms despite treatment, or ulcers accompanied by ongoing diarrhea.

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