

This Week's Citation Classic

Zollinger R M & Ellison E H. Primary peptic ulcerations of the jejunum associated with islet cell tumors of the pancreas. *Ann. Surg.* 142:709-28, 1955. [Dept. Surg. and Med. Ctr., Ohio State Univ. Coll. Med., Columbus, OH]

Non-insulin producing islet cell tumors of the pancreas were found in two patients with a fulminating ulcer diathesis which eventually required total gastrectomy. It was suggested that a distinct clinical entity resulted from a potent gastric secretagogue produced by these tumors. [The SCF[®] indicates that this paper has been cited over 475 times since 1961.]

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"Edwin Ellison and I simultaneously discovered that each of us was treating a patient who produced excessive gastric juice despite repeated radical surgical procedures culminating in total removal of the stomach. A planned total gastrectomy in one patient, a young girl, prompted a colleague, Hilger Jenkins, to suggest that I evaluate the pancreas, because he had observed ulcer recurrence in a patient who had an insulin-producing islet cell tumor. Peptic ulcer had been associated with insulinoma by R. Strøm and with other endocrine adenomata by P. Wermer.^{1,2} This patient, indeed, had two small lymph nodes near the pancreas, containing metastatic islet cell tumor of the noninsulin producing type. She is still living 23 years after total gastrectomy. The other

patient died, and autopsy disclosed a non-beta islet cell tumor in the pancreas.

"This chance experience with two rare cases stimulated Ellison and me to postulate a clinical entity comprised of hypersecretion, hyperacidity, and atypical ulceration associated with non-insulin producing islet cell tumors of the pancreas. We reported on the two patients in this 1955 article, and stated: 'If these observations accomplish nothing more than a renewal of interest in the ulcer problem with new avenues of study, we will feel justified in reporting these two cases.'

"Our hypothesis was accepted by many and challenged by many during the next five years. But within ten years, a thousand or more case reports established the clinical ulcerogenic Z-E syndrome (gastrinoma). Proof that these tumors were a rich source of gastrin by R.A. Gregory and H.J. Tracy of Liverpool stimulated great interest in the gastrointestinal polypeptides, which was implemented by the development of a reliable gastrin immunoassay by J.E. McGuigan.^{3,4}

"Ellison and I were amazed to observe the ramifications into many fields which followed our report of a daring concept based on two cases. Recently, the syndrome has been extensively cited because of the introduction of H₂ blockers, which for the first time permit drug control of the excessive gastric hypersecretion.

"Peptic ulcer remains a common and disabling disorder. While the original paper was concerned only with management of patients with the rare islet cell ulcerogenic syndrome, its thrust has been to challenge the research and clinical imaginations of many disciplines to solve the enigma of the gastrointestinal tract."

1. Strøm R. A case of peptic ulcer and insuloma. *Acta Chir. Scand.* 104:252-60, 1952.
2. Wermer P. Genetic aspects of adenomatosis of endocrine glands. *Amer. J. Med.* 16:363-71, 1954.
3. Gregory R A, Tracy H J, French J M & Sircus W. Extraction of a gastrin-like substance from a pancreatic tumour in a case of Zollinger-Ellison syndrome. *Lancet* 1:1045-8, 1960.
4. McGuigan J E & Trudeau W L. Immunochemical measurement of elevated levels of gastrin in the serum of patients with pancreatic tumors of the Zollinger-Ellison variety. *N. Eng. J. Med.* 278:1308-13, 1968.