



Peptic Ulcers

What Are Peptic Ulcers?

The stomach, intestines, and digestive glands produce acid and various enzymes, including pepsin, that break down and digest the starch, fat, and protein in food. The stomach itself is composed mostly of protein and must be protected from the same acid and enzymes, or it too can be attacked and broken down. Ulcers develop when an imbalance occurs between the digestive juices used by the stomach to break down food and the various factors that protect the lining of the stomach and duodenum (the part of the small intestine that adjoins the stomach). A peptic ulcer is an open sore or raw area in the lining of the upper part of the small intestine (duodenal ulcer) or the stomach (gastric ulcer). They average between one-quarter to one-half inch in diameter. In the US, duodenal ulcers are three times more common than gastric ulcers.

The primary digestive juices, hydrochloric acid and pepsin, are powerful substances necessary for breaking food down for use by the body. Acid is always present in the stomach, but, except at meal times, in relatively small amounts. A common misbelief is that excess acid is solely responsible for producing ulcers. Hydrochloric acid, secreted in the stomach, does indeed play a part in the development of ulcers, but it is not the only culprit. Pepsin, the other major digestive fluid, is an enzyme that breaks down whatever proteins are presented to it, including, if exposed, the stomach's own tissues.

Acid output in patients with duodenal ulcers does tend to be higher than normal, but in those with gastric ulcers, acid production is usually normal or lower. Abnormally large amounts of acid secretion occur in rare situations, such as in the genetic condition known as Zollinger-Ellison syndrome, in which acid is stimulated by tumors located in the pancreas or duodenum. In order for pepsin and hydrochloric acid to cause damage to the stomach or duodenum, however, the stomach's defense system must be altered or damaged. The mucous layer, which coats the stomach and duodenum, forms the first line of defense against acid and pepsin. In addition, the body secretes bicarbonate into the mucous layer, which neutralizes the acid. So while the contents of the stomach may be highly acidic, the stomach's own tissues are normally only



slightly acidic. Other factors in the defense system of the intestinal tract are hormone-like substances known as prostaglandins, which help keep the blood vessels in the stomach dilated, ensuring good blood flow and protecting against injury. Prostaglandins are also believed to stimulate bicarbonate and mucus production. If any of these defense mechanisms are disturbed, and acid and pepsin are allowed to attack the stomach lining, an ulcer can result.

What Causes Peptic Ulcers?

Helicobacter Pylori (H. Pylori)

Most healthcare consumers are still unaware that the major cause of peptic ulcers is the bacteria *Helicobacter (H.) pylori*. Before the discovery of *H. pylori*, the stomach was believed to be a sterile environment. The bacteria is seen as a major cause of or strongly associated with active chronic gastritis (inflammation of the stomach), active chronic duodenitis (inflammation of the duodenum), duodenal ulcers, and gastric ulceration. The bacterium is also strongly linked to stomach (gastric) cancer. *H. pylori*'s corkscrew shape is able to penetrate the mucous membrane of the stomach and attach itself there, where it is capable of causing damage in many ways. It causes changes in the immune system that allows it to survive for a person's lifetime. It thrives in the highly acidic stomach by producing the enzyme urease, which, in turn, generates ammonia, which neutralizes the acid and ensures the survival of the bacteria. *H. pylori* also produces a number of toxins that cause inflammation and damage to the lining.

Early studies reported that *H. pylori* is present in 90% of people with duodenal ulcers and in about 80% of people with gastric ulcers. As more people are being tested and treated for the bacteria, however, some studies suggest that the bacteria may be less prevalent than commonly thought. One study reported that 50% or less of duodenal ulcer patients harbored the bacteria. The risk was higher in African-American patients than in white patients. It should also be noted that *H. pylori* is found in about 25% of people who do not have peptic ulcers. The magnitude of *H. pylori* infection particularly in older people may not always predict the presence or absence of peptic ulcers. Other variables, then, must be present to actually trigger ulcers, such as chronic stress, genetics, or other factors (eg., possibly coffee-drinking) that increase susceptibility to the



organism. Some people harbor a particularly virulent genetic strain of *H. pylori* known as cytotoxin-associated gene A (cagA). CagA is strongly associated with damage severe enough to produce precancerous changes over time, although the gene varies widely among different populations. A cagA subtype called vacA (vacuolating cytotoxin) is also under investigation. Research is underway to determine if tests that detect the existence of the cagA or vacA gene can identify *H. pylori* carriers who are predisposed to ulcers.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) is the second most common cause of ulcers. The most common NSAIDs are aspirin, ibuprofen (Advil), and naproxen (Aleve, Naprosyn), although many others are available. NSAIDs reduce pain and inflammation by blocking an enzyme called cyclooxygenase (COX), which is involved in the production of prostaglandins. An excess of prostaglandins causes intestinal contractions and inflammation. Because NSAIDs reduce prostaglandins, they relieve pain, but, in doing so, they also impair the defense system in the intestine and increase the danger of damaging the mucous layer and causing ulcers and gastrointestinal bleeding. Even if an NSAID is injected intravenously the drug will still reach the stomach and duodenum through the bloodstream and inhibit prostaglandins. An ulcer will form if an NSAID is taken for a long period of time and the rate of damage inflicted by the drug exceeds the rate of repair conducted by the stomach. One study indicated that taking NSAIDs for only six months posed a risk for symptomatic ulcers that was greater than 1%. Regular use of even over-the-counter NSAIDs may be hazardous for anyone. The risk for bleeding is continuous for as long as a patient is on these drugs and may even persist for about a year after taking them. Taking short courses of NSAIDs for temporary pain relief should not cause major problems because the stomach has time to recover and repair any damage that has occurred. In people with existing ulcers, particularly gastric ulcers, however, even short-term use might increase the risk of bleeding. No NSAIDs should be used for long-term pain relief except under physician direction.



