



# Insight

www.irondisorders.org

Spring-Summer issue 2002

© IDI

## HELICOBACTER: *H. pylori*

A common bacterium often overlooked by physicians

*H. pylori*, a spiral shaped bacterium propelled by flagella, lives in the stomachs and small intestines of an estimated 40% of the world's population. Still, most physicians do not think to test for this germ, even when patients complain of symptoms that are classic for *H. pylori* infection, which include, stomach pain, nausea, acid reflux, intestinal discomfort and halitosis.

*H. pylori* is indicated in 90% of stomach ulcer cases and is considered the leading cause of stomach cancer. Before *H. pylori* was discovered, people with stomach ulcers were told that the cause was from stress or from eating spicy foods. These patients were instructed to relax, and to avoid stress and spicy foods.

### The Discovery:

The spiral shaped bacterium was first observed by Robert Koch, a 19th century scientist who was examining some specimens taken from the stomachs of ulcer patients. Koch disregarded his observation. He thought the curved shapes were artifacts on the pathology slide. After all, he upheld the well established belief that bacteria cannot survive the acidic environment of the stomach.

In the late 1970's, in Perth Australia, two scientists would disprove this widely accepted scientific assumption. J. R. Warren, a pathologist, observed the same curved microorganisms seen by Koch decades earlier. Warren first noticed that the bacteria were often present in many gastric biopsy specimens he examined for the presence of cancer. He also discovered that the tissue where the bacteria were found was inflamed.

Warren described the organism as similar in appearance to *Campylobacter*, a type of bacteria he knew capable of causing disease in the intestinal tract.

Barry Marshall, a young Australian physician intrigued by Warren's findings, joined Warren in his pursuit of the novel bacteria. Together they isolated and studied the organism. They found the bacterium to be unique, spiral shaped with helicopter like tentacles at one end. From this description they named their discovery *Helicobacter pylori*, or *H. pylori*.

Warren and Marshall were somewhat puzzled by what they had found, because until then, they too had believed as scientists before them, that bacteria could not survive the harsh acidic stomach environment. Their discovery would prove that this bacterium could not only survive in the stomach and small intestine, but that it used very clever techniques to do so.

In 1982 when Marshall and Warren posed the idea that a bacterium was the possible cause of ulcers, the two were ridiculed by their medical and scientific colleagues. The belief that bacteria could not possibly survive in the acidic stomach was difficult to dispel.

To prove their theory, Warren and Marshall are reported to have consumed sizable doses of the bacterium. Marshall waited until an ulcer developed and then treated his condition with the triad of Pepto-Bismol, antibiotic and anti-microbial medications. These findings revolutionized treatment for ulcers.

Continued on page four

## *in this issue*

**HFE Heterozygotes**  
increased risk of disease

***H. pylori***: a common bug  
often missed in diagnosis

**G6PD**: an enzyme  
deficiency that causes  
iron overload

**How Cost Effective  
is Screening for HFE?**

**Osteoarthritis &  
Hyaluronic injections**

**Selenium**: powerful  
antioxidant for the iron  
loaded heart

**Pernicious anemia  
and autoimmune disease**

**MCV-Guided Phlebotomy**  
A safe way to de-iron

Helicobacter, continued from the cover....

To date, *H. pylori* infection is still treated with Marshall's triad or triple therapy.

### How *H. pylori* survives and thrives:

*H. pylori* needs iron to thrive. It is one microorganism that is capable of getting iron both directly from heme in hemoglobin, and from iron bound to lactoferrin, which is found in human secretions such as saliva, tears, gastrointestinal fluids, Mother's milk, vaginal and seminal fluids. With an adequate supply of iron, *H. pylori* can thrive and proliferate to the extent of causing stomach cancer.

According to Marshall and Warren, Helicobacter is able to overcome the hostile environment of the stomach by burrowing into the thick protective mucus lining of the stomach lining. Here the bacteria enjoys an endless supply of nourishment in hemoglobin. Once *H. pylori* has infected the host's stomach lining, the bacterium protects itself by releasing an enzyme called urease, which converts urea into bicarbonate and ammonia. These two strong bases work like antacids to neutralize the acid in the area surrounding the bug. This creates an impenetrable, protective cover much like a raincoat repels water.

Even more clever, and somewhat ironic is that the presence of *H. pylori* sends a message to the immune system to dispense the infection-fighting white blood cells. The infection fighters cannot reach the source of infection because it has burrowed into the protective mucus lining of the stomach wall. The defense team doesn't give up; white cells (called neutrophils) and T cells remain, proliferate and die. As they die off, these cells dump destructive compounds (free radicals) onto the stomach lining.

As nutrients are sent to reinforce the defense team, the cycle is repeated and soon the host begins to experience symptoms of gastritis. Acid reflux, stomach pain, belching, nausea, bad breath and headaches are all signs that *Helicobacter* has taken up residence.

This immune response—also called the inflammatory response, rather than the bacteria itself according to Marshall and Warren is how the ulcer gets its start. Eventually if left unchecked, *H. pylori* infection can result in a gastric or peptic ulcer and even develop into gastric cancer.

