False Epistemologies: The Curious Case of *Helicobacter pylori* and Peptic Ulcer Disease

by Kelly Shaw
Anthropology / History

Faculty Mentor: Gautam Bhattacharyya, Chemistry
Faculty Mentor: James Mohr, History

If a theory is falsified, it is proven false; if it is 'falsified', it may well still be true. If we follow up this sort of 'falsification' by the actual 'elimination' of a theory, we may well end up by eliminating a true, and accepting a false, theory (a possibility which is thoroughly abhorrent to the old-fashioned justificationist).

Imre Lakatos
The Methodology of Scientific Research Programmes

The above quote by Lakatos predates the historical documentation of an incidence in the history of science in which the truth was passed over and the false was upheld. Lakatos predicted the occurrence of a false epistemology: an instance in which controversy raged over two facts, and the "false" fact was accepted by the scientific community while the "true" fact was denied importance. False epistemologies pose a problem for the continuation of the theoretical and technical growth of the sciences. Scientists often accept as unproblematic the facts and theories they use without understanding the history of how those facts and

theories were constructed or having in depth information about the empirical foundations supporting those facts and theories. As Bruno Latour (1987) has pointed out, the history of how and why certain facts and theories are accepted becomes silenced; they become black boxes with inputs and outputs. Black boxes may be used without knowing how or why the system inside of them works or understanding the history that produced them. If this occurs, whatever assumptions were built into the system are built into future research as well.

There is danger in science progressing this way. Scientists who accept without question the facts and theories handed down to them without any knowledge of how problems were solved may then base their research upon erroneous foundations. They may be convinced of a reality that does not exist. Everything built upon such a foundation is also false, and fallacies may be missed for a considerable amount of time.

This paper examines one instance of a false epistemology within the field of medical science pertaining to peptic ulcer disease (PUD) and *Helicobacter pylori,* identified in the latter part of the 20th century as the primary cause of type B gastritis and most forms of stomach and duodenal ulcers. Until that time, the medical community misunderstood the role of *H. Pylori,* even though it was first identified in 1875 in association with ulcers. Instead, physicians attributed ulcers and gastritis to acid-production in the stomach and focused treatments on eliminating acid and other gastric juices. Researchers were hard pressed to explain exactly why the over-secretion of acid occurred, or why some people seemed to be affected by ulcers while others were not. But without an understanding of the role of bacteria in breaking down

the mucus lining of the stomach, researchers' theories focusing on acid-production were the best theories of the disease they could produce.

During the 20th century, thousands of people died every year as a result of internal bleeding, stomach perforations, and cancer associated with PUD. Relapse rates for patients sometimes exceeded 50% of those treated for the disease. Additionally, peptic ulcer disease was one of the most common conditions known. Considering the prevalence and tenacity of PUD, one might have thought that new ideas and treatments for the disease came forth constantly, but the stability of ideas and methods for treating ulcers before the 1990s suggest another story. No cure was forthcoming, and it was not until the 1960's that new drug therapies began to be developed using the acid based etiology of the disease. Sunesson (1993) has argued that controversies in medicine tend to arise when significant pressure is applied to the profession to "do something" about an illness. The antacid therapies in use by physicians for the majority of the 20th century accounted for this 'something' that had to be done, even if it failed to cure patients of their afflictions. The frame of the disease was actually reaffirmed by the failure of the therapies because the standing etiology of the disease implied that reoccurrences would be common.

Today medical students are taught about *H. pylori* and associated bacteria as a standard part of medical training and an accepted part of medical science. Barry Marshall and J. Robin Warren were largely responsible for this shift, but their research alone does not explain how and why a bacterial etiology for PUD was accepted when it was and not much earlier. As Marshall discovered when performing his initial background research, stomach bacteria had been the

focus of research for over one hundred years, and much of that research centered on the potential pathological role of spirochetes in developing ulcers. Despite these past studies, when Marshall and Warren began their research, they thought that they were alone in their beliefs that certain bacteria lived in the stomach and that such bacteria could cause ulcerations and other pathologies. This was confirmed for them as they attempted to publish their findings and found an unsympathetic medical community. Their training, and that of their colleagues, left no room for spirochetes of the stomach.

Doctors' belief that ulcers were the result of the over-production of digestive fluids within the digestive tract was based on how medical science conceived the physiology of the stomach and its role in digestion. Within the stomach, hydrochloric acid and gastrin cooperate to break down foods to prepare them for absorption in the intestines. This same acid would break down the stomach except for its mucus lining. The mucus is an alkaline that, along with other alkalines produced by the pancreas and other organs, counteracts the acid and prevents damage to the internal organs. Since ulcers are perforations in the stomach lining where the mucus layer has been degraded, many concluded that perforations resulted from either overproduction of acid or an underproduction of mucus allowing the protective coating to be worn away.