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One medical center reported that between 50% and 80% of people who were hospitalized for gastrointestinal problems were taking NSAIDs. The elderly are at particular risk as are people who abuse alcohol. One study reported that those who took NSAIDs for rheumatoid arthritis had a higher risk for bleeding than patients who take them for osteoarthritis, but another found no difference. It is not yet known whether people who take NSAIDs and are infected with the H. Pylori bacteria face a significantly higher risk of ulceration than those with only one of these factors. The stomachs of younger, nonsmoking adults appear to adapt better to NSAIDs and have less risk for bleeding than those of older adults, particularly those who smoke.

One study ranked the sixteen most commonly used NSAIDs according to risk for ulcers and bleeding. Those at lowest risk were nabumetone (Relafen), etodolac (Lodine), salsalate, and sulindac (Clinoril). At medium risk were diclofenac (Voltaren), ibuprofen (Motrin, Advil, Nuprin, Rufen), aspirin, naproxen (Aleve, Naprosyn, Naprelan, Anaprox), and tolmetin (Tolectin). Drugs within this group, however, vary in risk. Studies show, for example, that short-term use of naproxen is twice as likely as ibuprofen to be associated with hospitalization from GI bleeding. Although ketoprofen (Actron, Orudis KT) was considered a medium-risk drug, another study reported that even one week of taking the drug at low doses causes significant GI injury. The highest risk for GI bleeding were flurbiprofen (Ansaid), piroxicam (Feldene), fenoprofen, indomethacin (Indocin), meclofenamate (Meclomen), and oxaprozin. Others not compared in this analysis were diflunisal (Dolobid), and ketorolac (Toradol). Buffered aspirin (coated with an antacid) is not protective against ulcers.

Zollinger-Ellison Syndrome

The third, and least common, major cause of peptic ulcer disease is the Zollinger-Ellison syndrome. In this condition, a tumor in the pancreas produces excessive amounts of gastrin, a hormone that stimulates gastric acid formation.



Other Causes

Rarely, other conditions may cause ulceration in the stomach or intestine, including radiation treatments, bacterial or viral infections, alcohol abuse, and physical injury or burns.

What Are The Symptoms Of Peptic Ulcers?

Dyspepsia and Other Symptoms of Peptic Ulcers

The most common symptoms of peptic ulcers are known collectively as dyspepsia, and they encompass a variety of problems in the upper abdomen, including pain, discomfort, bloating, fullness, nausea, heartburn, regurgitation, and belching. Dyspepsia may be persistent or recurrent. Pain can be either localized in one place or diffuse. It may be described as burning, gnawing, or aching in the upper abdomen or, in some cases, as a stabbing pain penetrating through the width of the gut. Sometimes pain radiates to the back or to the chest behind the breastbone where it seems like heartburn. Symptoms usually occur one to three hours after a meal and can include dyspepsia or even hunger and a feeling of being empty. Eating a meal usually relieves the pain of a duodenal ulcer but does not relieve pain from gastric ulcers and may even worsen them. Vomiting may relieve symptoms. Peptic ulcer disease can also occur with only a feeling of indigestion or mild nausea or even without dyspepsia or other symptoms at all, especially when they are caused by NSAIDs. Because ulcers can cause chronic and hidden bleeding, patients may experience the symptoms of anemia, including fatigue and shortness of breath.

Emergency Symptoms

A sudden onset of symptoms, such as severe abdominal pain even without vomiting or external bleeding, may indicate perforation and emergency conditions. Tarry, black or bloody stools, vomiting of blood, or vomiting of a substance with the appearance of coffee grounds could be the sign of a serious hemorrhage. Persons who experience any of these symptoms should go to the emergency room immediately.



Other Conditions that Cause Dyspepsia and Symptoms of Ulcers

Dyspepsia occurs in 20% to 40% of people who live in industrialized nations and the majority of these people do not have ulcers. Physicians refer to most of these cases as non-ulcer, or functional, dyspepsia. Such symptoms may also occur with gastroesophageal reflux disease, gastritis, or with stomach cancer.

How Serious Are Peptic Ulcers And H. Pylori?

Impaired Quality of Life

For most people with severe ulcers, the most significant problem is pain and sleeplessness, which can have a dramatic and adverse impact on the quality of life.

Bleeding and Perforation

Although peptic ulcers are rarely lethal, the disease can be very serious if it progresses to the point of hemorrhage or perforation of the stomach or duodenum. Of the people who get ulcers, up to 15% will experience some degree of bleeding. Fortunately, the incidence is declining with the introduction of effective treatments, but it is still one of the most common medical emergencies. Bleeding is more apt to occur with ulcers caused by nonsteroidal anti-inflammatory drugs (NSAIDs) than those caused by the bacteria *H. pylori*. NSAIDs cause bleeding in 1% to 2% of people who are taking them. NSAID-related stomach problems may be responsible for 60,000 hospital admissions and over 3,000 deaths each year in American patients. Because there are usually no symptoms until bleeding begins, physicians cannot predict which patients taking these drugs will develop bleeding, although elderly patients and those with serious conditions, such as congestive heart failure, are at greatest risk. The mortality rate for bleeding peptic ulcers is about 10%. The risk for a poor outcome is increased by certain factors, including ongoing bleeding, abnormal blood-clotting tests, low systolic blood pressure, mental instability, and the presence of another serious, unstable medical condition.



Obstruction

Ulcers that form where the small intestine joins the stomach can swell and scar, resulting in a narrowing or closing of the intestinal opening. In such cases, a patient will vomit the entire contents of the stomach and emergency procedures are necessary.

Stomach Cancer

Between 30% and 90% of stomach, or gastric, cancers are linked to *H. pylori*, and people with stomach ulcers from the bacteria are at twice the risk for stomach cancer than those without such ulcers. Those with duodenal ulcers, however, appear to be at lower risk for stomach cancer. Some evidence exists that people who harbor the specific, virulent *H. pylori* genetic strain called *cagA* are at even higher risk for stomach cancer.