The US Centers for Disease Control and

Prevention website provides that "Infection with *H. pylori*...causes duodenal and gastric ulcers. Infected persons have a 2- to 6-fold increased risk of developing gastric cancer and mucosal-associated-lymphoid-type (MALT) lymphoma compared with their uninfected counterparts."

According to physicians Linda Meurer and Douglas Bower of the Medical College of Wisconsin, Milwaukee, "*Helicobacter pylori* is the cause of most peptic ulcer disease and a primary risk factor for gastric cancer. Eradication of the organism results in ulcer healing and reduces the risk of ulcer recurrence and complications."

People who become infected with *H. pylori* may initially have anemia of chronic disease due to the inflammatory response. As the infection grows, pernicious anemia can develop because of the impaired absorption of vitamin B12 due to the reduced stomach acid. Eventually as disease advances and bleeding commences, iron deficiency anemia can result due to blood loss.

### **Iron deficiency anemia has been observed in *H. pylori* infected persons who do not have ulcers or cancer.**

The iron status (serum ferritin and hemoglobin) was measured in 2794 Danes ages 30-60 years. Those subjects who were positive for *H. pylori* had a higher incidence of iron deficiency than those not infected. The average serum ferritin of infected persons was less than 15ng/mL. Average normal ferritin range for adults is 25-75ng/mL. The investigators concluded that the anemia as indicated with the low ferritin level was caused by increased blood loss from the stomach.

Physicians at the Division of Pediatric Gastroenterology and Nutrition, Department of Pediatrics, Samsung Medical Center, Seoul, Korea investigated the prevalence of iron deficiency anemia in youths infected with *H. pylori*. Doctors Choe, Kwon, Jung, Kang, Hwang, and Hong obtained blood samples and completed questionnaires that included nutritional and economic status information from 440 high school students and 220 athletes.

Hemoglobin, serum iron, total iron-binding capacity, ferritin, and immunoglobulin G antibody to *H. pylori* were measured to compare the prevalence of IDA and *H. pylori* infection in the groups. Iron deficiency

anemia was three times more prevalent in those infected with *H. pylori* than youths that were not infected.

### ***Pernicious anemia, a vitamin B12 deficiency, is often found in people infected with *H. pylori*.***

In a recent study conducted at The Department of Hematology, Gulhane Military Academy, in Turkey, Dr. Kurad Kaptan and his colleagues found that "*H. pylori* was detected in 77 (56 %) of 138 patients with vitamin B12 deficiency and eradication of *H. pylori* infection successfully improved anemia and serum vitamin B12 levels in 31 (40 %) of the infected patients."

*H. pylori* impairs absorption of B12, and other vital nutrients, especially minerals, such as iron, by two different, but somewhat related ways. Scientists who have studied the relationship of pernicious anemia and *H. pylori* infection provide that the bacterium affects absorption of B12 in one type of gastritis and prevents the binding of cobalamin to intrinsic factor in a second type of gastritis.

Chronic atrophic gastritis (CAG) occurs when there is decreased activity of enzymes produced by the gastric mucosa, resulting in hypochlorhydria or achlorhydria and an unstable gastrin level. There are two types of gastritis. Type A gastritis is due to an autoimmune response; Type B gastritis is due to an allergic reaction, surgery or infection.

Type A chronic atrophic gastritis associated with *H. pylori* infection and pernicious anemia begins with *H. pylori*'s ability to mimic gastrin-producing cells. This ability is called genetic or molecular mimicry. How it works is fascinating. Stomach acid is necessary for normal digestion and the absorption of nutrients. The digestive process is dependent upon many factors, such as the presence of enzymes and hormones produced by the stomach for the release of stomach acid, or hydrochloric acid (HCL).

*H. pylori* is about to fool the immune system by mimicking the genetic structure of gastrin producing cells. When the bacterial infect a host, the immune system is alerted. White blood cells call leukocytes, and T cells from the lymph nodes, rush to attack the invading pathogen. Unfortunately, when the team arrives, it cannot distinguish the good guys from the bad because of the genetic similarities.

Therefore, while in the process of destroying the invading pathogen, some good and essential cells get destroyed too.

This destructive maneuver disrupts the production of stomach acid. Over time, low HCl or complete loss of HCl causes a diminished or total lack of absorption of B12, as well as other nutrients.

Normally the liver stores enough B12 to last about three years. B12 is also known as cobalamin. Vitamin B12 is contained in animal proteins such as beef, fish, chicken, eggs some cheeses and yeast. Stomach acid and an enzyme called pepsin release cobalamin from these proteins.

Free cobalamin is first bound to transcobalamin, a transport protein present in the stomach. Transcobalamin carries cobalamin to the small intestine, where another enzyme released by the pancreas digests the transport protein causing the release of cobalamin. Intrinsic factor, a hormone secreted from the gastric lining of the stomach then binds with cobalamin and transports it into the bloodstream to the liver, where B12 is stored.