These beliefs guided doctors in their treatments of peptic ulcers. The easiest way to treat an ulcer given doctors' understanding of the disease was to add alkaline agents to the patient's systems, neutralizing acid in the stomach and preventing it from doing further harm to the stomach wall. Thus, antacids have been used for hundreds of years to treat ulcer patients. A more advanced take on

this same principle are the H2 receptor blockers, such as Tagament ®, on the market today. These medications aim to prevent acid production.

If these methods failed to cure the patient or the patient relapsed a number of times, surgical means of ulcer prevention would have been pursued. This would result in a vagotomy, which would cut the vagus nerves. The vagus nerves provide sensory information to the ear and the tongue and provide motor functions for the esophagus and for parts of the abdomen as well. Their role in digestion is to stimulate both the chemical processes necessary for digestion (i.e. acid production) and to begin the churning action in the stomach that helps break up food. The gurgling sound the stomach makes after someone smells food is the result of the vagus nerves preparing the stomach for the digestion of food. By cutting these nerves, doctors hoped to preclude the production of acid that they believed resulted in ulcers.

In the case of PUD, stress became one of the primary factors thought to cause ulcers. Stress-based models of PUD predate all other theories of the disease. Dr. William Beaumont was the first to show that emotional stress could affect the gastric secretions of the stomach when he noticed such changes in his human subject, Alexis St Martin, whose stomach had been left permanently open after suffering a gunshot wound (Talley 1995). In 1824, Beaumont attempted to prove that these gastric secretions contained hydrochloric acid, and his findings were later confirmed by Heinrich Bidder and Carl Schmidt in 1852. In 1842, Golding Bird began to believe that abnormal secretion of these acids might be responsible for some stomach diseases when he noticed the presence of acid in the vomit of his patients. In 1868, A. Kussmaul began to prescribe

bismuth subnitrate, a known antacid, to sufferers of gastric pain, further perpetuating the stress and acid based frames of PUD. The stress-based paradigm, however, did not go unchallenged. The earliest research into a bacterial etiology of PUD was carried out by the German G. Bottcher and his French collaborator M. Letulle. They were able to demonstrate as early as 1875 that bacteria existed in the margins of ulcers (Bottcher 1875; Kidd and Modlin 1998). Both Botcher and Letulle believed that these bacteria played an essential role in the pathogenesis of ulcers. In 1888, Letulle used the *Staphylococcus pyrogenes* bacteria previously identified by the bacteriologist Alexander Ogston to inject guinea pigs in hopes that they would develop ulcers. His experiment was a success. Unfortunately he was unable to control the experiment sufficiently to show how the bacteria caused ulcerations (Letulle 1888; Kidd and Modlin 1998).

The timing of the work by Bottcher and Letulle could not have been better for the introduction of a bacterial etiology for diseases of the stomach. In 1876, one year after Bottcher's initial publication, Robert Koch demonstrated that bacteria were responsible for anthrax. After the work of Koch and his rival Louis Pasteur, viruses and bacteria were widely accepted for their pathogenic role, and many diseases were combated using immunization. Koch formulated four postulates that would continue to guide bacteriologists late into the 21st century. These postulates stated that 1) all infectious diseases are caused by microorganisms; 2) the microorganism must be obtainable in a pure culture; 3) it must be possible for the microorganism to reproduce in an animal; 4) it must be possible to recover the microorganism from the animal to create a vaccine from it.

Further research into stomach bacteria was carried out by J. W. Jaworski, Professor of Medicine at the Jagiellonian University of Cracow in Poland. In 1889, he published findings of spiral bacteria in gastric sediments that he called *Vibrio rugula*. Jaworski thought that the organisms might play some role in pathologies, but thought that their incidence would be rare. Similarly, in 1892, the Italian Giulio Bizzozero was able to demonstrate bacteria infecting the gland lumen of dogs. Bizzozero was the first person to show that bacteria actually lived under the mucus lining of the stomach. In 1906, Krienitz reported that he saw similar spiral shaped organisms in human biopsies in association with cancers of the stomach (Sarner and Babyatsky 1996).

