PEPTIC ULCER

A Guide for the Practicing Physician

M.I. Grossman
Editor

Peptic Ulcer

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By members of the staff of
The Center for Ulcer Research and Education (CURE)

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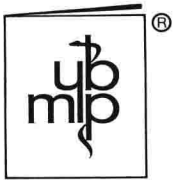

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PEPTIC ULCER

A GUIDE FOR THE PRACTICING PHYSICIAN

DEDICATION

We dedicate this book to the memory of our colleague and friend

RICHARD A. L. STURDEVANT

Richard Sturdevant died on April 22, 1978, of pancreatic cancer. He was 39 years old. The breadth of his interests and skills was formidable. In addition to an extensive knowledge of gastroenterology and gastrointestinal physiology, he was widely read in philosophy of science, symbolic logic, systems analysis, decision theory, and the theoretical principles of epidemiology and clinical trials. He knew how to focus this broad theoretical background on practical issues. He quickly established himself as an expert in the design, execution, and interpretation of clinical trials. Much of the work reported in this book was strongly influenced by Richard Sturdevant's precepts.

The process by which a physician could translate new scientific knowledge, particularly the results of clinical trials, into rational clinical practice was his special interest. (Excerpts from an editorial "How should results of controlled trials affect clinical practice?" by Richard Sturdevant appear on the following pages.)

Richard Sturdevant was the consummate scientific skeptic, but he did more than just criticize—he searched for ways to do things better. He had a talent for illuminating and clarifying the essential issues in any question.

We shall miss Richard Sturdevant not only because he did so many things so well, but also because he was a good and wise person whom we all loved.

(Excerpts from an editorial by Richard Sturdevant that appeared in Gastroenterology *73:1179–1181, 1977. Reprinted with permission.)*

HOW SHOULD RESULTS OF CONTROLLED TRIALS AFFECT CLINICAL PRACTICE?

Assuming that controlled trials indicate that a treatment is effective, how might a rational physician proceed to decide whether or not to recommend the treatment to his patients?

Three steps in the process from controlled trial to standard therapy are: (1) evaluation of the trial; (2) deciding if inductive inference of the conclusions from the trial to one's future patients is appropriate; and (3) deciding among competing treatments.

Measuring trials against standard criteria should help us decide whether or not to accept the conclusions of a particular trial. By "accept," I mean to accept that the conclusions are correct for the patients studied. If they are not accepted, the process stops.

The second step requires that we decide whether a treatment that met our therapeutic goal in a controlled trial will also meet that goal in our future patients. My view is that Karl Popper is correct—it is impossible to establish truth by inductive inference. If so, it is impossible to prove that the conclusions of a controlled trial will also be true in future patients. To decide whether inductive inference is appropriate, we are left to apply common sense, intuition, and bits and pieces of possibly relevant data from other animal and human studies, while trying to avoid conscious and unconscious bias.

But, in the third step, we have to act. If a treatment is available, we have to decide whether to use it or a competing treatment (which may be nothing, combinations of treatments, etc.). Conventional economic wisdom tells us to decide by "maximizing expected utility."

As a heuristic and educational tool, I believe that trying to maximize expected utility by the use of decision theory should be of value to physicians. As a method of solving (reaching agreement on) difficult and important medical decision problems, I am pessimistic about its potential value.

Do physicians now make decisions by methods that are consistent with decision analysis theory? Essentially no research results are available that attack this question.

Informally, patients and physicians appear to do something that resembles decision analysis. Consider two examples. First, hospitalization for a few weeks is believed to speed healing of gastric ulcer. Yet, patients are often treated as outpatients, indicating that the trial results are not compelling in the treatment decision. Apparently the

expected utility of a higher chance of complete healing after 3 or 4 weeks is less than the expected utility of outpatient management. In part, the explanation may be that the risk and discomfort of slower healing are small compared to the dollar cost and disruption of life-style of hospitalization.

Second, patients and physicians often choose elective surgical management of duodenal ulcer, despite the operative costs, the mortality, and the near certainty that a trial of elective surgery versus medical management would reveal greater dollar costs and more patients dead in the surgical group 30 days after enrollment. Apparently for these patients the expected value of improvement of future course of the ulcer is higher, even after subtraction of the negative utilities associated with operative death and with the dollar cost of the operation, than the expected utility associated with the natural (unoperated) history of ulcer. (I do not suggest that all of the important outcomes for these two problems are included in the discussion above.)

These considerations suggest some reasons why all physicians are not quick to transfer results of trials into clinical practice. Even if agreement can be reached at step one (evaluation), legitimate differences of opinion will, I believe, often remain at step two (induction). Step three (decision) is an even surer source of differences of opinion. For example, dollar cost and side effects of treatment regimens will not be valued the same by all patients and physicians.

