Current Comments

All About Ulcers, Antacids, and How Little We Know

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Even before I began high school, I can remember suffering regularly from hunger pains. These were not the normal pains of a growing boy, nor were they the result of poverty. We always had enough food, even though we were poor. Several years later at Fort Meade, Maryland, I developed intense stomach pains again. They were probably precipitated by stress in anticipation of combat. Fort Meade was the point of embarkation for the European theater of war.

After admission to the hospital, a barium X-ray series revealed a duodenal ulcer. I can remember my mother's tears of joy when the army surgeon told her that I had to be medically discharged. While the war in Germany was nearly over, Japan had not yet surrendered, and indeed many of my buddies arrived in Europe at the time of the Battle of the Bulge.

In those days, the so-called Sippy diet,[1] named after Bertram Sippy, was very popular in the treatment of ulcers. So the army nurses brought me delicious eggnogs made of milk and raw eggs. This was similar to the diet I had followed in school. In New York, for ten cents, you could get an enormous malted milk at almost any corner candy store. I often did, and the "hunger pains" went away.

About ten years ago, I went to see a Boston physician, Russell S. Boles, about my ulcer. After 25 years of just living with it, I had gone to see him at the urging of Harold Anderson, who formed the Randex Corporation with my friend, Murray Rosenberg. Boles spoke to me at length and gave me this rather philosophical recap on ulcers.

According to Boles, there are about a dozen different therapies for ulcers. All of them work, because if you wait long enough, most uncomplicated ulcers eventually heal by themselves. You might see an ulcer in an X-ray one day, and within days or weeks it is gone. Boles explained the cyclical nature of ulcers, and how they can often recur after healing. While in some cases the pain can be intense when it occurs, it inevitably goes away. In the interim, one adopts one of the "cures" to obtain temporary relief.

My position as president of a modern corporation conforms with the popular notion that ulcer victims tend to be hard-driving business executives. However, many professionals are obsessive about their work. And since they and I enjoy our work, it is simplistic to conclude that our life-styles are necessarily more stressful than the next person's. The popular notion of "executive ulcer" is, at best, oversimplified.[2,3] But beyond that, unequivocal answers about what causes peptic ulcers are hard to come by.

Peptic ulcers are actual holes that develop in the mucous membrane that lines the digestive tract, the mucosa. When they occur in the stomach, they are called gastric ulcers. More frequently, they occur in that part of the small intestine into which the stomach empties its contents, the duodenum. In

the US, about seven people develop a duodenal ulcer for every two who get gastric ulcer.[4] This ratio varies around the world. In India and Bangladesh, for example, it is estimated that 19 people suffer duodenal ulcer for every one person who gets gastric ulcer.[5]

Ulcers occur when digestive acids secreted in the stomach corrode the gastric or duodenal mucosa. As A.L. Blum and colleagues at the Triemli Clinic of the City Hospital of Zurich point out, " 'No acid—no ulcer' is the only unchallenged basic principle of ulcer formation."[6] But it is wrong to assume that ulcers afflict only those who secrete abnormally high amounts of acid. Many victims of duodenal[2] and gastric[7] ulcer secrete amounts of acid that are considered to be within the normal range, or even below normal. This leads researchers to conclude that for many patients, the problem is not the amount of acid secreted, but the ability of the mucosa to resist its corrosive effects.[8]

The most familiar symptom of peptic ulcer is a pain in the upper abdomen. The pain may be described as gnawing, burning, or simply as hunger. If the ulcer is duodenal, the pain usually occurs when the stomach is empty, although rarely before breakfast. The victim is often awakened from sleep by pain or "heartburn." Pain often radiates to the small of the back. Eating usually brings relief. Gastric ulcer symptoms don't follow this pattern, however, and eating often aggravates rather than relieves pain. Aside from this distinction, ulcer victims are typically unable to determine whether their ulcers are duodenal or gastric—a clinical diagnosis is needed. In both cases, antacids can relieve pain. Although the relationship between worry and the development of an ulcer is unclear, worry can make the pain of a duodenal ulcer more intense.[9] Duodenal ulcers occur most frequently in the fourth decade of life.[10] Gastric ulcers occur most frequently in the fifth decade.[11] But people of all ages can develop an ulcer, even teenagers.[3]

Ulcers are fairly common gastrointestinal disorders. It is believed that between 10% and 20% of Americans will develop one at some point in their lives.[4] For most of these people, ulcers will not pose a serious threat to health. Both gastric and duodenal ulcers often heal of their own accord in about two to six weeks, although recurrences of ulcers are common.[12] But for others, there are complications and other problems associated with peptic ulcers that can have serious consequences.