If *H. pylori* infects a child, by early adulthood the individual may develop a condition called atrophic gastritis, in which the stomach loses patches of glands that secrete protein and acid. New cells replace those destroyed but they do not produce enough acid to protect against carcinogens; over time, stomach cancer can develop. In developing countries where the rate of *H. pylori* in children is very high, the risk of stomach cancer is six times higher than in America. Onset of *H. pylori* infection in adulthood poses less of a risk, since the development of atrophic gastritis takes years and the patient is likely to die of other causes first. In the US, where *H. pylori* infects older individuals, less than 1% of people with *H. pylori* develop stomach cancer. (It should be noted that other factors, particularly diets low in fresh fruits and vegetables, might also influence the increased risk for stomach cancer reported in developing countries.)

Heart Disease

Some research had reported a very high rate of *H. pylori* infection in men with coronary artery disease, but more recent work has found no relationship between the bacteria and a risk for heart disease.



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Migraine Headaches

One study found an association between *H. pylori* and migraine headaches in people who also have gastrointestinal problems. Eliminating the bacteria reduced the frequency and intensity of migraines in half of these patients.

Who Gets Peptic Ulcers?

Peptic ulcer disease affects all age groups, including children, although it is rare in this population. Men have twice the risk for ulcers as women do. The risk for duodenal ulcers tends to occur first at around age 25 and continue until age 75; gastric ulcers peak in people between the ages of 55 and 65.

Risk Factors for *H. Pylori*

About 60% of Americans harbor *H. pylori* bacteria, and it occurs almost universally in people who live in crowded, unsanitary conditions. Almost 25% of children in the US and about half in developing countries harbor *H. pylori*. A minority, however, actually go on to develop ulcers caused by the bacteria, so other factors must be present to increase susceptibility.

The bacteria may be contagious, but little is yet known about its transmission. It is possible that young adults and children with the bacteria may be infectious, but many experts do not believe adults can easily transmit *H. pylori* to each other. It may be spread by sewage-contaminated water or by fecal-oral transmission (caused, for instance, by touching food with hands that weren't washed after a bowel movement). Some experts postulate that the common housefly may be an important agent in transmission.

Medical Conditions Requiring NSAIDs

Any condition that requires relief from persistent pain using NSAIDs increases the risk for ulcers. Such conditions include all forms of arthritis, chronic back pain, fibromyalgia, and many others.



As with *H. pylori*, however, not all people who take NSAIDs develop ulcers, and other factors are involved in susceptibility.

Factors that Increase Susceptibility to Ulcers

Genetic Factors. Genetic factors may be involved in increasing susceptibility to the effects of *H. pylori*. As examples, duodenal ulcers unrelated to NSAIDs seem to be two to three times more likely in relatives of people with ulcers, and identical twins have similar risks for developing ulcers. Genetic abnormalities might result in high levels of acid production, weaknesses in the mucosal layer, or production of abnormal nonprotective mucus. Inherited ulcers, however, are far less common than ulcers caused by NSAIDs or those associated with lifestyle factors that may increase a person's vulnerability to the ulcer-producing effects of *H. pylori*.

Caffeine, Cigarettes, and Alcohol. Coffee (both caffeinated and decaffeinated), soft drinks, and fruit juices with citric acid induce increased stomach acid production. Although no studies have proven that any of these drinks contribute to ulcers, consuming more than three cups of coffee per day may increase susceptibility to *H. pylori* infection.

Smoking increases acid secretion, reduces prostaglandin and bicarbonate production, and decreases mucosal blood flow. Results of studies on the actual effect of smoking on ulcers, however, are mixed. Some evidence suggests that smoking delays the healing of gastric and duodenal ulcers. One study reported that after ulcers healed, about half of nonsmokers relapsed after a year, but that all heavy smokers relapsed after three months. Other studies have found no increased risk for ulcers in smokers, and smoking does not appear to increase susceptibility to *H. pylori* or inhibit treatments for it. This should not give smokers any comfort, however, given the proven dangers from smoking.

Alcohol, too, has mixed reports. Some studies have shown that alcohol may actually protect against *H. pylori*. Drinking alcohol may, however, intensify the risk of bleeding in those who also take NSAIDs. In any case, everyone should avoid excessive use of alcohol.



Stress and Psychologic Factors. A host of studies have attempted to establish a correlation between the formation of ulcers and various types of occupations, stressful life events, lower educational or socioeconomic status, personality traits, and the ability to cope with stress, but most have found no causal relationship. Some experts believe, however, that the anecdotal relationship between stress and ulcers is so strong that attention to psychological factors is still warranted. It makes intuitive sense that stress probably plays some role in exacerbating or increasing susceptibility to peptic ulcer disease.

Blood Abnormalities. There seems to be an increased incidence of H-pylori caused ulcers in people who have Type O blood. In elderly people anemia may be a clue to the presence of an ulcer.

What Will Confirm The Diagnosis Of Peptic Ulcers?

Initial Approach for Patients with Dyspepsia

Medical and Family History. The physician will ask for a thorough report of their dyspepsia and other important symptoms, such as weight loss or fatigue, any present and past drug use (especially chronic use of NSAIDs), family members with ulcers, and drinking, and smoking habits.

Trial of Acid-Blocking Medication. Before proceeding to expensive and possibly needless testing in patients who are suffering a first attack of symptoms, physicians often recommend a four-week course of acid-suppressing medication. In such cases, the ulcer may heal. If symptoms persist, then further testing is needed.

Tests for Gastrointestinal (GI) Bleeding. The physician should administer a rectal exam and have other tests for GI bleeding performed, including a complete blood count and a fecal occult blood test (FOBT), which is used to detect hidden blood. (Blood in bowel movements is not always visible, in which case it is called occult blood.)



General Guidelines for Diagnostic Testing for H. Pylori

It is well established that H. pylori can be eradicated with antibiotics. Simple breath and blood tests can now detect H. pylori with a fairly high degree of accuracy. Endoscopy, an invasive test, however, allows a biopsy of stomach tissue and is the most accurate test for the bacteria.