It is naive to believe that controlled trials will dispose of disagreement among experts about therapy. Consider the continuing controversy surrounding oral hypoglycemic drugs and the University Group Diabetes Project trial. What possible trial can be conceived that would settle that controversy? More generally, in order for one treatment to be clearly superior to another, it is necessary that its expected utility be higher for all possible patients. This is unlikely

There are no controlled trials of the possible therapeutic value for ulcer of "a good physician-patient relationship" or of advice to alter work habits, employment, life-style, or goals, etc. These measures may have side effects of potentially great negative value. I suggest that their claimed positive values may be overrated, and formal trials of these therapies are in order.

My message is that results of controlled trials alone cannot be expected to define standard therapy. Rational therapeutic decision making requires judgments about issues that cannot be settled with certainty by controlled trials.

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Preface

ULCERS ARE COMMON and gastroenterologists are few, so most ulcer patients are diagnosed and treated by nonspecialists. This book is intended for use by those nonspecialist physicians who care for the largest share of ulcer patients. It was written by members of the staff of the Center for Ulcer Research and Education (CURE), an organization which has been engaged since 1974 in interdisciplinary research and education on the causes, cures, and prevention of ulcer disease.

From our experience in diagnosing and treating patients with ulcer, in conducting clinical trials and physiologic studies on such patients, and in reading and evaluating the literature on ulcer disease, we have tried to distill the essential information needed by the practitioner to diagnose and treat ulcer disease and to recognize those situations in which it is advisable to seek help from a specialist. This book represents a consensus of the staff of CURE, so we have not listed authors of individual chapters. While we have tried hard to get our facts straight and to make our judgments reasonable, it seems safe to assume that we have not always succeeded in these noble goals. We shall be grateful to those readers who take the time to let us know where we have gone astray. If it is a matter of fact, we will try to get the facts straight. If it is a matter of judgment, we will listen attentively and stand ready to change our opinions when that is warranted. CURE attempts to serve as a clearinghouse for all forms of information about ulcer disease. Criticisms or comments about this book or about any other aspect of peptic ulcer disease may be directed to Morton I. Grossman, Director, CURE, VA Wadsworth Medical Center, Los Angeles, California 90073.

The royalties from the sale of this book will be paid to the CURE Foundation, a nonprofit organization, and will be used to support its research and educational programs.

MORTON I. GROSSMAN

Contents

1 / What Are Peptic Ulcers and Where Do They Occur?

WHAT IS AN ULCER?

THIS BOOK is about peptic ulcers. Peptic ulcers occur in those parts of the digestive tract that are exposed to juice containing acid and pepsin secreted by the stomach (Fig 1–1). These include the lower end of the esophagus, the entire stomach, and the duodenal bulb. Rarely, more distal portions of the small intestine become exposed to gastric juice as the result of massive hypersecretion, surgical rerouting, or being adjacent to congenitally misplaced gastric mucosa such as in Meckel's diverticula (Table 1–1). The most common form of peptic ulcer is duodenal ulcer, and the next most common is gastric ulcer.

An ulcer is a hole in the tissue covering one of the surfaces of the body. Ulcers occur in the skin, the cornea of the eye, the lining of the mouth, and in the lining of various parts of the digestive tract.

Defects that do not extend through the entire thickness of the mucosal lining are called "erosions" to distinguish them from true ulcers, which involve the entire thickness of the mucosa and extend at least into the submucosa (Fig 1–2).

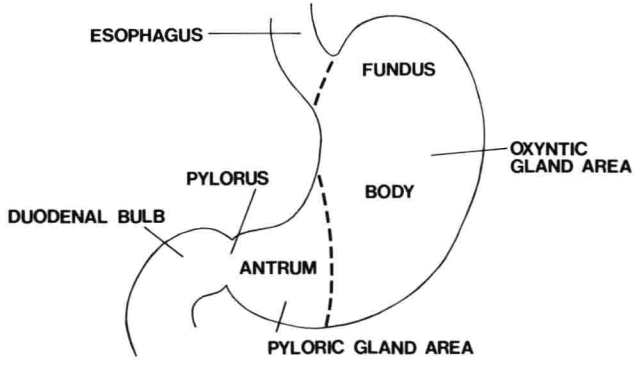

Fig 1–1.—Names of parts of stomach. Fundus and body contain acid-pepsin-secreting oxyntic glands. Antrum contains pyloric glands, which do not secrete acid-pepsin but secrete gastrin into blood.

