

Zollinger-Ellison Syndrome — Presentation, Diagnosis, Therapy

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Zollinger-Ellison syndrome is a rare condition that affects the duodenum or pancreas. Tumors (gastrinomas) form in the duodenum or pancreas, and they secrete huge amounts of gastrin, leading to excess acid production in the stomach. The excess acid results in symptoms and peptic ulcers.



Definition and Background of Zollinger-Ellison Syndrome

Zollinger-Ellison syndrome results from a **pancreatic tumor** in the **non-beta islet cells**, which stimulates the maximal activity of the **gastric acid-secreting cells**, resulting in **gastrointestinal ulceration** of the mucosa. **Multiple endocrine neoplasia type 1 (MEN 1)** is a familial autosomal dominant syndrome that includes Zollinger-Ellison syndrome; however, Zollinger-Ellison syndrome may occur sporadically.

The primary tumor is usually located in the **pancreas, abdominal lymph nodes, or duodenum**; however, it may be found in other **ectopic places** such as the **ovaries, gall bladder, kidney, liver, or heart**.

Pathophysiology of Zollinger-Ellison Syndrome

In Zollinger-Ellison syndrome, **hypertrophy** of the **stomach mucosa** is caused by **hypergastrinemia**, which increases the number of **parietal cells** and leads to **maximal output of acid**. Acid secretion also is stimulated by gastrin, leading to increased secretion of basal acid. Complications may result from increased acid, such as **ulcerations** of the gastrointestinal mucosa, **malabsorption**, and **diarrhea**. Malabsorption is caused by many factors, such as hypersecretion of gastric acid, inactivated pancreatic enzymes, and precipitation of bile salts.

Epidemiology of Zollinger-Ellison Syndrome

Approx. 75% of cases are sporadic, whereas 25% are associated with MEN 1, characterized by pituitary tumors, hyperparathyroidism, and pancreatic endocrine tumors.

Spread of Zollinger-Ellison Syndrome in the United States

About **0.1%-1%** of patients suffering from duodenal ulcers in the United States have Zollinger-Ellison syndrome. It is reported to have **a frequency similar to insulinomas**.

Spread of Zollinger-Ellison Syndrome Globally

The incidence **differs between countries**. For example, 0.5 cases per million patients per year have been reported in Ireland. In Sweden, the incidence is higher—**1 to 3** cases per 1 million patients per year.

Zollinger-Ellison Syndrome and Gender, Age, and Race

There is **no difference based on race**, and it appears that all races are equally affected. **Men have a slightly higher risk** of developing the syndrome than women, with a **1.3:1** ratio. Zollinger-Ellison syndrome rarely appears in very young or very old patients, and the **mean age of onset is 43 years**.

Presentation of Zollinger-Ellison Syndrome

History

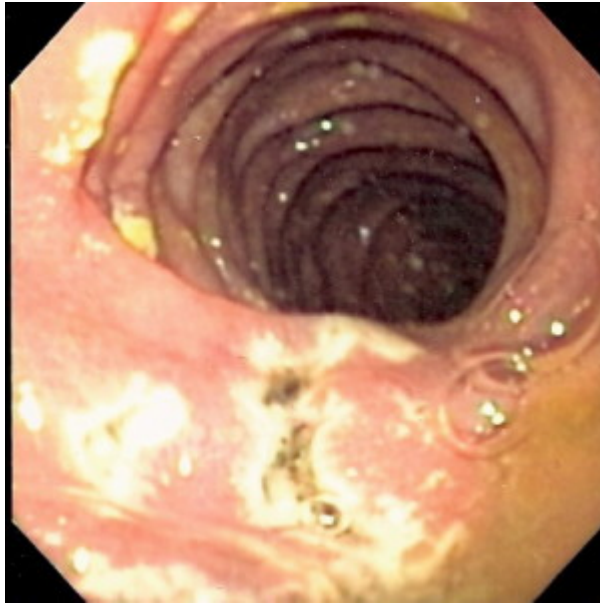


Image: Endoscopic image of multiple small ulcers located in the distal duodenum in a patient with gastrinoma (Zollinger-Ellison syndrome). By GNU FLD, License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Diagnosis of Zollinger-Ellison syndrome is based on a patient's **history, physical examination, and a high index of clinical awareness**. Main symptoms include:

- **Abdominal pain:** It is the **most common symptom**, presenting in more than **75%** of patients who ultimately are diagnosed with the syndrome. Abdominal pain is usually located in the **upper abdominal region** and resembles the pain felt with **peptic ulcer disease**.
- **Diarrhea:** Approx. **73%** of patients who ultimately are diagnosed with Zollinger-Ellison syndrome present with this symptom. In women, diarrhea is more common than abdominal pain. It is also more common in patients with MEN 1 Zollinger-Ellison syndrome than sporadic cases.
- **Heartburn:** This symptom resembles the pain associated with gastroesophageal reflux disease.