Clinicians, however, still face many questions: which individuals should be tested for H. pylori, which tests should be performed, and, if patients are infected with H. pylori should they be treated for the bacteria without further evidence of ulcers. Many individuals harbor the bacteria, but it causes ulcers in only a minority of those infected. Expert guidelines recommend testing for H. pylori only for certain individuals with dyspepsia: those with strong indications for ulcers, such as clear or alarming symptoms (weight loss, anemia, or indications of bleeding), patients with a history of active ulcers, and individuals who have risk factors for stomach cancer or other complications from ulcers. Some experts argue that testing for H. pylori may be beneficial even if symptoms are strongly associated with NSAID use, since the presence of the bacteria may significantly increase the existing risk for ulcers in such people.

Non-invasive Tests for H. Pylori

Breath Test. A simple test called the carbon isotope-urea breath test (UBT) is significantly reducing the need for invasive diagnostic testing although it is more expensive than blood tests. In order to qualify it, a patient must be off all antibiotics and not have taken any Pepto Bismol for one month before the test. The patient must also not eat or drink six hours before taking it. The patient is asked to swallow a special fluid or capsule containing urea that has been treated with carbon atoms. H. pylori, if present, converts the urea into carbon dioxide, which is then exhaled by the patient into the device. This test is proving to be very accurate for both initial detection of the bacteria and for checking recurrence after antibiotic treatment, which should be performed at least four weeks after therapy. Studies have found that the test can identify 95% of people who have H. pylori.

Blood Tests. Blood tests are used to measure antibodies to H. pylori with results available in minutes; some are reporting accurate diagnosis of between 80% and 90%. The tests, however,



are not useful for treatment follow-up, since even after successful therapy antibody levels may drop, but they still remain in the bloodstream.

Other Tests for H. Pylori. Other tests are under investigation including a saliva test and one known as polymerase chain reaction (PCR) that uses cells from gums or stools and makes multiple copies of the DNA, or genetic material, of H. pylori until the bacteria is detectable.

Endoscopy

Endoscopy with biopsy is the most accurate procedure for detecting the presence of peptic ulcers, stomach cancer, and for diagnosing H. pylori, but it is invasive and expensive. It is, therefore, usually reserved for only certain patients with dyspepsia: those over 45 (when the risk for stomach cancer increases), people at all ages with risk factors for stomach cancer, and people who have unexplained weight loss, gastrointestinal bleeding, vomiting, difficulty in swallowing, or anemia. Endoscopy (also often called gastroscopy, the specific name for this procedure) may be performed either in a hospital or in a doctor's office. The physician administers a local anesthetic using an oral spray and an intravenous sedative to suppress the gag reflex and to relax the patient. The physician then places an endoscope (a thin, flexible plastic tube) into a patient's mouth and down the esophagus into the stomach. A tiny camera in the endoscope allows the physician to see the surface of the esophagus (food pipe), stomach, and duodenum and to search for abnormalities. The physician will take about ten small tissue samples (biopsies) which will be used to test for H. pylori. Some studies suggest that simply testing the gastric juices obtained using endoscopy can detect H. pylori infection. The bacteria are likely to be present in over 90% of patients with high levels of urease, the enzyme produced by H. pylori.

Upper GI Series

The upper GI (gastrointestinal) series was the standard diagnostic method for peptic ulcers until the introduction of adequate tests for detecting H. pylori. The patient drinks a solution containing barium. Then x-rays are taken, which may reveal inflammation, active ulcer craters, or



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deformities and scarring due to previous ulcers. Endoscopy is more accurate, although more invasive and expensive.

Other Laboratory Tests

Stool tests may show traces of blood that are not visible, and blood tests may reveal anemia in those who have bleeding ulcers. If Zollinger-Ellison syndrome is suspected, blood levels of gastrin should be measured.

What Are The Treatments For Peptic Ulcers Caused By H. Pylori?

General Guidelines for Combination Therapy for the Eradication of H. pylori

Candidates for Antibiotic Treatment. Antibiotic regimens that eradicate H. pylori are now known to cure ulcers and reduce the risk for both peptic and duodenal ulcer bleeding. One computer analysis even suggests that eliminating H. pylori infection could significantly increase the lifespan of certain individuals with peptic ulcers, such as younger adults. Unfortunately, a 1998 report suggests that as many as two thirds of individuals with dyspepsia never seek medical care, and, as of 1997 about half of physicians were still giving patients with ulcer symptoms acid-blocking drugs without even testing for H. pylori.

Antibiotics are clearly indicated for patients with strong evidence, particularly from endoscopy, for both ulcers and H. pylori. Some experts even recommend antibiotics for patients who have dyspepsia and evidence of H. pylori from blood or breath tests even if the presence of ulcers has not been confirmed. Many believe that persistent dyspepsia is such a strong risk factor for ulcers that eliminating the bacteria in infected people may not only prevent them in many people but also lower the risk for stomach cancer. Studies report, in fact, that when patients with non-ulcer dyspepsia and H. pylori are treated only with the acid suppressor omeprazole and not antibiotics, acid secretion is reduced to such an extent that the intestinal tract might become very susceptible to intestinal infections and precancerous changes. Studies have been conflicting, however, over whether antibiotic treatments in cases of non-ulcer dyspepsia offer any significant relief compared to acid suppressors. Many physicians are also concerned that treating infected patients



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when there is no clear evidence of ulcers will lead to unnecessary prescriptions and increase the risk for the development of bacteria that are resistant to antibiotics.

