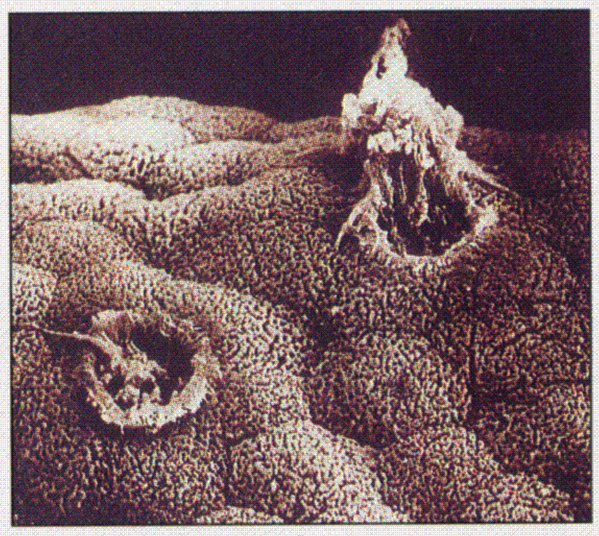
BODY

IN THE BELLY OF THE BUG:
Ulcer researchers report an unsuspected culprit that Americans can't stomach—bacteria

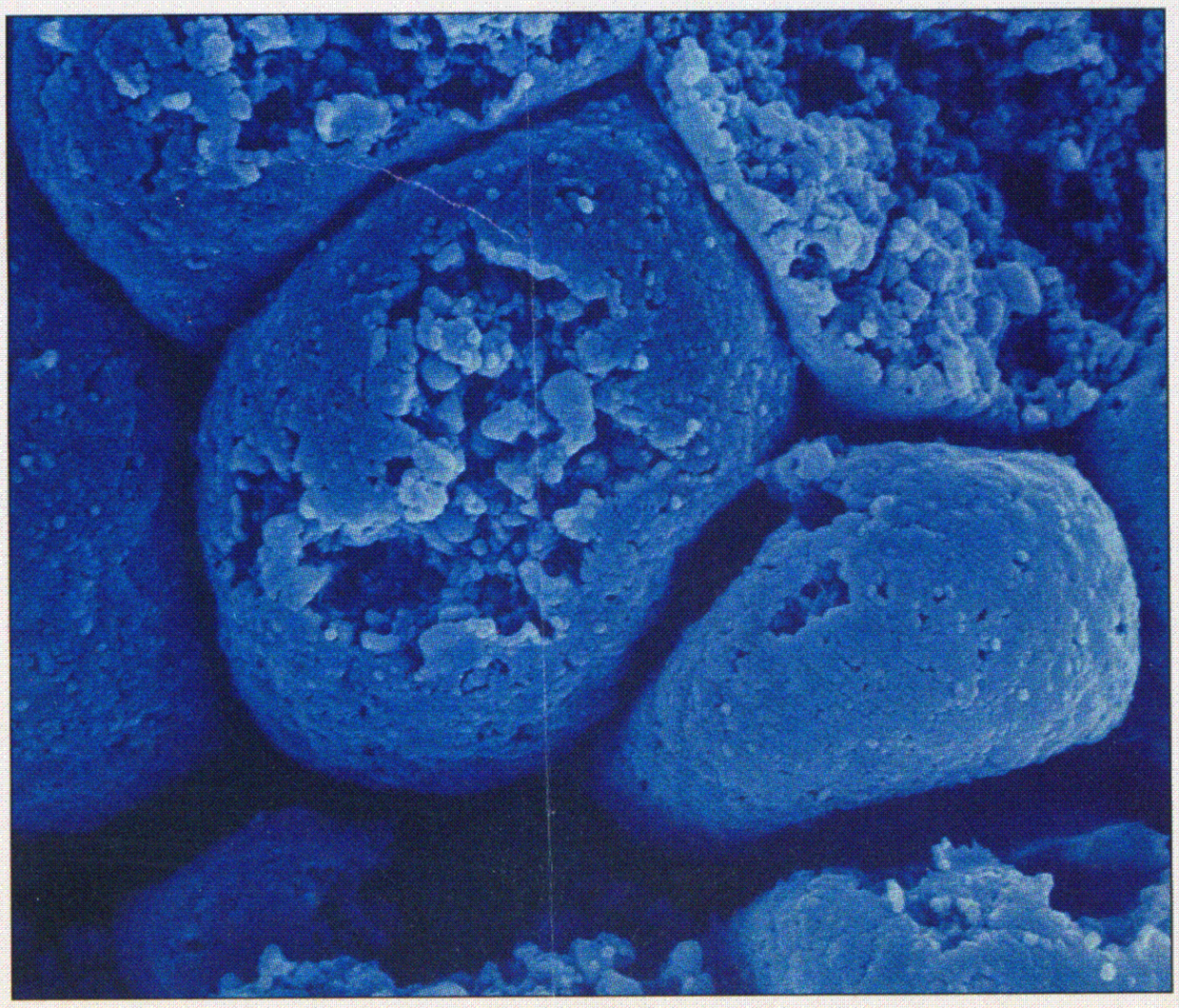
The co-worker you just saw bent over his desk in misery is more likely to be suffering from heartburn than heartache, and chances are the cause of his problem is a peptic ulcer. These painful irritations of the stomach's gastric lining and the duodenum (the entrance to the small intestine) strike 1 out of every 50 Americans each year. In 1987 alone the National Center for Health Statistics recorded a whopping 4,580,000 *new* cases of peptic ulcer.

