International Foundation for Gastrointestinal Disorders

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Peptic Ulcer: A Twentieth Century Disease

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Peptic ulcer of the stomach and duodenum was known in the 1700s because of its lethal complications of bleeding, perforation, and obstruction. However, it was not until the nineteenth century that ulcers were blamed for chronic abdominal pain. Only late that century did the disease become a common medical problem. In the twentieth century, ulcer disease constituted one of the greatest challenges facing Western Medicine.

However, at the dawn of this new century, have you lately heard of anyone having surgery for a peptic ulcer? The answer is likely "no," yet in most hospitals a generation ago ulcer operations often dominated elective surgery lists. Stomach operations were performed for pain when all other treatments failed. Now, such surgery is done only as a life-saving measure for complications of previously unsuspected ulcers. It is difficult to remember that in World War II the most common reason for invalidism in the armed forces was ulcer disease. Now it rarely causes hospitalization, and most young surgeons are inexperienced in ulcer surgery. What are the reasons for these changes? Why does peptic ulcer appear to be a disease of the twentieth century? The answers are sometimes ironic and pertinent to the study of functional gut disorders.

Diagnosis

The disease was not easily diagnosed before the 1880s, and ulcer pain was ignored or attributed to something else. Postmortem examinations were uncommon and tiny craters in the stomach and duodenum may have been overlooked. With the new surgical possibilities offered by the discovery of anesthesia, physicians and surgeons became more aware of ulcers and their potential for pain, suffering, and death. Pain and discomfort in the upper abdomen, what we now call dyspepsia, became connected with ulcers and the search for treatments began.

Was the disease a sleeping giant in centuries past? It's impossible to know. Nevertheless, through the work of surgeons and pathologists over 100 years ago, peptic ulcer became recognized as a very prominent and frequently lethal twentieth century disease.

Research

One reason why peptic ulcer cure was so long in coming was an almost obsessive interest in stomach acid as the means by which ulcers occurred. Through the work of Pavlov and others, and later Dragstedt, acid secretion was believed to be the clue to cure. Most twentieth century gastroenterologists studied gastric secretion in order to understand better their ulcer patients. "No acid, no ulcer!" was the motto and ever more sophisticated surgical and medical techniques were devised to control acid secretion and permit the ulcer to heal. The requirement for acid in causing ulcer disease is true, and many people were helped and even saved through the results of acid controlling procedures. However, subsequent events showed the cause of ulcers to lie elsewhere. It could be argued in retrospect that the acid theorem delayed the discovery of an ulcer cure. We failed to look "outside the box," even when the real cause presented itself.

Acid Controlling Drugs

The greatest accomplishment of gastric acid study was the development of drugs that control stomach acid secretion. In the late 1970s, a drug, the histamine H_2 receptor antagonist cimetidine (Tagamet), was released and physicians at last had a means to effectively control ulcer pain. The need for elective gastric surgery declined. Other H_2 antagonists came later [e.g., nizatidine (Arid), famotidine (Pepcid), and ranitidine (Zantac)]. But the crowning pharmaceutical achievement was the late 20th century development of the proton pump inhibitor (PPI), omeprazole (Prilosec). [More recent PPIs include lansoprazole (Prevacid), rabeprazole (Aciphex), and pantoprazole (Pantoloc/Protonix).] The proton pump inhibitors, powerful acid suppressants, could heal almost any ulcer if appropriately prescribed, and hospitalization and elective ulcer surgery became a thing of the past.

Nevertheless, cure was not yet at hand. Healed ulcers recurred requiring more drugs. The drugs were of little immediate help when ulcers bled, perforated, or obstructed. It is a further irony that these drugs, which were developed to treat ulcers, are now principally used to treat gastroesophageal reflux disease (GERD).