Drug Regimen

At least five effective drug combinations are being used with success rates as high as 90% although cost varies widely. The best results are achieved using two antibiotics and a drug called a proton pump inhibitor, usually omeprazole (Prilosec), which suppresses acid production. A typical triple-drug regimen consists of omeprazole, clarithromycin (Biaxin), and amoxicillin. Other effective regimens substitute metronidazole (Flagyl) for clarithromycin or amoxicillin. (*H. pylori* resistance to metronidazole is increasing, however.) Such three-drug regimens are well tolerated and effective, but very expensive. A less costly three-drug regimen using omeprazole, Bismuth (Pepto-Bismol), and tetracycline may be a good alternative, although it is less effective, side effects can be very distressing, and many patients cannot tolerate it. Another regimen uses Biaxin and a newly developed drug that combines ranitidine with bismuth citrate (Tritec). Two-drug regimens are being developed that use omeprazole and one antibiotic or two antibiotics. So far, they are slightly less effective than taking three drugs but are still more effective and less expensive than acid-blocking therapies that treat only symptoms. Most regimens need to be taken for at least 14 days; only the three-drug combination Prilosec, Biaxin and Flagyl requires just seven days, and, in one study, taking this combination for even only three days appeared to be effective. [For descriptions of these drugs, see [What Are the Specific Drugs Used for Peptic Ulcers?](#) below .]

Side Effects and Noncompliance .

Although antibiotic treatment is very effective against both gastric and duodenal ulcers, patient compliance is poor. The triple-drug regimens are complicated and require many pills a day. Side effects from one or more of these drugs occur in up to 30% of patients. Cases of severe diarrhea have occurred during treatment. One study indicates that the long-term side effects of treatment



include weight gain. Eliminating the bacteria also may increase risk for gastroesophageal reflux esophagitis (a cause of severe heartburn).

Follow-up and Success

Cure rates after antibiotic treatments range from 70% to 90%. Symptom relief after treatment does not always indicate success, nor, on the other hand, does persistence of dyspepsia necessarily mean that treatment has failed. Follow-up testing for the bacterial should be conducted no sooner than four weeks after therapy. (Test results before that time may not be accurate.) Studies are indicating that, at least in developed countries, once the bacteria is eliminated, ulcers recur at an annual rate of less than 10%. (Reinfection with the bacteria may be possible, particularly in areas where the incidence of *H. pylori* is very high and sanitary conditions are poor.)

Other Treatments for Ulcers Caused by *H. Pylori*

Elderly patients with ulcers caused by *H. pylori* but who cannot tolerate the side effects of the antibiotic therapy may continue to benefit from H₂ blockers, the older treatment for peptic ulcers. Some experts recommend H₂ blockers for people who test positive for *H. pylori* but have symptoms only of dyspepsia and no sign of peptic ulcers. Their argument is based on reducing costs; young people who meet this criteria but who have other risk factors for ulcers should discuss options with their physician. Some researchers are also concerned that eradicating *H. Pylori* may not be effective against bleeding episodes from existing ulcers and that H₂ blockers will remain important for treating this condition. By decreasing acid production, the body has the opportunity to heal itself. H₂ blockers temporarily heal up to 95% of ulcers after eight weeks, but they do not prevent recurrence of ulcers. One study, for example, showed that long-term therapy with the H₂ blocker ranitidine (Zantac) significantly prevented recurring bleeding in people who had experienced severe hemorrhaging from non-NSAID-induced ulcers. [For information on H₂ blockers see [What Are the Specific Drugs Used for Peptic Ulcers?](#) below.]



What Are Preventive Measures For Peptic Ulcers Caused By Nsaids?

Proton Pump Inhibitors

Taking a proton pump inhibitor, such as omeprazole (Prilosec), in combination with long-term NSAIDs may prevent the development of ulcers. [See What Are the Specific Drugs Used for Peptic Ulcers, below.]

Antibiotics for H. Pylori-Infected NSAID Users

Considerable debate is underway on whether antibiotic treatments should be used for individuals who are infected with H. pylori and require long-term NSAIDs. There is some evidence that such people are at even greater risk for ulcers than individuals who have these conditions independently and that the use of antibiotics may cut their risk for ulcers by half. Other studies, however, have found no association and, indeed, one analysis of studies indicated that that H. pylori infection had a protective effect against NSAID-induced gastric, but not duodenal, ulcers. More research is needed. At this time experts do not recommend testing NSAID users for H. pylori.

Alternatives to NSAIDs

COX-2 Inhibitors. Aspirin-like drugs, including celecoxib (Celebra) and rofecoxib (Vioxx), called COX-2 inhibitors target a specific prostaglandin-producing enzyme called cyclooxygenase 2 (COX-2) without affecting COX-1, an enzyme that generates stomach-protective prostaglandins and which NSAIDs block. Both drugs are effective pain relievers for chronic arthritic pain. Vioxx only needs to be taken once a day. One study suggested Vioxx was more effective in relieving acute pain than Celebra, but the results may have been due to the use of higher doses in the Vioxx group. Research is strongly indicating that COX-2 inhibitors may allow high doses to relieve pain without incurring the same risk as NSAIDs have for ulcers and bleeding. Long-term side effects are still unknown. Early reports cite an increased risk in bleeding in patients who are also on anticoagulant drugs. Of some interest and concern is a study on rats that indicated that COX-2 had a late protective effect against lung inflammation after 48 hours. The study suggests that the agents that block COX-2 may not be beneficial over the long



term, although studies are needed to determine if these same effects occur in joint tissue of humans.

Arthrotec. A combination of the NSAID diclofenac and misoprostol (Arthrotec) has now been approved that may reduce the risk for gastrointestinal bleeding. One study found that patients taking Arthrotec had 65% to 80% fewer ulcers than those who took NSAIDs alone.

Acetaminophen. Acetaminophen (Tylenol, Anacin-3, Panadal, Phenaphen, Valadol, and other brands) is the most common alternative to NSAIDs, although many patients report less pain relief with acetaminophen than with an NSAID; acetaminophen is not an anti-inflammatory agent. Acetaminophen can be used alone or in combination with NSAIDs with some success. Liver and kidney damage are potential serious side effects of acetaminophen. Alcohol use with acetaminophen increases the risk for liver damage. Experts recommend taking no more than eight extra-strength tablets each day.

NO-NSAIDS. Experimental agents are being developed that combine nitric oxide with NSAIDs (NO-NSAIDs). Nitric oxide increases blood flow in the mucous lining and secretions of mucus and bicarbonate. Combining nitric oxide with NSAIDs may provide benefits similar to the COX-2 Inhibitors.

