

## Peptic Ulcer and Stress

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### Evidence and controversy

- At 5:46 AM on 17 January 1995, a major earthquake devastated the Hanshin-Awaji area of Japan. More than 6000 people were killed, and 300,000 had to be evacuated from their homes. During the next two months there were three times as many bleeding ulcers detected at local hospitals as in the same period of the previous year.
- During 1971-75, the National Health and Nutrition Examination Survey asked 2511 Americans how much “strain, stress, or pressure” they were under. Ten years later, those who had felt under a great deal of stress were 3 times as likely to have an ulcer than those who felt no stress at all.
- Researchers found that 44% of English patients with new ulcers had been having serious, objective life difficulties during the last six months, as compared with only 9% of healthy people of similar age and background.
- Among Italian patients who had recently developed ulcers, those who scored in the highest third on an anxiety questionnaire were four times as likely to remain unhealed after a standard course of treatment.
- In a study of 2109 Swiss ulcer patients, those classified by their physician as under stress were twice as likely to relapse during the first year after cure.

There is a wealth of research demonstrating that people who are experiencing life stress are more likely to develop an ulcer of the stomach or the duodenum, and that their ulcers are harder to cure. The stereotype of the frazzled executive reaching for his bottle of Maalox every time he slams down his telephone is misleading only in its suggestion that ulcers are more common in the rich than in the poor (in fact it’s the other way around).

On the other hand, in recent years it has been widely stated that ulcers are caused not by stress but by an “ulcer germ,” *Helicobacter pylori*. Since the early 1990’s, the discrepancy between these two rival explanations has been confusing physicians as well as the lay public about the role of psychological factors in ulcer disease.

The hunch of an Australian scientist, Barry Marshall, who believed that bacteria might be involved in ulcers, was so revolutionary that it took 15 years to convince the medical community. We now know he was right: *Helicobacter pylori* lives in the stomach of most ulcer patients, and many people who suffered from ulcer pain for decades have been given permanent relief by a single brief course of antibiotics. The *Helicobacter* story has not only clarified the origins of one specific disease and improved the lives of many patients but has opened the door to a paradigm shift in medical science by suggesting that infectious agents may play a role in many chronic diseases, including heart attacks and cancer.

The relation between Helicobacter and ulcer is not so simple, however. It's true that most people with ulcers are infected, but so are a large percentage of healthy adults: half of Americans over age 60, and 90% of all African adults, have Helicobacter pylori in their bodies, many of them without a twinge of indigestion. And, contrariwise, as many as one ulcer in four develop in people who have never had a Helicobacter infection, confirming that the ulcer story is larger than just Helicobacter pylori.

Helicobacter pylori usually settles into the body during childhood, but ulcers rarely develop before the age of 30, and only one in five people with Helicobacter pylori infections ever develop an ulcer. Clearly additional factors, psychological or non-psychological, must be involved if a person's relationship with his or her resident Helicobacter makes the leap from peaceful coexistence to ulcer. Similarly, only a small proportion of people who are coughed on by somebody with tuberculosis, or who have strep in their throats, become ill.

Barry Marshall himself has warned against overstating the implications of his discovery. To determine the toxic effects of Helicobacter pylori, Marshall once bravely downed a concoction of live bacteria. When he then looked inside his own stomach, he saw that the bacteria had caused inflammation — but not an actual ulcer. Based on this and other evidence, Marshall wrote that according to Koch's criteria, the standard method for proving that a given infectious agent causes a given disease, his germ had not been demonstrated to cause ulcer.

Important as it is to avoid overestimating the role of Helicobacter pylori in ulcer disease, it is equally vital to recognize a series of pitfalls that can lead to overestimating the role of stress.

For one thing, sick people like having explanations for their sickness, and stress is a popular one, especially when the disease is as notoriously "psychosomatic" as ulcer. Furthermore, being sick is in itself stressful. Ulcer patients have been consistently found to be more anxious, depressed, and hostile than control groups. But having constant stomach pain could itself lead to anxiety, depression, and irritability, so the psychological characteristics could result from the disease instead of the other way around.

Socioeconomic status constitutes a special pitfall in ulcer research. The poor are particularly likely to have ulcers, both because Helicobacter pylori infection is rampant in conditions of crowding and inferior hygiene, and because heavy physical labor increases ulcer risk. Since the poor are also particularly likely to have stressful lives, a study which looks at the general population is likely to show an artifactually strong association between stress and ulcer.

#### How ulcers develop

To understand the role of psychological factors it is useful to review a few medical facts. An ulcer (sometimes called "peptic" after pepsin, an enzyme found in gastric juices) is an open sore where stomach acid has eaten its way into the lining of either the stomach itself or the duodenal bulb, located where the stomach ends and the intestine begins. Ulcers don't ordinarily occur lower down in the intestine, because bicarbonate pours into the mix just inches past the bulb, and neutralizes the stomach acid.

In a way it's a miracle we don't all have ulcers. Glands inside the stomach are constantly churning out hydrochloric acid, which gets the process of digestion going by reducing the food we've eaten to pulp. When a hungry person smells a juicy steak, the acidity of the stomach contents can be ten times stronger than vinegar.

So why doesn't that same acid reduce the stomach itself to pulp?

One answer is that the entire gastrointestinal tube is coated with a thin layer of protective mucus. A second answer is buffering of acid by food: stomach acidity hits its peak as we start eating, but the acid starts to be neutralized by the first chewed-up bite as soon as it emerges from the far end of the esophagus.