Until recently doctors considered ulcers a life-style disease brought on by too much stress or excessive consumption of alcohol, coffee, spicy food, or even aspirin. Ulcer patients got lectures on changing their habits, along with prescriptions for widely heralded "miracle drugs" like Zantac and Tagamet, introduced a decade ago, which work by inhibiting the secretion of stomach acids to give ulcerous lesions a chance to heal. Because ulcers tend to recur, patients who relied on these drugs could generally expect to do so for a lifetime.

Researchers have now announced a startling discovery that could lead to an outright cure—rather than just a treatment—for ulcers. The most common cause of these stomach disturbances, they say, is a corkscrew-shaped microorganism called *Helicobacter pylori,* which burrows into the wall of the stomach, making victims susceptible to virtually any irritant. Once research determines the best protocol of antibiotic treatment, doctors should be able to cure ulcers within a few weeks of diagnosis. Further down the line some researchers envision vaccinating everyone against both gastritis and ulcers soon after birth.



Robin Warren, a pathologist at Royal Perth Hospital in western Australia, first spotted the germ in 1979 when he took stomach biopsies from patients with a variety of intestinal ailments. Colleagues greeted his discovery with skepticism, however: The standard wisdom held that the stomach was too acidic to support a resident microbe. No one took Warren very seriously until 1981, when Dr. Barry Marshall, a gastroenterologist now at the University of Virginia Medical Center in Charlottesville, confirmed the findings. Marshall isolated *Helicobacter* and showed that it shields itself from acid by invading the mucus sheathing the inside of the stomach. Once in place, the bug appears to trigger an inflammation of the lining characteristic of gastritis or, in severe cases, an erosion of the wall that develops into full-fledged ulcers. Clearly, *Helicobacter pylori* was not the only organism that could cause such trauma, but it did seem to be a leading suspect: Marshall extracted the germ from 90 percent of gastritis patients and 80 percent of those with ulcers.



Vaccinating babies against ulcers would ensure that a healthy stomach (top) stayed that way; an antibiotic cure can be expected soon for the treatment of ulcers (right).

Similar findings emerged from a large study conducted in Ireland in 1988 by Dr. Cornelius Dooley, now an assistant professor of medicine at the University of Southern California. Dooley found *Helicobacter* in 85 percent of patients with ulcers, 80 percent of those with gastritis, and 50 percent of those suffering from an inflammation of the esophagus.

While doctors gradually began to accept *Helicobacter*'s association with gastric disturbances, many believed that it was a cofactor rather than a cause. They argued that the organism might be an opportunist that had simply found an already weakened stom-

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ach an attractive site to colonize. It took an unorthodox demonstration to settle the matter. Marshall swallowed a batch of *Helicobacter*—and promptly came down with an acute case of gastritis. Biopsies showed that his stomach was infiltrated with the bacterium.