H. Salomon was the first to attempt to show that bacteria could be used to infect animals. In 1896, using bacteria obtained from the gastric mucosa of dogs, Salomon tried to infect dogs, cats, and other animals with the bacteria. He was unsuccessful in every case except that of white mice, in which he was able to use the bacteria to infect the parietal cells. Kasai and Kobayashi (1919) repeated Salomon's experiments with greater success. They were able to infect cats, dogs, rats, and several other animals. Kasai and Kobayashi subsequently demonstrated the presence of ulcers in rabbits that had been infected, becoming perhaps the first to fulfill Koch's postulates. To Kasai and Kobayashi's benefit, their early 1919 publication was thorough enough to include illustrations of the bacteria with which they worked. These illustrations clearly show the spiral shape and flagella of *H. pylori* and show that Kasai and Kobayashi were dealing with the bacteria known today to cause PUD.

Several important advances occurred during the early part of the

twentieth century that affected how the physicians and researchers viewed the physiology and pathology of the stomach. Some of that work indirectly affected how PUD was framed during most of the century. In 1904, I.P. Pavlov received the Nobel Prize for his research on digestive processes and the role of the vagal nerves in regulating secretions of the stomach. Pavlov's research may have helped reinforce the stress-based models of PUD by showing how psychological conditions could affect the production of digestive juices. In his experiments, he was able to show that dogs would begin producing saliva and digestive acids at the ring of a bell when the sound became associated with feeding. Eventually no food was required; the sound of the bell was sufficient to produce the digestive juices that Pavlov was trying to study. While this discovery on his part was unintentional, it was important because it showed that psychological conditions could affect physiology. Specifically it showed that the mental state of the individual could affect the secretion of gastric acids. Since it was thought that ulcers were probably the result of the over-secretion of gastric juices, Pavlov's findings made it feasible to forge a connection between the mental and emotional state of a patient and the resulting physiological condition. In 1907, I. Boas and P. Cohnheim began to argue against the bacterial foundations of PUD. Boas found that the spiral shapes Jaworski had seen were common in most gastric sediments. Further research by Boas and Cohnheim showed how to alter normal cells chemically to make them take similar spiral shapes, meaning that such cells could be normally occurring in the stomach as the result of the digestive process. This was a double blow to bacterial-based etiologies for stomach diseases, as previous evidence supporting the possibility of stomach bacteria was deflated, while further evidence

suggested that the stomach's own acid was responsible for altering some cells. By 1910, K. Schwartz was piping the dictum "no acid no ulcer" that dominated how both researchers and physicians understood and treated ulcers of the stomach and duodenum (Sarner and Babyatsky 1996; Schwartz 1910).

L. R. Dragstedt's 1917 study showed the limits of this dictum and could have shifted research interests back towards bacteria. Dragstedt was interested in studying how gastric juices affected the rate of healing in ulcers. He chemically induced ulcers in dogs and performed surgical operations on them to give them Pavlov pouches so as to monitor the amount of digestive fluid present in their stomachs. He found two important things. First, to his surprise, he was unable to find a relationship between the amount of digestive fluid secreted and the rate of healing. Second, during histological examinations of the dogs, Dragstedt noted that bacteria had infected the margins of the ulcers, even though the ulcers had been stimulated chemically. The bacteria he saw were the same as those reported in humans, and he concluded that they probably came from the alimentary tract. Had the ulcers not been chemically induced, it is possible that Dragstedt would have attributed greater importance to his finding. The importance of both of his findings, however, went unnoticed by the greater medical community.

In 1938, J.L Doenges observed the presence of spiral bacteria in the stomachs of Rhesus monkeys and in human autopsies. His findings prompted Freedberg and Barron to study the presence of bacteria in human stomachs. Taking samples of gastric tissue from 35 patients, 19 with stomach cancer, 14 with ulcers of the duodenum, and 2 with stomach ulcers, Freedberg and Barron (1940) examined these for evidence of bacteria living in human gastric mucosa. Altogether

they found spirochetes in 37.1 % of the samples, but noted that they were more common in individuals with ulcers than those without ulcers. In total, 52.3 % of individuals with ulcers showed signs of bacteria, while only 14.2% of individuals without ulcers had the bacteria. They concluded that such organisms were not natural to the stomach, and following their article F.D. Gorham noted in his discussion that further research was necessary to understand the role of bacteria in diseases of the stomach. Specifically Gorham called for investigations of potential bacteria that could live in the acid environment of the stomach (Freedberg and Barron 1940).

