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Microorganism (Helicobacter pylori) Related with Asthma, Obesity and Cancer of the Esophagus in Children

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Most people feel a twinge of regret at reports that an animal or plant is becoming rare. Should they feel the same pangs for a bacterium? With *Helicobacter pylori*, (**Figure 1**) so-called because of its twisty-turny shape, and famous for causing stomach ulcers and gastric cancer, the reaction would probably be "good riddance". And *H. pylori* is, indeed, endangered in many parts of the planet. It is fast vanishing from the rich world, thanks to antibiotics and improved hygiene. Yet, as conservationists of larger organisms are quick to remind you, extinctions can have unexpected consequences. And that may prove to be the case with *H. pylori*. *Helicobacter pylori* has a reputation for causing ulcers and cancer. Hunting it to extinction, however, may be a mistake.

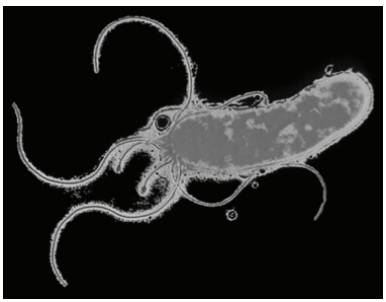

Figure 1. *Helicobacter pylori*
(Source: Science Photo Library)

Martin Blaser, a microbiologist at the New York University School of Medicine, and his team from the National Cancer Institute have already linked the microorganism's disappearance with increased levels of obesity and with the rise of cancer of the esophagus [1-2]. In 2009 they added asthma to the list by publishing a study showing that children who had not been infected by *H. pylori* were more likely to suffer from the condition than those who had [3].

It is a mistake, according to Blaser, to think of *H. pylori* as just another pathogen. He reckons that it is better perceived as a symbiont that is sometimes helpful and sometimes harmful. The evidence suggests that its relatives have been living in mammalian stomachs since the mammals began, some 150m years ago. It, itself, has been around for at least 60,000 years and until about 50 years ago it infected 70-80% of the human population. Now, as a consequence of the routine use of antibiotics for such things as ear infections, only 5% of American children have it. That change, he thinks, is having consequences.

Give and take

Blaser has discovered, for example, that *H. pylori* helps to regulate stomach-acid levels in a way that is usually helpful to both itself and its host. If the human

side of the loop gets too strong, and the stomach becomes too acid, the bug may produce a substance called cag. The intended effect of this, Blaser thinks, is to say "turn down the acid level". However, cag also has a side-effect. It is toxic to the stomach lining, and it is this toxicity that provokes the ulcers and cancers for which *H. pylori* is notorious.

The obvious medical temptation—and, indeed, what has happened in practice—is to annihilate the bacterium with antibiotics. That works as an anti-ulcer treatment, but when *H. pylori* goes its homeostatic effect goes with it, allowing the strength of the stomach acid to rise chronically. This acid has a tendency to spill out of the top of the stomach and into the esophagus. That has unpleasant consequences. In fact the recent drop in *H. pylori* infections has almost exactly matched the rise in gastroesophageal reflux disease (which feels like bad heartburn). Over time, the damage the excess acid does to the walls of the esophagus may cause cancer.

The link with asthma has a different mechanism. When Chen and Blaser [3] analysed a health and nutrition database called the National Health and Nutrition Examination Survey [4], they found that American children between the ages of three and 13 who are infected with *H. pylori* are 60% less likely to have asthma than their uninfected contemporaries. They believe this is because *H. pylori* makes the immune system more robust. The lack of it lowers the threshold for responding to a foreign protein that might come from a pathogen. As a result, things like pollen and mites trigger responses even though they are not, actually, dangerous. This idea is similar to the "hygiene hypothesis" that the super-clean environment of the modern world fails to challenge children's immune systems enough for their own good, and thus opens the way for conditions such as asthma. It differs, however, in that Chen & Blaser think humanity has co-evolved with the bugs that prime the immune system, rather than picking them up at random. This study [3] was the firs to report an inverse association between *H. pylori* seropositivity and asthma in children. The finding indicates new directions for research and asthma prevention.

Moreover, even the link between *H. pylori* and gastric cancer and ulcers is complicated. Just having the bacterium does not automatically mean you will get an ulcer. In the past, most people were infected with *H. pylori* from their childhoods until they died. Ulcers, however, generally emerge when a patient is in his 30s or 40s. In addition, they are three times more common in men than in women. *H. pylori*-infection rates, however, are the same in both sexes. In their study [2] they calculated the population attributable risks (PARs) identified for esophageal adenocarcinoma, gastric adenocarcinoma, esophageal squamous cell carcinoma and noncardia gastric adenocarcinoma for various risk factors in 293 patients that presented these conditions. Smoking, alcohol consumption, low fruit and vegetable consumption, being overweight, history of gastroesophageal reflux and *H. pylori* infection could be related to these cancers. These results suggest that the incidence of these cancers maybe decreased by reducing the prevalence of smoking, gastroesophageal reflux, being overweight and by the increasing the consumption of fruits and vegetables.

H. pylori also has an effect on two of the hormones that control appetite—ghrelin, which makes you feel hungry, and leptin, which does the opposite. People without *H. pylori* produce more ghrelin than those with. Though the connection has not been established for sure, Blaser and his group [1] suspects the bacterium's disappearance could thus be contributing to the epidemic of obesity that is sweeping the rich world.

What all this suggests is that rather than trying to eradicate *H. pylori*, a better strategy would be to manage its relationship with humanity in a more sophisticated way. Some people are, genetically, more susceptible to ulcers and gastric cancer than others. For these unfortunates eradication may be the best option. However, if your genes predispose you to asthma or obesity, eradication may be unwise.

Moreover, people are not born with *H. pylori* in their stomachs. Rather, they get infected when they are young. That means a parent or doctor could choose which strain of the bacterium a child ends up carrying, rather than leaving the matter to chance. *H. pylori* is genetically variable (not all strains, for example, make cag). Blaser envisages a future in which doctors run routine checks on babies' genes to find out their susceptibilities, and then colonise those babies' stomachs with the strain or strains that are best for them. If that happens, *H. pylori* can come off the endangered species list for good [5].

References

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