Ulcer Surgery

Elective ulcer surgery began in the 1880s. At first, the ulcers were simply cut out, only to recur. As knowledge of acid secretion physiology accumulated, surgeons attempted to reduce the stomach's acid production through first removing the acid producing area of the stomach, later removing the antrum of the stomach [the lower part of the stomach], which produces the acid stimulating hormone gastrin, and finally removing the neurogenic stimulus for acid secretion by

cutting the vagus nerves that supply the stomach. While they often cured the ulcer disease, these operations had many complications and gastric impairment was common in Gastroenterology clinics during the last half of the century. Ironically again, development of a safe, effective surgical procedure called highly selective vagotomy coincided with the arrival of effective drug treatment. Aside from treating perforation, obstruction, and rarely bleeding, peptic ulcer surgery has become virtually obsolete.

Helicobacter Pylori

A peptic ulcer cure became possible when bacteria called *Helicobacter pylori* (*H. pylori*) were recognized on the surface of the stomach lining. Another irony of the ulcer story is that these bacteria were observed at least three times between 1898 and 1983, but their significance was missed. Students of gastric acid secretion could not believe that any bacteria could survive in the acid stomach. Rather than ulcer scientists, it was an Australian pathologist, JR Warren, and a Gastroenterology resident seeking a research project, BJ Marshall, who connected *H. pylori* and ulcers. Even so, it took almost a decade after their 1983 report in the journal *Lancet* before the medical establishment came to believe that these bacteria caused peptic ulcers, and that eradication with antibiotics cured the disease. Provided the diagnosis was made, ulcers could be cured in doctor's offices.

The Passage of Time

We have seen how improved pathological observations, the study of acid secretion, the rise and fall of ulcer surgery, the development first of healing drugs, and then curative treatments for peptic ulcer created the appearance that peptic ulcer was a twentieth century disease. The final irony is that before these treatments and cures, the prevalence of ulcers in Western countries had begun to decline spontaneously. It's as if the "demons of illness" realized that ulcers were about to be curable and decided to meddle elsewhere. The truth is something different.

The means of transmission of *H. pylori* from person to person is poorly understood. It appears to require the transmission of gastric juice from one person to another. It is often found in people with infected parents, large families, overcrowding, poverty, and unsanitary conditions. With the revolution in living standards, the prevalence of *H. pylori* in Western countries is fast declining. While still present in over half of our elderly population, the organism is uncommon in the young. Coincident with these developments has been a natural decline in peptic ulcer disease.

Remaining Challenges

It would be a mistake to leave the impression that peptic ulcer poses no challenges for the twenty-first century. *Helicobacter* and the resulting ulcers and other diseases are still very common as lingering sources of misery in the third world. While ulcer dyspepsia is fading, non-ulcer dyspepsia remains as one of the most frustrating and costly conditions in modern Gastroenterology. Is *H. pylori* a possible cause? Not likely it seems. How should nonulcer dyspepsia (functional dyspepsia) be investigated? How can it be treated? The organism does seem to be a cause of gastric cancer. We need a low-cost, efficient, and safe means of eradicating *H. pylori* from the population. Current methods are costly and risk side effects and antibiotic resistance. Perhaps, someday a vaccine will rid large populations of the organism. While *H. pylori* are responsible for most ulcers, another cause is the use of non-steroidal analgesic drugs (NSAIDs) for arthritis. This is an increasing and potentially lethal problem, especially for elderly females.

Conclusions and Lessons for the Study of Functional GI Disorders

- Some diseases appear to emerge and decline for reasons that are not well understood.
- Improved living standards and public health are important (some say most important) in the prevention of disease.
- When a hypothesis fails to be proven as the cause of a disease after many decades of intensive research, new ideas should be sought.
- Such new ideas will emerge from unprejudiced young people with professional/ scientific backgrounds. Like Warren and Marshall, young Fredrick Banting was a doctor with an idea for treating diabetes that was outside established thinking. While few believed that bacteria could live in gastric acid, even fewer believed Banting's hypothesis that diabetes-controlling insulin could be extracted from the destructive enzyme-producing tissues of the pancreas. Without research funding, these doctors required great personal effort to prove their ideas.
- It seems likely that someone will discover the cause of functional gastrointestinal disorders with an idea that is not apparent today. Such a person should be challenged (and funded) to prove it.

References

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