Advances toward an etiological role for bacteria in diseases of the stomach, however, did not last. In 1954, E.D. Palmer published a report of gastric biopsies he had gathered using a vacuum tube from one thousand patients. These patients were all in various states of gastric health, including those who had ulcers and carcinomas and those who did not. He took 180 additional biopsies from individuals already in his study. In no case did he find any bacteria present. His conclusion was that previous researchers who had demonstrated bacteria through biopsies and through autopsies had in fact demonstrated commensals of the mouth that had contaminated their materials. Thus, he was able to counter much of the research that had been put forward advancing a bacterial etiology for PUD. Palmer's method of obtaining the samples using a vacuum tube may have led to his inability to demonstrate the presence of bacteria, as the vacuum may not have been strong enough to pick up lit microorganisms from the stomach wall. After his publication, however, the stomach was viewed as sterile, and over-secretion of digestive juices continued to be considered the primary factor leading to PUD.

Between the time Palmer published his findings and J. Robin Warren and Barry Marshall re-discovered the bacteria *Helicobacter pylori,* little research was carried out concerning the presence of bacteria in the stomach. The controversy that had existed, to the extent that there had been one, no longer attracted the attention of researchers. Medical texts taught each new generation of doctors to treat a peptic ulcer as though it were caused by the over-secretion of acid in the stomach. New research into treatments was based upon this framework and eventually produced a series of drugs that were H2 receptor blockers designed to prevent the secretion of acid in the stomach. The first of these drugs, Tagament ®--produced by Smith, Kline, and French--became the most prescribed medicine on the planet.

Researchers around the world independently discovered that bacteria caused PUD. Most notable of these was the discovery of *H. pylori* in The Royal Perth Hospital in Australia by Barry Marshall and J. Robin Warren (see Marshall 1988; 1989; 2002; Warren 2002).

The modern discovery of *H. pylori* began on June 11, 1979, when J. Robin Warren noticed an unusual blue line in the biopsy of a patient suffering from chronic gastritis. After magnifying the line, he saw small bacilli close to the epithelial cells of the stomach. Excited about his finding, he showed the biopsy to one of his colleagues, Dr. Len Matz, who, despite Warren's enthusiasm, could not see the small bacteria. Based upon his observations, Warren thought that the bacteria might actually be causing the damage to the mucus lining of the stomach. He began to look for more of the bacteria, taking more biopsies and using Warthin-Starry silver stains to see the bacteria. To his surprise the bacteria he had seen were quite common in these biopsies. So began Warren's preoccupation

with stomach bacteria.

Warren had the problem of finding clinicians to help him study the bacteria. Most believed that the bacteria were secondary to the inflammation and wondered why the bacteria had not been seen earlier (Warren 2002; 154). Only later did Warren realize that these bacteria had been studied for over 100 years and that their association with chronic gastritis had been noted much earlier (see Bottcher 1875; Kidd and Modlin 1998). In the meantime, Warren needed someone to help him get more biopsies and to perform more studies on the bacteria and their association with chronic gastritis. In 1981, he met a young trainee named Barry Marshall who was in the process of trying to find a small research project to aid him in his internship. At first, according to Warren (2002), Marshall was not convinced by the biopsies or by Warren's hypothesis that bacterial infections were causing gastritis and peptic ulcer disease. Marshall agreed, however, to look into biopsies from 25 patients taken from sections of the stomach that looked normal based upon endoscopic inspection. Simultaneously, Marshall began to culture the bacteria that he found in these biopsies.

The problem that Marshall encountered at this point was the wide range of symptoms experienced by people infected with the bacteria. Though most patients had dyspepsia, other symptoms ranged from ulcers to no symptoms at all. This made it difficult to associate the bacteria with any specific pathology (Marshall 1988). While his findings were inconclusive, they were enough to convince Marshall to continue working on the problem. Marshall and Warren began a 100-patient clinical study to further understand the bacteria.

Initially, no one was sure what the bacteria were or from

where they had come. Warren suspected that the organisms were *Camplylobacter* like organisms (CLO), based upon previous studies of these bacteria in relation to intestinal pathology. Warren and Marshall developed three main ideas about the possible origin of the bacteria. The first was that they were commensals of the mouth, as other spirochetes were known to be. Chicken was also thought to be a potential source, as it was known that *Camplyobacter jejuni* was passed through chicken and infected the intestines. Finally, they thought that it might be possible for the bacteria to colonize the stomach after patients had ingested antacids, H2 receptor antagonists, or other medications that might reduce the acidity of the stomach (Marshall 1988).