Although Marshall made a full recovery within two weeks, another doctor who volunteered his stomach to science was not so fortunate. Three years after consuming a *Helicobacter* culture, he still had a belly full of the bug. What finally cured him? A whopping dose of antibiotics and a lot of Pepto-Bismol.

The best strategy for eradicating the organism incorporates that time-honored remedy for digestive ills. As far back as 1915 doctors advocated salts of bismuth (the active ingredient in Pepto-Bismol) as a cure for upset stomachs. Although physicians eventually dropped the treatment, their patients continue to rely on it to this day. As it turns out, there's more to the soothing effect of Pepto-Bismol than the "protective coating action" cited in its ads: Salts of bismuth kill *Helicobacter.*

By itself, however, a salts of bismuth preparation can keep the organism in check only by temporarily reducing its numbers. To completely clear the gut usually requires a course of two antibiotics—tetracycline and metronidazole—taken over a two-week period.

Although compounds like Zantac and Tagamet, which reduce the acid content of the abdomen, promote recovery from ulcers, the relief is usually short-lived. The germ invariably flares up again. "Antacid drugs are a treatment, not a cure," says Marshall. "People often have to take these medications on and off for life." The advantage of the one-two combination of bismuth salts and antibiotics, he argues, is that it eliminates the disease at its roots, greatly reducing the likelihood of a relapse.

To prove his point, Marshall recruited 100 ulcer patients testing positive for the bug and randomly assigned them to two treatment groups. He reported the results in the December 1988 issue of the British medical journal *Lancet:* The group treated with bismuth–antibiotic therapy had an 80 percent cure rate a year later. In contrast, 15 percent of the group receiving only Tagamet were symptom-free after 12 months.

Don't expect your local physician to offer the antibiotic therapy anytime soon, however. For one thing, the only test for *Helicobacter* currently available requires passing a narrow tube called an endoscope through a patient's mouth and down his esophagus to obtain biopsies of stomach or intestinal tissue. And although blood tests and breath tests to detect *Helicobacter* exist, they're not expected to become commercially available for two years.