What Are The Specific Drugs Used For Peptic Ulcers From All Causes?

Antacids

Many antacids are available without prescription and are the first drugs recommended to relieve heartburn and mild dyspepsia. They are best used alone for relief of occasional and unpredictable episodes of heartburn. All of the many brands available rely on various combinations of three basic ingredients and work by neutralizing the acid in the stomach. It has recently been suggested that they may also stimulate the defensive processes of the stomach, causing increases in bicarbonate and mucus secretion. There are three basic salts used in various antacids: magnesium, calcium, and aluminum. Magnesium salts are available in the form of magnesium carbonate,



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magnesium trisilicate, and, most commonly, magnesium hydroxide (Milk of Magnesia). The major side effect of magnesium salts is diarrhea. Calcium carbonate (Tums, Titralac, and Alka-2) is a potent and rapid-acting antacid. It can cause constipation. There have been rare cases of hypercalcemia (elevated levels of calcium in the blood) in people taking calcium carbonate for long periods of time. This can lead to kidney failure and is very dangerous. None of the other antacids have this side effect. The most common side effect of antacids containing aluminum salts (Amphogel, Alternagel) is constipation. People who take large amounts of antacids that contain aluminum may also be at risk for calcium loss and osteoporosis. Long-term use also increases the risk for kidney stones. People who have recently experienced GI bleeding should not use aluminum salts if possible. Maalox and Mylanta are combinations of aluminum and magnesium, which balances the side effects of diarrhea and constipation.

It is generally believed that liquid antacids work faster and are more potent than tablets, although some evidence suggests that both forms work equally well. Antacids can interact with a number of drugs in the intestines by reducing their absorption. These drugs include tetracycline, ciprofloxacin (Cipro), propranolol (Inderal), captopril (Capoten), and the H₂ blockers ranitidine (Zantac) and famotidine (Pepcid). These interactions can be avoided by taking these other drugs one hour before or three hours after taking the antacid. Conversely, some antacids, such as Maalox and Mylanta, increase the potency of certain drugs, including valproic acid, sulfonylureas, quinidine, and levodopa.

Antibiotics

For treating *H. pylori*, amoxicillin or tetracycline are effective drugs, and either can serve as a second antibiotic in a three-drug regimen. *H. pylori* is very sensitive to both. Amoxicillin can cause diarrhea and allergic reactions. Tetracycline may cause staining of the teeth, which can be permanent in children. It should not be given to pregnant women. Clarithromycin (Biaxin) is an antibiotic that is similar to erythromycin but more effective against *H. pylori*. It causes changes in taste that might be unpleasant and is the most expensive of the antibiotics used against *H.*



pylori . Resistance to this drug is already between 2% and 3% and researchers fear that this rate will increase as usage against H. pylori increases. Ciprofloxacin (Cipro) is another potentially effective antibiotic. Antibiotics may also be useful for patients infected with H. pylori who have duodenal ulcers caused by NSAIDs. Patients who harbor the bacteria and who have stomach ulcers caused by NSAIDs, however, do not appear to derive any additional benefit from antibiotics.

Bismuth

Compounds that contain bismuth are often used in the three-drug antibiotic regimens. They destroy the cell walls of the H. pylori bacteria and are an effective addition to the regimen. The only available bismuth compound available in the US has been bismuth subsalicylate (Pepto-Bismol), although a drug combination of the H₂ blocker ranitidine and bismuth citrate (Tritec) has been released. High doses can cause vomiting and depression of the central nervous system, although the doses given for ulcer patients rarely cause side effects.

H2 Blockers

H₂ blockers block or antagonize the actions of histamine, a chemical found in the body that encourages acid secretion in the stomach. H₂ blockers were the standard treatment for peptic ulcers until the development of antibiotic regimens against H. pylori . They cannot cure or prevent ulcers, however. Nevertheless, at least some of these drugs still may have value for preventing and treating ulcers caused by NSAIDs. Four H₂ blockers are currently available over the counter in the US: famotidine (Pepcid AC), cimetidine (Tagamet), ranitidine (Zantac), and nizatidine (Axid). All have good safety profiles and few side effects .

Famotidine (Pepcid AC) is the most potent H₂ blocker and the only one to date found to be effective at all for NSAID-induced ulcers. (H₂ blockers in general may actually mask the symptoms of ulcers in people who take NSAIDs.) The most common side effect of famotidine is headache, which occurs in 4.7% of people who take it. Famotidine is virtually free of drug interactions. A trial of NSAID-users who took 40 mg of famotidine (Pepcid AC) twice a day



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reported that only 8% of patients taking the drug developed stomach ulcers and 2% developed duodenal ulcers, while 20% of patients who did not take famotidine developed stomach ulcers and 13% duodenal ulcers. In one study of NSAID-users who had existing ulcers, the ulcers healed in 82% of patients who took famotidine, even though they continued taking the NSAIDs. After six months, the ulcers had recurred in only 25% of the patients who took famotidine compared to recurrence in over half of those who did not. It is not known whether the drug is effective in people whose ulcers have developed to the point that they are causing symptoms. Some experts are concerned that although famotidine appears to prevent and perhaps even heal ulcers, the use of acid-blocking drugs may actually increase the risk for serious complications including perforation, internal bleeding, and possibly even stomach cancer. In cases of patients taking NSAIDs for long periods, some experts advise acid-blocking drugs only for those who are at risk for ulcers (eg., if they have a history of ulcers, are over 70, or are also taking corticosteroids).