Marshall began to do background research on the bacteria and on *Campylobacters.* To his amazement, he found historical references that included electron micrographs of CLO on gastric epithelial cells (Marshall 2002; Ito 1967). He was able to reconstruct the trail leading backward in time to Vial and Orrego (1960), E.D. Palmer (1954), Freedberg and Barron (1940), Doenges (1938), Salomon (1896) and Bizzozero (1892). Discovery of the bacteria itself was not much of an accomplishment after all. What was important was the means of associating the bacteria with gastritis so as to prove a pathological role. Earlier researchers had attempted to make that connection, but lacking the techniques available to modern scientific medicine, no one had been able to prove that the bacteria was not a post-mortem contamination.

Culturing the bacteria proved to be more difficult than initially anticipated. Since Marshall and Warren suspected the bacteria was a *Campylobacter,* they used the same methods for culturing new samples. *Campylobacter* cultures were retained for only three days if they did not show growth. Complicating the matter, the cultures

themselves were being cared for by lab technicians who were otherwise working on fecal samples, resulting in the disposal of the samples after only two days (Marshall 2002). Culturing the bacteria under these circumstances was impossible because *Helicobacters* required longer incubation times, and as a result the process was set back six months. Luck fortunately intervened in April 1982. After accidentally leaving a sample for five days over the long Easter holiday, the cultures showed considerable growth. After realizing that longer incubation times were required, Marshall and Warren successfully cultured bacteria from nearly every infected biopsy. They decided to name the bacteria *Camplyobacter pyloridis,* a name which was eventually changed to *C. pylori* and finally to *Helicobacter pylori* in 1989 (Romaniuk et al. 1987; Goodwin et al. 1989).

In the 100-patient study, *Helicobacters* were present in all 13 of the patients who had duodenal ulcers. Altogether, 65% of the patients had bacterial infections. The bacteria was present in 26 of the 30 ulcer cases. In the four remaining cases of ulcers without the presences of bacteria, Marshall attributed ulceration to the use of non-steroidal anti-inflammatory drugs (NSAIDs), which were known to cause ulceration in patients who used these drugs excessively. This meant that non-drug induced cases of ulcers occurred only in the presence of *Helicobacters.* Statistically this one-to-one association between *H. pylori* and stomach ulcers provided a strong correlation. After the bacteria had been cultured and a synthesis of the 100-patient study obtained, Marshall and Warren decided to publish their findings. They each sent letters to The Lancet in January 1983, but it was not until June of that year that their findings were published (Warren 1983; Marshall 1983).

The fight was not over for Warren and Marshall, however, as they still needed to fulfill Koch's third and fourth postulates to prove the infectious nature of the bacteria. Fulfilling Koch's postulates required that the bacteria itself be used to infect an animal and have that animal develop the disease associated with the bacterial agent. When Marshall and Warren sent their letters to The Lancet in 1983, they still had not shown that the bacteria could infect people, and that infection could cause gastritis. Instead, they had shown only a strong correlation between the presence of the bacteria and the existence of ulcers. Without being able to directly infect an animal with the bacteria they would be unable to show that the bacteria were not commensals of the mouth that entered ulcers after the ulcers had already occurred. To remedy this, Marshall and his colleague Stuart Goodwin began attempting to infect pigs with the bacteria in 1984. The idea was simply to perform biopsies on the pigs and culture the bacteria from these biopsies. Unfortunately the experiments failed; the pigs did not demonstrate either gastritis or any sign of the bacteria.

Marshall began to treat patients successfully with antibiotics, curing their ulcers and freeing them of stomach bacteria at the same time. He began to refine the antibiotic combinations used to treat the bacteria and was able to define a 14-day treatment plan that worked despite the natural resistances of the bacteria to antibiotics. Eradication of the disease did not seem a problem at this point. Given continued difficulties with infecting pigs, and the fact that the pigs were getting larger and harder to handle, Marshall realized that he needed to show that the bacteria was infectious. He had difficulty publishing his findings in journals because of the lack of researchers studying bacteria of the stomach who could review

his articles and because of the general resistance of the medical community to his ideas (Marshall 2002). Realizing that he needed to act and knowing that he had eradicated the infection in many of his patients, Marshall decided to try and infect himself with the bacteria so as to induce gastritis and fulfill Koch's postulates. On June 12, 1984, Marshall ordered an endoscopy performed on himself to show that his stomach showed no sign of the bacteria. On the same day, he was able to culture the bacteria from a 66-year-old man who had dyspepsia but not an ulcer (Kidd and Modlin 1998). From this a broth of bacteria was made, which Marshall consumed. Seven days later he awoke early in the morning to vomit. He had successfully developed gastritis with hypochlorhydria. He then treated himself with antibiotics and eradicated his condition. He had fulfilled Koch's postulates (Marshall 2002).

