

Nobel Came After Years of Battling the System

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Published: October 11, 2005

When two Australian scientists set out in the early 1980's to prove that a bacterium, *Helicobacter pylori*, caused stomach inflammation and [ulcers](#), they met opposition from a medical-industrial complex entrenched in the belief that psychological stress was the cause.

Opposition to their radical thesis came from doctors with vested interests in treating ulcers and other stomach disorders as well as from drug companies that had come up with Tagamet, which blocked production of gastric acid and was becoming the first drug with \$1 billion annual sales.

Ulcer surgery was lucrative for surgeons who removed large portions of the stomach from patients with life-threatening bleeding and chronic symptoms. Psychiatrists and psychologists treated ulcer patients for stress.

The concept of curing ulcers with [antibiotics](#) seemed preposterous to doctors who had long been taught that the stomach was sterile and that no microbes could grow in the corrosive gastric juices.

A bacterial cause "was just too wild a theory for most people" to accept, and something so ingrained as stress causing ulcers was too difficult to dismiss, Dr. J. Robin Warren, one of two who won the 2005 Nobel Prize for Physiology or Medicine on Oct. 3, said in a telephone interview.

Blame focused on psychological stress in part because many patients had stressful lives and scientists lacked another explanation.

Also, Tagamet and similar drugs, known as H2 blockers, safely made ulcers and their symptoms disappear. But the H2 blockers were not one-shot cures. Ulcers often recurred, requiring repeated courses of the drugs, providing a steady stream of profits.

"The opposition we got from the drug industry was basically inertia," said Dr. Barry J. Marshall of the University of Western Australia, the other Nobel winner, and "because the makers of H2 blockers funded much of the ulcer research at the time, all they had to do was ignore the *Helicobacter* discovery."

"If the drug companies were truly into discovery, they would have gone straight after the *Helicobacter*," Dr. Marshall said, but they did not because of the success with H2 blockers.

"Had these drugs not existed, the drug companies would have jumped on our findings," he added.

Then, too, the fresh thinking was coming from what many doctors regarded as a medical outpost, Perth.

All the factors created a type of rigidity that many doctors say still exists for better or worse.

Further, Dr. Marshall said, "The fact that the big drug companies who were supporting the journal articles ignored H. pylori was far more effective than actually saying that a bacterial cause was not true because if they had said it was false, or not important, they would have created a controversy and maybe media interest."

Right from the moment in 1979 when Dr. Warren, a pathologist, first saw bacteria in stomach biopsies at the Royal Perth Hospital, he said: "I met skepticism from my colleagues who mostly did not want to know, or believe, what I was describing. Anyone could see the bacteria through a microscope, but the clinicians did not want to see them."

Why was he the only one seeing the bacteria? Why had others not described them earlier? He did not know, Dr. Warren said in answer to the skeptics who asked. "Once I started looking for them, they were obvious," he said, "but convincing other people was another matter."

Even doctors who peered down the barrel of a microscope and did agree bacteria were present said they must be opportunists, not the cause of stomach ailments.

Dr. Warren pointed out that the bacteria were all the same, not the variety that would be expected of secondary invaders. But, he said, "It was hard for me to prove them wrong."

Proof took years.

Early support came from Dr. Marshall's efforts in the library and laboratory. Aided by a librarian in Perth, Dr. Marshall painstakingly searched for papers published decades earlier than those listed in the United States National Library of Medicine's electronic data base that starts about 1965.

Although a few doctors had described the curved bacteria in the late 19th century, the findings were passed over in the hundreds of peer-reviewed articles published thereafter. Then Dr. Marshall performed a famous self-experiment in which he swallowed a culture of H. pylori, got sick, documented that he developed an inflamed stomach and was cured of the gastritis with an antibiotic.

Many critics took notice of the bacterium's dangers, Dr. Warren said.

As a practicing gastroenterologist, Dr. Marshall saw many patients go to surgery for ulcers and some die from internal bleeding.

His top priority was to determine which combinations of antibiotics cured ulcers. "There was a lot of urgency to publish data because" the medical world wanted convincing proof, Dr. Marshall said.

But many American researchers, he said, "seemed more interested in carefully studying the mechanism of how H. pylori produced stomach damage rather than driving straight in to treat people."

There were many reasons for the different tacks.

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Dr. Warren said that "the medical profession is brought up to be very careful with new findings, and that is probably a good thing for most patients because you have to be fairly careful with new findings or otherwise you may do something stupid."

A cardinal rule of medicine is: First, do no harm. Experience has taught that rushing to use a new therapy without the backing of findings from controlled trials can have serious, if not lethal, outcomes. One example was that freezing the stomach cured ulcers, when it sometimes resulted in dead tissue.

It can be hard for doctors, like others, to admit error. Sometimes the caution is excessive and it, too, can cost lives.

Dr. Alfred Sommer, the former dean of the Johns Hopkins Bloomberg School of Public Health, recalled how medical leaders in the 1980's rejected evidence that inexpensive vitamin A pills could prevent death from infections as well as blindness.

Now it is standard therapy.

Dr. Samuel Hellman, a former dean of the University of Chicago's Pritzker School of Medicine, said that doctors "often fall in love with a hypothesis, and that holds in my field, [cancer](#)."

Medicine's peer-review system for deciding what articles to publish and which grants taxpayers should support "discriminate against the truly inventive, exciting, far-out ideas, Dr. Hellman said.

Peer review "tends to adhere to things that are consistent with prevailing beliefs and models," he said, and "really new ideas usually just get thought of as crazy."

The National Institutes of Health, a federal agency, supports biomedical research at its campus in Bethesda, Md., and in medical schools and centers throughout the country and abroad. But, Dr. Hellman said, "innovation does not get funded at the N.I.H. right now because it can pay for only a very low percentage of approved grants."

When this reporter interviewed American medical leaders about the Australian findings in 1984, some dismissed them as unimportant because a bacterial cause of ulcers had not been discussed at recent national scientific meetings.

Reflecting on his road to the Nobel Prize, Dr. Marshall said: "In the 1970's and 1980's there was a bit of a mind-set that all the important stuff in medicine had been discovered.

"So maybe we started something that was more important than we thought because Helicobacter has opened people's minds to the possibility of an infectious cause of all those other diseases whose cause is unknown."