For example, gastric ulcers may sometimes result from a malignancy, although duodenal ulcers almost never do.[12] If either type of ulcer burrows into an artery or vein, hemorrhaging will result. This is called bleeding ulcer. This is presumably what happened to me five years ago in Paris. It is an experience one should avoid. Vomiting blood or the presence of blood in stools are both signs of bleeding ulcer. The latter can sometimes go unnoticed or be mistaken as diarrhea.

Sometimes, an ulcer can burrow clear through the gastric or duodenal wall and into the abdominal cavity, causing a real medical emergency. This is called perforation. A person whose ulcer has become perforated will have no trouble knowing something is wrong. A fact sheet published by the Digestive Diseases Information Center, Bethesda, Maryland, dryly reports: "The extreme pain associated with . . . [perforation] insures that the patient will seek medical help promptly." The Center notes that perforation occurs in about 5% of ulcer victims.[3] An overview of surgical procedures available to physicians in treating perforated ulcers appeared recently in the *British Journal of Clinical Practice*.[13]

Research into ulcer cures has traditionally focused on combating digestive

acids rather than strengthening the mucosa's ability to resist them. Until recently, physicians had to rely exclusively upon antacids in treating uncomplicated ulcers. And antacids are still widely used to both relieve pain and promote healing. There are a large variety of antacids available, and a knowledge of their differences is important.

The most effective antacids are usually some combination of aluminum or magnesium hydroxide. These are *amphoteric,* i.e., in the presence of an acid, they act as a base, and in the presence of a base, they act as an acid. The objective is presumably to maintain a particular pH, although exactly what a "normal" stomach pH is has not been established.[2] The product Amphojel, produced by Wyeth Labs in Philadelphia, is named for its amphoteric properties. Mylanta, produced by Stuart Pharmaceuticals, is a combination of aluminum hydroxide, magnesium hydroxide, and simethicone which relieves excess gas. Amphojel consists simply of aluminum hydroxide.

The major differences among Amphojel, Mylanta, and other over-the-counter antacids are their effects on bowel movements. Some have a constipating effect, while others tend to cause diarrhea. Were it not for these side effects, one might be able to consume large quantities without discomfort. However, prolonged use may cause other problems such as kidney dysfunction.

Another popular antacid is Digel, which contains magnesium carbonate in addition to the ingredients found in Mylanta. Rolaids and Tums may be the most widely advertised antacids on the American market. Their television ads are, to say the least, ubiquitous. Rolaids is nothing more than dihydroxyaluminum sodium carbonate. According to the manufacturer's insert in the *Physicians' Desk Reference,* each Rolaids tablet "has acid neutralizing capacity of 75-80 ml of 0.1N hydrochloric acid and the ability to maintain the pH of the stomach contents close to 3.5 for a significant period of time."[14] (p. 636)

Tums, however, is primarily calcium carbonate. According to the manufacturer, Tums "neutralizes 10 mEq. of 0.1N HCl. This high neutralization capacity combined with a rapid rate of reaction makes Tums an ideal antacid for management of conditions associated with hyperacidity. . . . It effectively neutralizes free acid yet does not cause systemic alkalosis [extreme loss of acid] in the presence of normal renal function."[14] (p. 586) Tums is a much stronger product, and I believe one should exercise caution in use. It does not act slowly, but quickly and *violently* as would any pure carbonate. Moreover, as Jerome Rotter of the Center for Ulcer Research and Education (CURE), Los Angeles, points out, calcium carbonate is currently out of favor with gastroenterologists. Although the compound initially reduces the level of gastric acid, the calcium stimulates acid production after it is absorbed, a phenomenon known as acid rebound.[15]

The neutralizing of stomach acids is obviously desirable for ulcer patients. But a new drug, cimetidine, helps to prevent secretion of acid in the first place. The drug, marketed by SmithKline under the trade name Tagamet, works by blocking histamine-2 receptors.[16] Receptors are chemical groupings on the surfaces of specialized cells that react to specific substances. And histamine-2 is believed by many to be a principal mediator, or inducing agent, in gastric acid secretion. However, more physiological data are needed to determine the exact relationship between histamine-2 and gastric acid production.

Cimetidine first became available in Great Britain in November of 1976. It wasn't until nine months later that it was approved by the US Food and Drug Administration.[17] The drug has generated an enormous amount of scientific lit-

erature. My *ASCA*® report on cimetidine and related drugs includes from 10 to 20 citations per week.