By 1985, a bacterial cause for gastritis was documented and research had begun around on the globe on what was then known as Camplyobacter pylori. Marshall and others were finding it easier to publish partially because of the momentum created by a greater numbers of researchers around the globe who were aware of the bacterial cause of PUD and who could critically review new research. There has since been an explosion of research into *H. pylori* and its role in PUD, with thousands of articles being published between Marshall's and Warren's first letters to The Lancet in 1983 and the year 2000. In 1994, the National Institute of Health released a consensus statement saying that sufficient evidence had been produced regarding *H. pylori* and the ability to cure PUD with eradication therapies that standard treatment of individuals expressing bacteria caused gastritis and associated conditions should include antibiotics in addition to antacids and

H2 receptor blockers.

It is still not clear how or why exactly *H. pylori* was missed as long as it was. There are four main problems that require more research. First, methodological and technological constraints may have prevented early investigators from being able to isolate the bacteria in samples from living patients who expressed signs of PUD. Rebuttals like Palmer's (1954) against earlier research emphasized these problems by suggesting that bacteria were contaminations. Also, it was impossible for investigators like Kasa Kobayashi to show that the ulcers they believed were in association with the bacteria were not pre-existing conditions. Palmer's use of a vacuum tube to biopsy patients may have likewise been inefficient to detect the presence of bacteria in living patients. These constraints were no longer present when Marshall and Warren began investigating *H. pylori* and its association with PUD.

The second problem may have been how research was framed. The presence of bacteria in the stomach was noted multiple times by independent investigators, but often these same individuals failed to make the necessary connection between the bacteria and pathologies of the stomach. In some cases, such as that of Dragstedt, the existence of the bacteria was more of a curiosity than the subject of serious investigations. Had Dragstedt begun looking at the stomach of dogs with a frame of reference that might have applied more importance to the presence of bacteria, then he might have followed his findings in a different way, or interpreted his data in a different light.

Equally important were frames of the stomach and of peptic ulcer disease that contradicted a bacterial etiology. Palmer's empathetic 1954 assertion that the stomach was sterile precluded further research

into stomach bacteria because it essentially framed the histology of the stomach in such a way that it would be ludicrous to search for bacteria there. That microbiologists studying the stomach had noted the presence of bacteria meant little because they themselves were not directly interested in attributing a pathological role to the bacteria, or even in its study. If the researchers discovering bacteria in the stomach did not associate them with a pathological role then there would be no reason to investigate that association. Normal research concerning other pathological factors would have been carried on without reason for reference to published material on bacteria in the stomach. Therefore, although bacteria were found in association with the stomach, the meaning of that finding might not have been elucidated under these circumstances.

Further, the acid-based frame of the disease provided everything that medical science required except a cure, and the particular way that the disease was framed prevented a cure from being necessary. There are many chronic conditions today that continue to be treated in the same light as had PUD before the acceptance of *H. pylori.* Not all maladies are treatable in the same way that bacterial infections are, and unless a specific condition is thought to be related to some form of infectious agent, there is no reason for a medical professional to attempt to combat it in that way.

The third problem requiring closer examination brings us back to the therapies used to treat PUD. Since the frame of peptic ulcers and gastritis did not make it necessary to cure the disease, there was little reason to question the failings of medical science to do so. Better therapies were forthcoming, such as the H2 receptor blockers, allowing for treatment of patients in new ways. These medicines represented breakthroughs in science because they made

possible and made use of manipulations of the chemical signals in the human body that are responsible for so many of biological functions. They represent a moment where the technical features of science were succeeding, even when the theoretical frame guiding that research was false or misleading.

Essentially, the theoretical understanding possessed by physicians and researchers persuaded them to interpret their empirical findings in such a way that they were self-validating regardless of their actual findings. Whether acid therapy treatments worked mattered little. More important was that the histology of the stomach dictated that certain precautions and measures be taken. Those measures included neutralizing some of the digestive fluids present in the stomach so as to reduce the amount of erosion these would cause to the internal stomach wall. Many patients were aided by these treatments, if only temporarily, and the physician could not be blamed for the stomach's lack of healing afterwards.

Finally, the lack of knowledge possessed by doctors and researchers about the history of PUD also played an important role in the continuation of this false epistemology. Had Warren and his colleagues been aware of prior research on bacteria living in the stomach, they might not have been so surprised when it showed up as a blue line in the biopsy of a patient. An understanding of how the controversy over a bacterial or physiological cause for PUD was resolved might have led other investigators to question their textbooks sooner. Additionally, publishing findings may have been easier as well had the medical community possessed a general awareness of the intricacies of the social history of the disease.