If the stomach is not acidic enough, the entire B12-transport system is impaired. Cobalamin misses the bus, so to speak, since it loses its ability to meet up with and bind with intrinsic factor. A vitamin B12 deficiency develops and pernicious anemia is the consequence.

How does a person get *H. pylori*?

The bacteria can be transmitted oral-oral, the gastro-oral or the fecal-oral route. Oral-fecal transmission occurs by eating or drinking water or food contaminated with fecal matter very similar to the way viral hepatitis A is transmitted. People who do not wash their hands when using the toilet can contaminate foods that are eaten by others, who become infected.

Researchers at the VA Medical Center in Johnson City, Tennessee used molecular analysis to detect *H. pylori* in 88 gastric biopsy, 85 saliva, and 71 fecal specimens. In saliva specimens, *H. pylori* DNA was identified in 57 of the 68 patients with proven gastric *H. pylori* infection and in three of the 17 patients without gastric *H. pylori* infection. These investigators concluded that the oral-oral route is a prominent method of *H. pylori* transmission.

Another possibility is that *H. pylori* might be transmitted from the stomach to the

mouth in regurgitated fluids, when a small amount of the stomach's contents is forced up into the esophagus from reflux, vomiting or belching. The bacterium could then be transmitted to someone who drinks or eats from eating utensils, beverage containers or shares a toothbrush used by the infected person.

Who is at risk of getting *H. pylori*?

People who live in developing countries or people who are poor are more likely to be infected with *H. pylori*. In the USA, *H. pylori* affects about 20% of persons below the age of 40 years, and 50% of those above the age of 60 years. The prevalence of *H. pylori* infection among Hispanics and African Americans of all ages is higher than among Caucasians, especially those with iron overload.

Excessive levels of iron provide an environment rich in the nutrient that helps *Helicobacter* thrive. Lactoferrin in saliva, may likely give *H. pylori* its initial nourishment. It is one bacteria that is capable of getting iron from lactoferrin, whose purpose is to withhold iron from harmful pathogens. Anyone stockpiling iron may have elevated levels of iron-binding proteins such as lactoferrin and therefore, an abundant supply of iron for *H. pylori* to acquire.

*Helicobacter* is more common in children than previously believed.

From 1975 to 1996 Scientists at the Department of Medicine, Veterans Affairs Medical Center and Baylor College of Medicine, Houston conducted a study to determine the prevalence of *H. pylori* in children. Dr. Malaty and his colleagues monitored 224 children ages 1-3; 99 of the children were black, 125 were white. At the beginning of the study each child was tested for *H. pylori* infection; 18 of the children or 8% were infected.

**By the time these children reached 18-23 years of age, nearly 25% were infected.**

The investigators found that the incidence of *H. pylori* infection was highest among children ages four to five and that black children were three times more likely to be infected with *H. pylori* than whites.

*Helicobacter* infection is also seen in animals. Over 16 strains of *Helicobacter* have been identified. Some are gastric specific, colonizing in the stomach; others are non-gastric, colonizing in the intestine. *H. mustelae*, *felis* and *acinonyx* are gastric

**Yeah, we ferrets can get this *Helicobacter* infection too. According to Dr. Leslie Johnston a veterinarian and super smart guy, we ferrets get the same medicines that humans are given to cure our infection!**



strains found in ferrets, cats, dogs and cheetahs. Non gastric strains have been found in humans and rodents. The gastric strain causes problems of absorption, ulcers and stomach cancers, where the non-gastric type causes hepatitis and liver cancers.

Symptoms and findings:

Some people infected with *H. pylori* have no symptoms whatsoever, including anemia. However, *H. pylori* infection should be suspected when a patient complains of acid burning in the throat (esophagus) and stomach, is bloated, belching, nauseated, has frequent headaches, has a problem with flatulence, or bad breath. Other findings might include fever.

How is *H. pylori* detected?

Infection of *H. pylori* can be determined in several ways. Blood tests can detect anti-bodies. A breath test can detect infection. An endoscope and examine the stomach directly and obtain a tissue sample, or biopsy. A fecal stool *H. pylori* antigen test is a relatively new test. It is ideal for pediatric patients. The parent or the patient collects a stool sample at home and drops the sample off at the physician's office. The sample is checked for *H. pylori* antigens, which are proteins that cause the production of specific antibodies. A positive result on the stool antigen test can confirm the diagnosis. When positive seven days after completion of therapy, the infection is still present and further therapy is needed.

Treatment:

Treatment of patients with *H. pylori* infection typically involves a quadruple-drug regimen given for a period of 10 to 14 days. Bismuth commonly sold as Pepto-Bismol is used along with lansoprazole, brand names: Prevacid, Prilosec, to coat the stomach and to reduce stomach acid production so that ulcers, if present can heal. An antimicrobial such as Flagyl is used along with an antibiotic such as amoxicillin or tetracycline for those who are allergic to penicillin.

Ulcers take about 6 to 12 weeks to heal and may require an extended regimen of drugs such as Prevacid, or Prilosec. ■