The other common acid blockers, ranitidine, cimetidine, and nizatidine, have not been proven to be very effective for NSAID-induced ulcers. Still, they heal (not cure) ulcers caused by *H. pylori* and may be helpful for those who fail antibiotic treatment. Cimetidine (Tagamet), the first H₂ blocker, was one of the widest-selling drugs in the world. It has few side effects; approximately 1% of people taking cimetidine will experience mild temporary diarrhea, dizziness, rash, or headache. Because cimetidine interacts with a number of commonly used medications such as phenytoin, theophylline, and warfarin, however, patients should always inform the physician of any drugs they are taking. Long term use of excessive doses (more than 3 grams a day) of cimetidine may also cause impotence or breast enlargement in men; these problems resolve after the drug is discontinued. Ranitidine (Zantac) was the second H₂ blocker to be introduced. Ranitidine's advantage over cimetidine is that it interacts with very few drugs. Even so, the physician must always be aware of any other drugs a patient is taking. In a recent study, ranitidine provided more pain relief and healed ulcers more quickly than cimetidine in people under 60 years old, but there was no difference in older patients. A common side effect



associated with ranitidine is headache, which occurs in about 3% of the people who take it. Nizatidine (Axid) is the latest H₂ blocker and is nearly free of side effects and drug interactions.

Metronidazole

Metronidazole (Flagyl) was the mainstay in initial combination regimens for *H. pylori*, but resistance to the drug is very high (about 25% of *H. pylori* bacteria). Consuming alcohol while taking the drug can cause flushing and severe gastrointestinal problems, so should be avoided during therapy and for three days afterward.

Misoprostol

Misoprostol (Cytotec) increases prostaglandin levels in the stomach lining, thus conferring protection against the major intestinal toxicity of NSAIDs. Misoprostol can reduce formation of ulcers in the upper small intestine by two-thirds and in the stomach by three quarters. It does not neutralize or reduce acid, however, and so, although the drug is used for preventing NSAID-induced ulcers, it is not generally used to heal existing ulcers. Diarrhea and other gastrointestinal problems are side effects that are severe enough to cause 20% of patients to stop taking the drug. Taking misoprostol after meals should minimize these effects; one study indicated that taking the drug two or three times a day instead of the standard regimen of four times may prove to be just as effective and cause fewer side effects. Misoprostol can induce abortion or cause birth defects and should not be taken by pregnant women. If pregnancy occurs during treatment, the drug should be discontinued at once and the physician contacted immediately.

Proton-Pump Inhibitors

Omeprazole (Prilosec), lansoprazole (Prevacid), and rabeprazole (Aciphex) are known as Proton-pump inhibitors. They work by inhibiting the so-called gastric acid pump that is required for the stomach's cells to secrete acid. They are very effective suppressers of acid production. Either drug can be used as part of the triple-drug regimen for *H. pylori*. These drugs do not eradicate the bacteria, but they reduce the acidity in the intestinal tract, thereby increasing the effectiveness of the bacteria-fighting drugs being used in the regimen. One study also reported that in people



whose ulcers were not cured by H. pylori therapy, lansoprazole helped maintain remission after temporary ulcer healing for more than a year.

Proton-pump inhibitors are proving to be very effective for NSAID-users who have large gastric ulcers. Taking omeprazole with NSAIDs can both heal and help prevent ulcers. In a comparison study between omeprazole and misoprostol, the two drugs were about equally effective in the short term, but after eight weeks of maintenance therapy, omeprazole was superior. It was also more effective than the H2 blocker ranitidine. It was not compared to famotidine, however, which is an H2 blocker with some proven effectiveness against NSAID-induced ulcers [see below].

Proton-pump inhibitors are also useful in the treatment of ulcers caused by Zollinger-Ellison syndrome.

Side effects are uncommon but may include an allergic reaction, headache, stomach pain, and diarrhea. Proton pump inhibitors should not be used unless necessary by pregnant women or nursing mothers, although recent studies suggest that they do not pose an increased risk of birth defects. There is some evidence that the use of proton-pump inhibitors in people with H. pylori reduces acid secretion to such extent that it causes a condition called chronic atrophic gastritis, in which protection against carcinogens in the stomach is impaired. Eradicating H. pylori should eliminate this risk, although if such precancerous changes already exist, the danger may persist. Of particular concern in this regard is the long term use proton-pump inhibitors to relieve symptoms in H. pylori -infected people with nonulcer dyspepsia, who are not given antibiotics because they do not have full-blown ulcers. This effect does not seem to occur in patients taking proton-pump inhibitors who are not infected with H. pylori , although one study indicated that taking them for a long period of time may pose a small risk for polyps in the upper part of the stomach.



Sucralfate

Sucralfate (Carafate) seems to work by adhering to the ulcer crater and protecting it from further damage by stomach acid and pepsin. It also promotes the defensive processes of the stomach. Through these dual mechanisms, sucralfate has proven to have a duodenal ulcer healing rate similar to that of H2 blockers. Other than constipation, which occurs in 2.2% of patients, the drug has few side effects. Sucralfate does interact with a wide variety of drugs, including warfarin, phenytoin, and tetracycline. It is not approved for gastric ulcers.

Vaccines and Experimental Treatments

There is some urgency in pursuing development of alternative treatments to antibiotics because strains of the bacteria are emerging that are resistant to many common antibiotics. Vaccines, including an oral form called Ora Vax, are showing promise in producing an immune response against *H. pylori* although availability is still years away.

Researchers have recently analyzed the entire genetic sequence of *H. pylori*. This means that eventually they may be able to develop drugs that block proteins that are essential for bacterial growth.

How Are Bleeding Ulcers Treated?

Approach to the Patient with Bleeding Ulcers

Bleeding stops spontaneously in about 70% to 80% of people with bleeding ulcers. For massive bleeding, fluid replacement is essential and blood transfusions may be required. Diagnosis is confirmed using endoscopy, which involves tubes that are passed down into the stomach.

Physicians are able to detect signs of bleeding that include active spurting or oozing blood from arteries, swollen but nonbleeding blood vessels, and nearby blood clots. Depending on the intensity of the bleeding, patients can be released from the hospital within a day or kept up to three days after endoscopy. Patients who have the *H. pylori* bacteria, even if NSAIDs caused the bleeding, should be treated with antibiotic therapy to eradicate the bacteria. People on NSAIDs should discontinue them if possible.