Under ordinary circumstances there is a nice balance between acid production on the one side and protective forces like mucus and food on the other, so the lining of stomach and the duodenum remains intact. Ulcer-promoting factors throw off that balance either by increasing gastric acid or by decreasing the protective forces.

*Helicobacter pylori* disturbs the balance chiefly by degrading the quality of the protective mucus. Cigarette smoking and having type O blood help *Helicobacter pylori* to do its damage; they do not seem to cause ulcers in people who are not infected. Nonsteroidal antiinflammatory drugs such as aspirin or ibuprofen, the chief causes of non-*Helicobacter* ulcers, also degrade the mucus defenses.

Other risk factors act by increasing the quantity of acid that ulcer-susceptible tissues are exposed to. A high level of pepsinogen in the blood, which runs in families, is associated with high rates of acid secretion, as is heavy physical labor. Abnormal gastric contractions can cause acid to stagnate at length in the stomach or to be dumped copiously into the duodenum. And skipping breakfast increases the contact between acid and the stomach and duodenal lining by prolonging the nighttime period when there is no unbuffering by food.

### Mechanisms of stress

So how do psychological factors promote ulcers? The classic explanation is that stress puts the lining of the upper gastrointestinal tract at risk by stimulating the stomach to secrete high levels of acid. This is correct as far as it goes, since acid production is in fact stimulated by stress in human beings (though, curiously, not in monkeys, our close animal relatives).

But other physiological mechanisms seem at least as important in the pathway between stress and ulcer formation. Stress decreases blood circulation in the gastrointestinal tract, rendering it more susceptible to damage, and it can also affect gastrointestinal contractions. Life stress is known to interfere with the process of wound healing, which may contribute to the poor prognosis of ulcers in patients who are chronically anxious or experiencing a particularly difficult period. Psychological factors may directly disrupt a long-standing equilibrium between *Helicobacter* and its host, both because *Helicobacter pylori* flourishes in the presence of high acid levels and, conceivably, by affecting immune defenses against *Helicobacter*.

Stress can also promote ulcer formation indirectly, by influencing behavior. Many behavioral patterns associated with life stress and psychological distress — heavy alcohol consumption, cigarette smoking, irregular eating habits, sleeplessness — are

also risk factors for ulcer. People also take more nonsteroidal antiinflammatory drugs when they are under stress, whether because they are getting more headaches or in the hope an aspirin will calm them down or help them sleep. These behavioral concomitants of stress are extremely important, explaining about half of the causative effect of stress on ulcers. It is therefore vital for health care workers to discuss food and sleep rhythms and substance use with ulcer patients, emphasizing the chain of causality from stress to unhealthy behavior patterns to disease.

Beyond such counseling around health risk behaviors, there does not seem to be a major place for psychologically-oriented interventions in the average patient with an ulcer. Modern medical therapy heals nearly all ulcers rapidly and easily, while chronic disease can almost always be avoided using *Helicobacter pylori* eradication therapy, early treatment of symptom recurrences, or in the worst case non-toxic maintenance regimens. The modest effect on ulcer symptoms from dynamically oriented individual psychotherapy or cognitive interventions hinted at in two clinical trials is dwarfed by the efficacy of modern medical therapy. In the one published head-to-head trial a psychologically-oriented intervention (group counseling) was significantly inferior to maintenance therapy with H<sub>2</sub>-receptor blockers, and was in fact indistinguishable from placebo. In yet another trial cognitive intervention was associated, disconcertingly, with significantly increased ulcer recurrence rates.

Mid-century medical lore held that hospitalization, by removing the ulcer patient from a stressful life situation, was in itself therapeutic. Recent confirmation that anxiety impedes ulcer healing lends credence to these older concepts, the weak results of published trials being due in large part to their enrolling unselected ulcer patients. Psychotherapy or cognitive-behavioral therapy may indeed have something to offer in the treatment of peptic ulcer, but only in a few highly-motivated patients with high perceived stress levels and resistant disease.

#### Past and future

Ulcers were uncommon in 19th century Europe and America but burgeoned after 1900, to the point that one out of eight people born around 1910 was destined for an ulcer. The ulcer epidemic happened to correspond with the rise of psychoanalysis and of psychosomatic medicine, whose proponents spotlighted the apparently overwhelming association of peptic ulcer with stress and the success of rest and relaxation in healing it. What was known at the time of ulcer physiology, which focussed chiefly on excess secretion of gastric acid, jibed perfectly with a psychosomatic cause.

Ironically, as the origins of peptic ulcer were becoming clear in the 1980's, the epidemic was already receding — probably because hygienic improvements were preventing children from acquiring *Helicobacter pylori* from older friends and family members. So concepts of peptic ulcer have changed radically: in the middle of the twentieth century it was a common and disabling disease, often required surgery, and was a model for the ability of psychological distress to cause disease. Fifty years later, ulcer is relatively uncommon, can usually be eliminated with a brief course of medication, and is a model for the ability of bacteria to cause unexpected damage.

It is tempting to take sides and consider the cause of ulcers either as stress or as *Helicobacter pylori*. The truth is more complex and more interesting: there is no single

culprit. Peptic ulcer results from the massed effect of various risk factors, with different combinations active in any individual patient. In the same way coronary artery disease has long been conceptualized in terms of risk factors, which include both high cholesterol and psychological stress. It is by now well-accepted that stress can influence heart attacks, angina pectoris, and sudden death, but this discovery has not prompted fruitless debates over whether psychological factors are “the cause” of heart disease. As the novelty of *Helicobacter pylori* wears off, the medical community is likely to arrive at a willingness to embrace the complexity of mind-body interactions in understanding the causation of peptic ulcer as well.

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