Other less common symptoms include:

- Nausea
- Vomiting
- [Gastrointestinal bleeding](#)
- Weight loss

If a patient has a history of **hypercalcemia, pituitary disorders, or nephrolithiasis**, then **MEN 1** should be suspected.

Physical Examination

Physical examination **may be normal** and may not reveal any signs or findings. However, signs may be present, including:

- Epigastric tenderness
- Jaundice, if the tumor is causing compression over the common bile duct
- Paleness due to gastrointestinal bleeding
- Dental erosions
- Hepatomegaly, which suggests metastasis to the liver

Differential Diagnosis

The following clinical scenarios are similar to Zollinger-Ellison syndrome:

- Retained gastric antrum syndrome
- Antral G cell hyperplasia
- Gastric outlet obstruction

Diagnosis of Zollinger-Ellison Syndrome

Laboratory Studies

- **Fasting serum gastrin:** This is the **best screening test** for Zollinger-Ellison syndrome. Serial measurements of fasting serum gastrin should be performed on different days because of fluctuations in gastrin levels from day-to-day.
- **Gastric acid secretory tests:** Zollinger-Ellison syndrome is suspected if **the basal acid output is greater than 15 mEq/h**. Zollinger-Ellison syndrome also should be suspected in the case of large gastric volume and **gastric pH less than 2.0**.
- **Serum calcium levels:** MEN 1 is suspected in cases with high serum levels of calcium.

Imaging Studies

- **Computed tomography (CT) scans:** Even though CT scans are **not highly sensitive** for the localization of a primary tumor (50% sensitivity), they can be used to **localize some tumors**, especially when a tumor is **larger than 1 cm**. CT scans also can help clinicians evaluate metastatic disease.
- **Somatostatin receptor scintigraphy:** This is the **imaging study of choice** for the detection of Zollinger-Ellison syndrome, and it is the **most sensitive** imaging modality for the detection of both primary and metastatic tumors.
- **Endoscopic ultrasonography:** This is a new method used to localize gastrinomas.
- **Abdominal ultrasound** and **magnetic resonance images** also can be used; however, they have **lower sensitivity** than somatostatin receptor scintigraphy and CT scans.

Procedures

- **Esophagogastroduodenoscopy:** This procedure is used to look for **gastric fold hypertrophy** and **duodenal ulcerations**.

Management of Zollinger-Ellison Syndrome

Medical Treatment

The main therapy is surgical removal of the tumor. However, medical treatment is used first to **control gastric acid hypersecretion**. Once that is controlled, imaging studies help determine the size and location of the tumor so that it may be resected surgically.

Proton pump inhibitors are the main medications used to control gastric acid

hypersecretion. **Histamine 2 receptor blockers** also can be used; however, proton pump inhibitors are superior. **Interferon, octreotide, and chemotherapy** may be used in the management of patients with **metastatic disease**. Hepatic metastasis may be treated by liver transplantation.

Surgical Intervention

The main treatment for a tumor in Zollinger-Ellison syndrome is surgical resection, especially in patients with no surgical contraindications and no metastasis. Surgical resection **decreases the risk of hepatic metastasis**.

In cases of **MEN 1**, **surgical intervention rarely cures the condition**; however, it decreases the risk of metastatic disease.

Follow-up after surgical resection is mandatory to make sure there is no recurrence. This should include **secretin test, serum fasting gastrin levels, and somatostatin receptor scintigraphy**. Follow-up evaluation should be done **3-6 months after surgical resection** and then every year thereafter.

Proton pump inhibitors may be continued after surgical resection.

Complications

Some common complications are:

- Abdominal perforation as a sequela of ulceration
- Gastric outlet obstruction
- Esophageal atresia secondary to gastric acid reflux
- Gastric carcinoids
- Gastrointestinal bleeding
- Bowel obstruction

Prognosis

- Morbidity and mortality are low in Zollinger-Ellison syndrome because of improved management. Fewer than 5% of patients develop complications.
- Prognosis is good without associated metastatic disease.

References

Praveen K Roy. Zollinger-Ellison Syndrome.

What Is Zollinger-Ellison Syndrome?. WebMD.

Zollinger-Ellison syndrome. MAYO CLINIC.

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