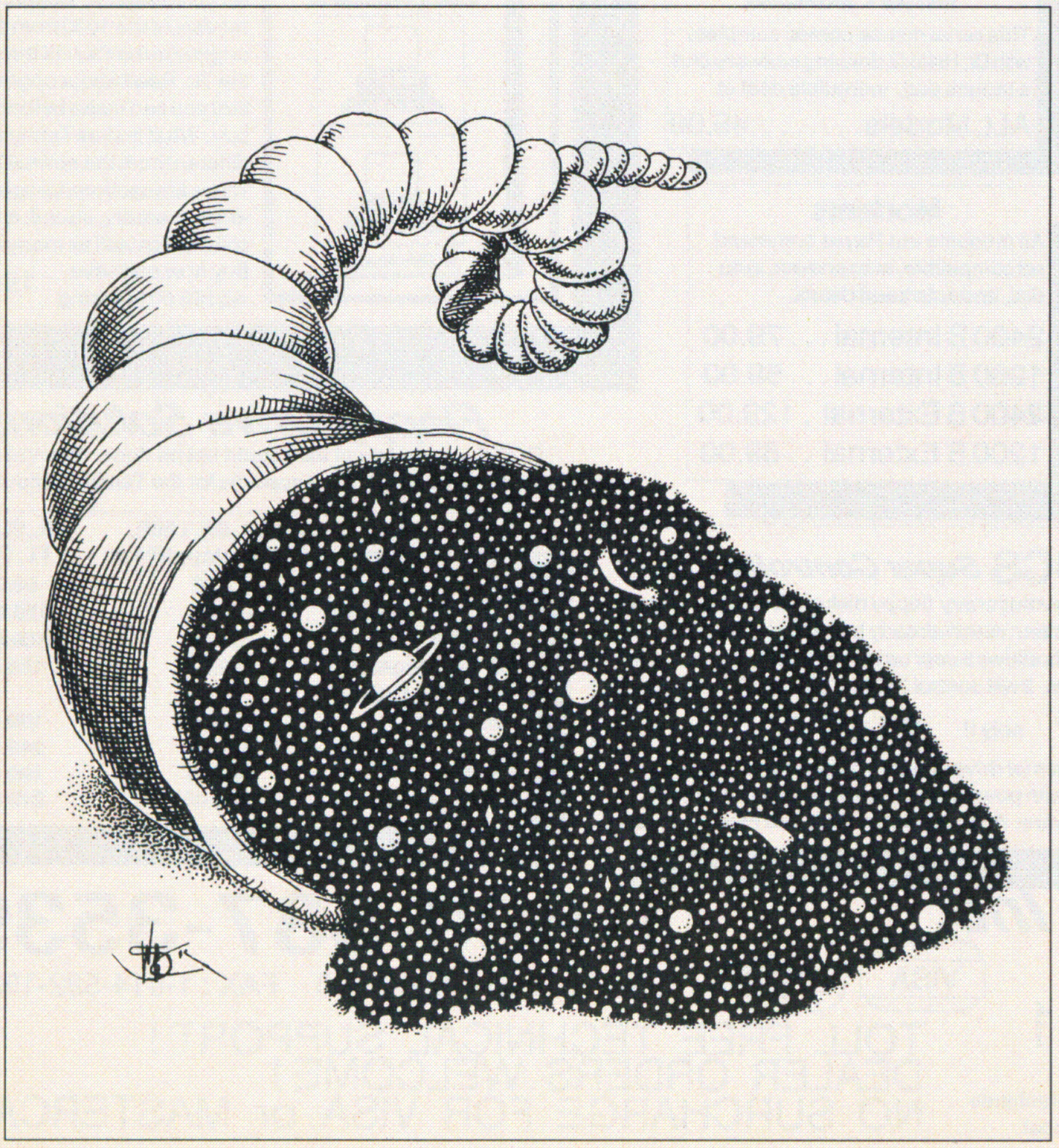
Furthermore, researchers are likely to face continued resistance from mainstream practitioners. "We've spent the last seventy years thinking that excess acid caused gastritis and ulcers," says Dr. James Barthel, assistant director of endoscopy at the University of Missouri School of Medicine in Columbia. "So the discovery of this germ is causing a tremendous upheaval in common medical thought."

The antibiotic approach is troubling to some physicians because it produces severe side effects—including nausea, vomiting, and diarrhea—in 30 percent of patients. "It's probably worth the risk of an adverse reaction if the ulcer or gastritis is severe and persistent," acknowledges Dooley. "But if symptoms are mild, patients should be forewarned that the cure may be worse than the disease." Yet another drawback of the treatment: It's not *always* effective. Although antibiotic-resistant strains of the bacteria account for many treatment failures, as-yet-unidentified factors also seem to play a role.

"Antibiotic therapy is still highly controversial," cautions Dr. David Graham, chief of digestive disease at Baylor College in Houston. "Until we have a proven, safe, and effective therapy to eradicate the infection I believe we should stick to treatments that already have a proven track record in helping patients." Graham says he is concerned that prescribing currently available antibiotic protocols to kill *Helicobacter* infections could backfire by ultimately making some strains resistant to more specific drugs on the horizon.

Undoubtedly, better antibiotics will soon be available. The sheer size of the ulcer market has made banishing the bug an extremely attractive research target. In the United States alone, 10 percent of the population will suffer from ulcers at some time in their adult lives, and many more will develop gastritis. "It's the most common infection in the world," says Marshall.

Fortunately, most people have such low-level infections that they never develop symptoms. But the germ clearly exacts a huge toll from aching bellies around the globe. "Once we have developed safer, more effective antibiotics against it," says Barthel, "the next step is to prevent ulcers and gastritis altogether. The ultimate goal may be to vaccinate everyone in infancy—just like we do for polio."—Kathleen McAuliffe



For more information about the process of testing for and treating Helicobacter pylori *infections, call the School of Medicine of the University of Virginia at (804) 924-9970.*