While all of these factors played a role in the social history of PUD, no one is more important than the others. They are interrelated

and played off of each other in dynamic ways. Lack of more advanced methodologies and technologies led to the acceptance of a frame of PUD that was acid based rather than bacteria based. The ability to treat the disease within that frame led to complacency and its continued acceptance. As better technologies and methods developed, the medical facts that had already been derived from previous research were no longer under question and thus failed to receive new attention. The black and white of medical textbooks gave little reason for doctors to delve into the social history of peptic ulcer disease or to question the findings of previous generations. Warren and Marshall do not serve as an exception to this rule because their research occurred only after an anomaly was identified and not as the result of pointed criticism of what they were being taught.

The example of PUD illustrates how interdependent the growth of knowledge can be on the surrounding epistemology and how deeply this epistemology is steeped in its own specific history. Given any other case in the history of science or medicine and a completely different set of factors may have revealed themselves. As an example of a false epistemology, the social history of PUD serves to illustrate how easily perceptions can become self-validating and maintained over long periods.

References

Bizzozero G. "Ueber die schlauchformigen Drusen des magendarmakanals und die Bezienhungen ihres Epithels zu dem oberflachenepithel der Schleimhaut" Arch Mikr Anat Vol. 42: 82-152.1983.

Blaser, Martin, Ed. *Camplylobacter pylori* in Gastritis and Peptic Ulcer Disease. New York. Igaku-Shoin press: 1989.

Boas, I. Diseases of the Stomach. Davis. Philadelphia. 1907.

Bottcher, G. Dorpater Med Z 1875; 184.

Chen, Thomas and Peter S. Chen. "Chronology" in The History of Gastroenterology Ed T.S. Chen and P.S. Chen. Parthenon Publishing group, New York. 1995.

Goodwin, C. Stewart, John A. Armstrong, Terry Chilvers, Michelle Peters, M. David Collins, Lindsay Sly, William McConnell, and William E. S. Harper. "Transfer of *Campylobacter pylori* and *Camplyobacter mustelae* to *Helicobacter* gen. nov. as *Helicobacter pylori* comb. nov. and *Helicobacter mustelae* comb. nov., respectively." International Journal of Systematic Bacteriology Vol. 39 (4): 397-405. 1989.

Dragstedt, L.R. "Contributions to the physiology of the stomach: Gastric juices in duodenal and gastric ulcers" JAMA Vol. 158:330-333. 1917.

Doenges, J.L. "Spirochaetes in gastric glands of macacus monkeys and human without definite history of disease" Proc Soc Exp Biol Med Vol. 38:536-538. 1938.

Dunn, Bruce E., Hartley Cohen, and Martin J. Blaser. "*Helicobacter pylori*" Clinical Microbiology Reviews Vol.10 (4): 720-741. 1997.

Enriquex H. and R. Hallion. "Ulcère gastrique expérimental par toxine diptheritique." Co Re Soc Biol Vol 45: 1025. 1893.

Figura, Natale, and Laura Bianciardi. "Helicobacter were discovered in Italy in 1892: an episode in the scientific like of an eclectic pathologist, Giulio Bizzozero" in *Helicobacter* Pioneers Ed Barry Marshall. Blackwell publishing. Victoria. 2002.

Freedberg, A.S., and L.E. Barron. "The presence of spirochetes in human gastric mucosa" American Journal of Digestive Disease Vol.7: 443-5. 1940.

Hoffman, Albert. "Experimental gastric and duodenal inflammation and ulcer produced with a specific organism fulfilling Koch's postulates" American Journal of the Medical Sciences. Vol 127: 212-219.

Ito, Susumu. "Anatomic Structure of the Gastric Mucosa" in Handbook of Physiology: Section 6; Alimentary Canal Vol. 2 Eds. Heidel, U.S. and C.F. Code. American Physiological Society. Washington D.C. 1967.

Jaworski W. "Podrecznik Chorob Zoladka" Wydawnictwa Dziel Lekarskich Polskich Vol 32. 1889.

Kasai, Katsuya and Rokuzo Kobayashi. "The stomach spirochete occurring in mammals" Journal of Parasitology Vol.6 (1):1-11. 1919 .

Kidd, Mark and Irvin M. Modlin. "A century of *Helicobacter pylori*: Paradigms Lost-Paradigms regained" Digestion Vol. 58: 1-15. 1998.