TABLE 1-1.—MUCOSAL SURFACES BATHED BY ACID-PEPSIN AND WHICH ARE THEREFORE POTENTIAL SITES OF CHRONIC PEPTIC ULCER

Duodenal bulb (commonest site)
Gastric antrum, the non-acid-secreting distal part of the stomach (next commonest)
Jejunum that has been anastomosed to the stomach during surgical treatment of ulcer
Acid-secreting part of stomach, oxyntic gland area, especially after it has been afflicted by gastritis and lost its ability to secrete acid
Lower end of the esophagus, particularly if metaplasia to gastric-type epithelium (Barrett's epithelium) has occurred
More distal parts of duodenum and upper jejunum in patients with extreme hypersecretion
Intestinal mucosa adjacent to acid-pepsin-secreting mucosa in some Meckel's diverticula

When the terms "peptic ulcer," "duodenal ulcer," or "gastric ulcer" are used without further qualification, a chronic ulcer is implied. An ulcer is chronic if it has existed long enough—say, two weeks or more—to have evoked the formation of granulation tissue that will in turn leave a scar when the ulcer heals. By contrast, erosions heal by migration of surrounding epithelium into the defect without scar formation.

Defects that do not extend through the entire thickness of the mucosa are erosions; true ulcers involve the entire thickness.

As the ulcer burrows through the wall, it may erode into a large artery and cause severe hemorrhage (Table 1-2). Most ulcers go no deeper than the muscular layers. However, a few, known as "penetrating ulcers," excavate through the entire thickness of the gastric or duodenal wall and may even extend into an adjacent organ that happens to be touching at that point, such as the pancreas or liver. An ulcer may form a fistula into an adjacent hollow viscus such as the colon or gallbladder. If no organ is touching at the serosal side of a through-and-through excavation, then a free perforation into the peritoneal cavity occurs—a life-threatening situation demanding immediate treatment.

Peptic ulcers tend to be round or oval, but occasionally are linear or irregular. They vary from a few millimeters to a few centimeters in largest dimension, but most are less than 2 cm. Most chronic ulcers are single. Occasionally, two or even three may occur in the same person.

One of the most distinctive features of chronic peptic ulcers is their tendency to heal and then recur months or years later.

Multiple superficial erosions of the stomach and duodenum—often

TABLE 1-2.—SOME POSSIBLE CONSEQUENCES OF EXTENSION OF ULCER THROUGH THE ENTIRE THICKNESS OF GASTRIC OR DUODENAL WALL

Erosion of large blood vessel, usually an artery, with severe bleeding
Penetration into an adjacent solid organ such as pancreas or liver
Perforation into an adjacent hollow viscus, such as colon or biliary tract, with formation of a fistula
Perforation into free peritoneal cavity, where spillage of gastric contents causes severe chemical peritonitis

called "stress ulcers"—occur frequently in patients with a wide variety of severe injuries or diseases such as extensive burns or severe head injuries. A few of these may progress to acute ulcers and may extend deeply enough to involve large arteries with life-threatening hemorrhage. Acute "stress ulcer" is a separate disease from chronic peptic ulcer; it is discussed in Chapter 17.

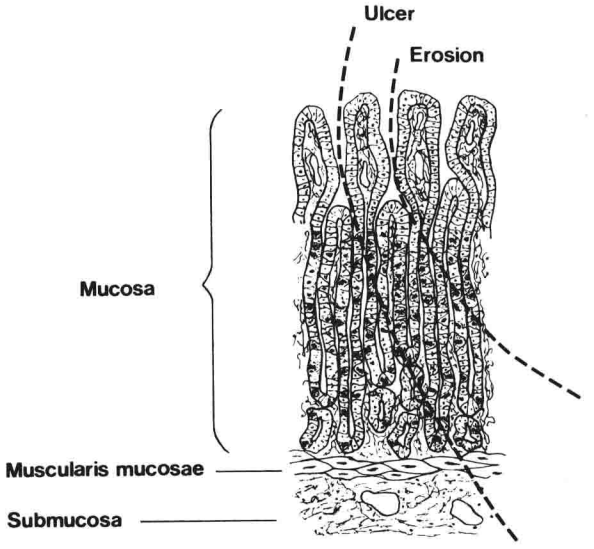

Fig 1–2.—Schematic diagram of oxyntic gland area of stomach. Surface epithelial cells, which secrete mucus, line surface and pits of entire stomach. Oxyntic glands contain parietal cells, which secrete hydrochloric acid and intrinsic factor, chief cells, which secrete pepsinogen, and some mucus-secreting cells. Pyloric glands of gastric antrum lack parietal and chief cells and so do not secrete acid and pepsinogen but have mainly mucus-secreting cells and some gastrin cells, which secrete gastrin into blood. Erosion does not extend beneath muscularis mucosae, which marks lower boundary of mucosa. Ulcer extends through muscularis mucosae into submucosa or deeper. Beneath submucosa are muscular and serosal layers.