Cimetidine is particularly effective for treating duodenal ulcers, although for gastric ulcers the drug fares no better than traditional antacid treatment.[18] Recently, the FDA has approved the use of cimetidine as a prophylactic against recurrence of duodenal ulcers that have healed.[17]

A research team headed by G. Shaw of Prince Henry's Hospital, Melbourne, Australia, recently compared the effects of cimetidine against those of Mylanta II, an over-the-counter antacid. They found a healing rate of 81% for cimetidine against 61% for the antacid.[19] Kermit Knudsen and Walter Dyck, Texas A&M University College of Medicine, observe that although cimetidine is often prescribed in combination with antacids, there are no controlled studies indicating whether or not such combinations have any particular value.[20]

Most researchers concur that the side effects of cimetidine are mild and rare.[16,21] But some have adopted a go-slow attitude. There have been reports that cimetidine may cause dizziness in patients,[22] and that the drug may temporarily lower a patient's sperm count.[23] Recently, Barry Kisloff, University of Pittsburgh School of Medicine, reported the first case of a human patient who proved immune to the acid-inhibiting effects of cimetidine.[24] Nevertheless, the drug has been well-received by the research community, despite concern over its indiscriminate use.[25]

Until cimetidine came along, a common drug used for ulcers was Pro-Banthine, an anti-cholinergic which acts on the vagus nerve to reduce hyperacidity. It may often be used as an intermittent therapy so that one can avoid uninterrupted use of cimetidine.

Researchers now recognize the heterogeneity of peptic ulcer.[26,27] As Rotter notes, ulcers may be many different diseases. He likens an ulcer to anemia, where any number of physiological disorders may result in a depressed level of red blood cells. "To say that someone has an ulcer," according to Rotter, "may be no more specific than saying that someone has anemia."[15]

It now seems clear that the physiological traits that predispose one to peptic ulcer can be inherited.[28] It has long been observed, for example, that ulcers occur more frequently in people who are close relatives of other ulcer victims.[29] Recent work indicates that a high blood level of a certain enzyme, pepsinogen I, is genetically determined, and that high concentrations of pepsinogen I identify people who are prone to develop one form of duodenal ulcer.[30]

Heredity seems to be a strong factor in determining whether or not one will develop an ulcer. But it is not the only one. Certain characteristics of the population of ulcer victims change over time in a way that cannot be explained by genetics. In Britain, for example, 19th-century women developed ulcers more frequently than men.[31] But by the mid-20th century, the overwhelming majority of ulcer victims in Britain and throughout the world were male. In 1938, more than four British men developed ulcers for every woman who developed one.[5] But today, the male-female ratio of duodenal ulcer in Britain has narrowed to 1.9:1.[5] In fact, women are developing a greater share of both duodenal[32] and gastric[33] ulcers throughout the industrialized world. Such changes in the incidence of ulceration would seem to be caused by factors other than genetics.

The scientific literature has curiously little to say about why more women are getting ulcers. Most theories focus on modern living habits. For example, a team of Australian researchers attribute an increase of gastric ulcers among Australian women to increased consumption of aspirin.[34] Researchers in

other countries have endorsed this view regarding their own countrywomen.[7] In short, the question of why more women are getting ulcers is not usually considered apart from the question of why anyone gets them.

Aspirin has been suspected to be harmful to the stomach mucosa since at least 1938.[35] Since that time, an accumulating body of evidence has firmly linked regular consumption of aspirin to gastric ulcer.[36] Few would claim that occasional use of aspirin is harmful. But there is some concern that many people take aspirin unwittingly. A 1974 article in the *New England Journal of Medicine* listed about 200 products that contain aspirin, many of which do not have the word "aspirin" in their trade names.[37]

Another living habit, if you can call it that, which may be a factor in ulceration is cigarette smoking. I have discussed the danger of nicotine addiction in a previous essay.[38] Researchers report a significant statistical relationship between cigarette smoking and ulcers.[39] But it is not known why cigarette smoking or nicotine should affect ulceration at all. There have been a number of studies to determine if cigarette smoking can raise the level of acid secretion, but the results are mixed.[40-42] Most authors stop short of asserting a direct cause and effect relationship between smoking and ulceration. There is evidence, however, that ulcer victims who smoke develop larger ulcers than non-smoking victims.[43]

Alcohol consumption and smoking often are combined. But contrary to popular belief, there is no evidence that alcohol consumption per se causes ulcers, or even inhibits their healing. Heavy drinkers do not get significantly more ulcers than moderate drinkers.[3] However, at least one research team asserts that alcohol and aspirin in combination are so powerfully ulcerogenic that the two should never be taken together.[44] In my own experience, most dry wines will produce symptoms very quickly, while others, like Japanese plum wines, will not; nor will mixed drinks like pina-colada, which contains a combination of rum, coconut, and pineapple juice. Canned juices of almost any kind are excessively acidic, while absolutely fresh orange juice is not.