Konturek, J.W. "Discovery by Jaworski of *Helicobacter pylori* and its pathogenic role in peptic ulcer, gastritis, and gastric cancer" Journal of Physiology and Pharmacology Vol. 54; S3: 23-41. 2003.

Latour, Bruno. Science in Action Harvard Press. Cambridge 1987.

Letulle, M "Origine infectieuse de certains ulcères simples de l'estomac ou doudénum" Soc Med Hop. Paris 1888.

Lee, Adrian, Michael Phillips, and Jani O'Rourke. "We grew the first Helicobacter species and didn't even know it" in *Helicobacter* Pioneers Ed Barry Marshall. Blackwell publishing. Victoria. 2002.

Marshall, Barry "Unidentified Curved Bacilli on Gastric Epithelium in Active Chronic Gastritis" The Lancet 1273-1275. 1983.

-- "The *Campylobacter* story" Scandinavian Journal of Gastroenterology Vol. 23 (s146): 58-66. 1988.

-- "History of the Discovery of *C. Pylori*" in *Camplylobacter pylori* in Gastritis and Peptic Ulcer Disease. Ed. Martin Blaser. New York. Igaku-Shoin press. 1989: 7-24.

-- "The Discovery that *Helicobacter pylori*, a spiral bacterium, caused peptic ulcer disease" in *Helicobacter* Pioneers Ed Barry Marshall. Blackwell publishing. Victoria. 2002.

Modlin, I. M., Mark Kidd, I.N. Marks, and Laura Tang. "The pivotal role of John S. Edkins in the discovery of gastrin" World Journal of

Surgery Vol. 21:226-234 1997.

NIH Consensus Statement. *Helicobacter pylori* in Peptic Ulcer Disease. 1994 Jan 7-9; 12(1): 1-23. 1994.

Palmer, E.D. "Investigations of the Gastric Mucosa Spirochetes of the Human" Gastroenterology Vol. 27: 218-220. 1954.

Rigas, Basil and Efstathios D. Papavassiliou. "John Lykoudis: the general practitioner who in 1958 discovered the etiology of, and a treatment for, peptic ulcer disease" in *Helicobacter* Pioneers Ed Barry Marshall. Blackwell publishing. Victoria. 2002.

Romaniuk, P.J., B. Zoltowaska, T.J. Trust, D.J. Lane, G.J. Olsen, N.R. Pace and D.A. Stahl. "*Camplyobacter pylori* the spiril bacterium associated with human gastritis, is not a true *Camplyobacter* spp." Journal of Bacteriology Vol 169; 2137-2141. 1987.

Sarner, Andrea, and Mark W. Babystsky. "Peptic Ulcer Disease: Paradigms Lost" Mt Sinai Journal of Medicine Vol. 63: 387-398. 1996.

Salomon, H. "Uber das spirillum des saugetiermagens und sein Verhalten zu den Belegzellen" Zentralbl Bakteriol Vol. 19: 433-442. 1896.

Sunesson, Sune. "Comparing 'Tool Controversies': Science, Contexts, institutional Power, and the Development of Medical Controversies" in Controversial Science; From Content to Contention Ed. Thomas Brante, Steve Fuller, and William Lynch. Pg 193-224 Suny Press, New York. 1993.

Swartz, K. "Uber penetrierende magen-und jejunal geshcwure" Beitr Klin Chir 76: 96-128. 1910.

Talley, Nicholas J. "Dyspepsia and non-ulcer dyspepsia: an Historical Perspective" in The History of Gastroenterology Ed T.S. Chen and P.S. Chen. Parthenon Publishing group, New York. 1995.

Unge, Peter. "*Helicobacter pylori* treatment in the past and in the 20th century" in *Helicobacter* Pioneers Ed Barry Marshall. Blackwell publishing. Victoria. 2002.

Vial, J.D. and H. Orrego. "Electron microscope observations on the fine structure of parietal cells" Journal of Biophysical and Biochemical Cytology Vol. 7: 367-72. 1960.

Warren, J. Robin "Unidentified Curved Bacilli on Gastric Epithelium in

Active Chronic Gastritis" The Lancet 1273-1275 1983.

"The Discovery of *Helicobacter pylori* in Perth, Western Australia" in *Helicobacter* Pioneers Ed. Barry Marshall. Blackwell publishing. Victoria. 2002.

Wurtz, R and R Leudet. "Recherces sur l'action pathogène du bacilli lactique." Arch Méd Exp Anat Pathol. Vol 3: 485. 1891.