Surgical Treatment for Bleeding Ulcers

Those who show signs of continued or recurrent bleeding require immediate emergency treatment. About 30% of patients who come to the hospital for bleeding ulcers require endoscopy or other surgical procedures.

Endoscopy. Endoscopy is the procedure most often used for treating bleeding ulcers, although not everyone is a candidate, and some patients require more invasive surgery [see below]. Endoscopic treatment of bleeding generally involves using a probe passing through the endoscopic tube that applies electricity or heat to coagulate the blood and stop the bleeding. An injection of epinephrine (commonly known as adrenaline) directly into the ulcer increases the effectiveness of endoscopic treatments. In one study, bleeding recurred in only 8.7% of patients treated with epinephrine plus endoscopy; it should be noted that the procedure was performed by highly experienced physicians. (Other studies have reported 15% to 25% recurrence rates in patients given either the agent or the procedure as sole treatments.) Epinephrine plus a combination of blood clotting factors termed fibrin glue may prove to be even more effective. Between 15% and 20% of patients who have had endoscopy experience a recurrence of bleeding. Those at highest risk for bleeding recurrence are those with large or deep ulcers, severe clotting abnormalities, other serious medical conditions, very low blood pressure, or whose bleeding started after a patient was hospitalized. This may require major surgery, although repeat endoscopy performed by experienced doctors is proving to be effective. In one study repeat endoscopy successfully stopped further bleeding in 73% of patients; the others required surgery.

Major Surgery

Major surgery is now generally performed only when endoscopy is not appropriate. Before this procedure and the advent of antibiotic therapies for *H. pylori* , major surgery was often the primary treatment in patients with severe ulcers. Surgical procedures include vagotomy, which cuts the vagus nerve and interrupts messages from the brain to the stomach that stimulate acid secretion. This surgery may impair stomach emptying; a recent variation that cuts only parts of the nerve may reduce this complication. Antrectomy removes the lower part of the stomach that



manufactures the hormone responsible for stimulation of digestive juices. Pyloroplasty enlarges the opening into the small intestine so that stomach contents can pass into it more easily.

Antrectomy and pyloroplasty are usually performed with vagotomy. Surgery is not effective for upper GI ulceration caused by chronic NSAID use.

Medical Treatments for Bleeding Ulcers

Researchers are also looking for medical alternatives to surgery for bleeding ulcers. Intravenous administration of the proton-pump inhibitor omeprazole is now often used after endoscopy or certain surgeries to prevent recurrent bleeding. Somatostatin, a hormone used to prevent bleeding in people with cirrhosis, and a similar agent called octreotide (Sandostatin) have been found to reduce persistent peptic ulcer bleeding or the risk of recurrence. In one study, somatostatin was significantly more effective than either omeprazole or an H₂ blocker in preventing bleeding recurrence. Such drugs may also be useful for initial bleeding episodes if endoscopy is unsuccessful, inappropriate, or unavailable.

What Are Lifestyle Changes For Peptic Ulcers And Dyspepsia?

Diet

It was common in the past to restrict people suffering from peptic ulcers to frequent intake of small amounts of bland foods and milk. Exhaustive research conducted since then has shown that a bland diet is not effective in reducing the incidence or recurrence of ulcers, and that frequent small meals throughout the day are no more effective than consumption of three meals per day. (Large amounts of food should still be avoided because stretching or swelling of the stomach can result in painful symptoms.) Milk was found to actually encourage the production of acid in the stomach, although moderate amounts (two to three cups a day) can be drunk without harm. Coffee may increase susceptibility to *H. pylori*, and, in any case, cutting down on coffee (both decaf and caffeinated) and carbonated beverages may help reduce stomach acid.

The good news is that a diet rich in fiber may cut the risk of developing ulcers in half and speed healing of existing ones. Fiber found in fruits and vegetables is particularly protective; vitamin A contained in many of these foods may increase the benefit. In one study, apples and yams



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appeared to be especially helpful. Apples, celery, cranberries, onions, red wine, and green and black tea are also high in natural chemicals known as flavonoids, which appear to inhibit H. pylori growth and have many other health benefits.

Studies conducted on spices and peppers have yielded conflicting results. The rule of thumb is to use all these substances moderately, and to avoid them if they irritate the stomach.

Although no vitamins have been shown to protect against ulcers, H. pylori appears to impair absorption of vitamin C, which may play a role in the higher risk of stomach cancer.

Other Lifestyle Changes

Some evidence exists that exercise may help reduce the risk for ulcers. Stress relief programs have not been shown to promote ulcer healing, but they may have other health benefits.

Herbal Remedies

One well-conducted 1999 study indicated that an herbal preparation (Iberogast) combined with extracts from a bitter candy reduced dyspepsia in 82% of subjects compared to 39% who had taken a placebo. Other herbal remedies are marketed for dyspepsia but few have been seriously studied and no one should take any untested medication, even so-called natural ones, without consulting a physician.

Where Else Can Information About Peptic Ulcers Be Obtained?

National Digestive Diseases Information Clearinghouse, Two Information Way, Bethesda, MD 20892-3570. Call (301-654-3810) or on the Internet (<http://www.niddk.nih.gov/>). Offers patient information and educational materials.



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American Gastroenterological Association, American Digestive Health Foundation, 7910 Woodmont Avenue, 7th Floor, Bethesda, MD 20814. Call (301-654-2055 or toll-free 800-NO-ULCER) or on the Internet (<http://www.gastro.org>).

American Society for Gastrointestinal Endoscopy, 13 Elm Street, Manchester, MA 01944-1314. Call (978-526-8330), fax (978-526-8330) on the Internet (<http://www.asge.org/>)

Helicobacter Pylori Foundation, P.O. Box 7965, Charlottesville, VA 22906-7965. On the Internet (<http://www.helico.com/>). Includes FAQ's, links, and on-line discussion.

Centers for Disease Control and Prevention. Call toll-free (888-MY-ULCER) or on the Internet (<http://www.cdc.gov>). Their web site contains an excellent, searchable database of articles.

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