A forthcoming book from CURE will discuss the latest developments in ulcer research. The book, entitled *Peptic Ulcer: A Guide for the Practitioner,* will be edited by Morton I. Grossman of CURE. It will be published by Yearbook Medical Publishers, and should appear sometime in February of next year.

In recent years, the role of diet in ulceration has been downplayed in developed nations. It used to be that doctors warned against spicy food and prescribed bland diets for ulcer patients. Now patients are told to eat more or less what they wish. Certain foods may cause discomfort among individual ulcer victims. But in general, diet is not thought to affect the healing of an ulcer one way or the other.[3]

But many ulcer studies originating from Third World countries do consider the relationship between diet and ulceration. In a study on duodenal ulcer in Nigeria, E.A. Lewis and E.A. Aderoju state that certain foods may play a causative role.[45] They note that ulcer in Nigeria is more common among the lower socioeconomic classes. People in these groups, the authors speculate, cannot afford good protein sources such as milk, eggs, and green vegetables. They therefore eat traditional foods containing chili peppers and cassava roots which, Lewis and Aderoju found, aggravated existing ulcers. And cassava preparations contain a small amount of cyanide, which the authors regard as significant.[45]

Another study, from India, indicates that the incidence of duodenal ulcer is higher in areas where rice is a staple food than in areas where people eat wheat.

However, there were other factors that differed between the two populations, including ethnicity and climate, and the author of the study makes no conclusions regarding the role of diet.[5]

The climatic conditions in the Indian study mentioned above involved humidity. It was found that people living in humid areas get ulcers more frequently than those who live in dry areas.[5] This was also found to be the case in several parts of Africa.[46]

It has been traditionally assumed that peptic ulcer, particularly duodenal ulcer, can have psychosomatic causes. Literature concerning the effects of emotional states on alimentary processes has appeared since the turn of the century. A comprehensive review of the literature on psychosomatic illnesses in the first half of this century can be found in the 1954 volume *Emotions and Bodily Changes,* by Flanders Dunbar.[47] Most authors from that period explained the psychological causes of ulcer in Freudian terms. For example, in a 1950 paper, one author described an ulcer as an "internal digestive bite . . . provoked by remorse on account of oral aggressive wishes against the mother's frustrating breast."[48] Several authors endorsed the view that ulcer victims have strong oral-receptive tendencies, that is, the need to be loved and cared for. These tendencies are repressed, the theory went, because of the ego's desire for independence. Ulcers may, therefore, be manifestations of the ensuing emotional conflict.[48,49]

Today, psychosomatic causes of ulceration receive less attention. But research in this area has not been abandoned entirely. Stress is still thought to be a possible factor in the development of ulcers. In 1970, for example, M. H. Alp and colleagues at the Queen Elizabeth Hospital in Adelaide, Australia, found that a preponderance of gastric ulcer victims were experiencing domestic and financial stress.[50] Some have questioned, however, whether stress in ulcer victims is a cause or an effect of the ulcer.[2] Blum and colleagues flatly state, "On the basis of personality structure, there is no such thing as an 'ulcer type.'" They add, "Psychiatric methods for the treatment of ulcers are of doubtful value."[2]

During the past decade, researchers have begun to examine other aspects of ulceration. One study, for example, showed that male ulcer victims tend to be leaner than their ulcerless counterparts.[51] Another study found an intriguing relationship between blood pressure and ulcers: those with lower blood pressures tend to get them more frequently.[52] There has also been speculation that herpes-simplex virus may play a role in ulceration, but there are no conclusive studies.[53] A recent paper in *Science* indicates that there may be a link between the hypothalamus and gastric acid levels.[54] Developments in this area promise to be worth watching.

It is heartening to follow the continuing improvements made in the treatment of peptic ulcer. Aside from cimetidine, better surgical techniques have recently been found to treat ulcers that are resistant or have developed complications.[55,56] But much work remains to be done on the question of why we must suffer ulcers at all. The voluminous literature on the causes of peptic ulcer makes for fascinating reading, but unfortunately provides few answers. Still, I'm pleased to note that in 1978, Eden Medical Research, Inc., St. Albans, Vermont, began an *Annual Research Reviews* series devoted exclusively to duodenal ulcer.

While science goes its slow, persistent way, I've worked out a combination of techniques that seem to work for me. I hope this review will provide some insights that will lead others in the right direction.

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