

Woe Is Me: Gastrin and the Regulation of the Gastrointestinal System

by

Marilyn H. Moss

Department of Biology

Sacred Heart University, Fairfield, CT



Part I – Presentation

G.I. Akin, a 30-year-old man, is struggling with bouts of abdominal pain. Suspecting that he may have an ulcer, Mr. Akin has tried many different over-the-counter medical regimens to treat his ulcer, but nothing seems to work. In desperation, Mr. Akin makes an appointment with a gastroenterologist, a digestive system specialist. The physician, Dr. Jones, also suspects an ulcer, which is an erosion of the mucosa lining of the digestive tract, and schedules an upper GI endoscopy. The test involves inserting a thin tube, an endoscope, down through the GI tract as far as the duodenum. The tube has a light and camera attached which allows the operator to examine the organs of the upper digestive tract. During the endoscopic procedure, Dr. Jones notes two, large ulcers, both in the duodenum. Additionally, prominent gastric folds are located in the stomach. The occurrence of two ulcers and the prominent gastric folds prompts Dr. Jones to consider causes of increased stomach acid or hyperacidity, particularly Zollinger-Ellison syndrome (ZES). ZES is a rare disorder caused by a gastrinoma, a tumor that secretes gastrin. The tumor is usually located in the duodenal area, but can be found elsewhere, such as in the pancreas. The excess gastrin causes excess acid secretion in the stomach that can lead to mucosal disruptions/ulcers and hyperplasia (proliferation) of the acid-producing cells of the stomach.

Questions

1. Gastrin is a gastrointestinal hormone. Define *hormone*. Does gastrin fit the description of a hormone? Explain.
2. What are the functions of gastrin?
3. In healthy individuals, which cells usually secrete gastrin? Where are those cells located?
4. Which cells secrete acid? What is the role of acid in the stomach?
5. What other important substance do the cells in Question 4 release? Describe the function of that substance.
6. Gastrin causes proliferation of the cells in Question 4, which may account for the increased gastric folds noted on endoscopy. How might this proliferation affect the symptoms and the course of ZES?
7. Explain how the release of gastrin is usually regulated. Why doesn't this regulation work for Mr. Akin?
8. One of the main functions of gastrin is to regulate acid secretion in the stomach. How is acid generated and released in the stomach?

Part II – Diagnosis

The diagnosis of ZES requires documentation of inappropriate excess gastrin secretion. Dr. Jones receives the following blood results for Mr. Akin.

Table 1. Fasting gastrin

Normal	150 pg/mL
ZES	>1000 pg/mL
Mr. Akin	1650 pg/mL

Questions

- Measuring fasting gastrin levels provides the most accurate results. Why should the gastrin level be measured during fasting?
- What abnormalities are revealed in Mr. Akin's blood results? Are these consistent with the diagnosis of ZES?

Part III – Additional Evidence

Although not true for Mr. Akin, sometimes the gastrin test results are equivocal. In such cases, the secretin stimulation test is done to confirm the diagnosis of ZES. Normally, secretin, another gastrointestinal hormone, inhibits gastrin secretion. Gastrinoma cells, however, are stimulated by secretin, causing a significant rise in the level of gastrin. A rise of >100pg/mL over fasting gastrin levels is suggestive of ZES; a rise of >200 pg/mL is considered diagnostic.

Questions

- What are the functions of secretin?
- Compare how secretin works in a healthy individual and how it works in someone with ZES.
- Hypothesize how the paradoxical action of secretin in ZES might play a role in the pathophysiology of the disease.

Part IV – Treatment

ZES is caused by a gastrinoma, a tumor. Mr. Akin, therefore, needs to be further evaluated for the location of the tumor, as well as for the potential malignancy of the tumor and the possibility of metastatic lesions. Dr. Jones refers Mr. Akin to an oncologist and an oncologic surgeon for further evaluation and treatment. Surgical intervention has the potential to cure the disease, but there are often more than one gastrinoma and the surgical procedure may be poorly tolerated. Most physicians recommend surgical exploration in those without documented metastatic disease. With metastatic disease, direct surgical intervention is not recommended.

While Mr. Akin awaits the outcome of his medical evaluation, Dr. Jones prescribes a proton-pump inhibitor (PPI) to treat Mr. Akin's ulcers. This medication works very well to help control acid secretion in the stomach.

20–30% of individuals with ZES may have MEN type 1 (multiple endocrine neoplasia). This rare, autosomal dominant disorder puts individuals at risk for developing certain endocrine tumors, including gastrinoma. Mr. Akin will need careful evaluation of the other glands which might be involved, usually with the guidance of an endocrinologist. Treatment for ZES patients with accompanying MEN type 1 are controversial. Usually, these individuals are not considered for surgical cure, but may need surgery to manage complications from the tumor.

Questions

- Hypothesize how you think a proton-pump inhibitor may work to control acid levels in the gastrointestinal tract.
- ZES is associated with MEN type 1. Do some research on this disease, including clinical manifestations and epidemiology. Prepare a short presentation discussing your findings.