Editorial

*Helicobacter pylori* in the faeces?

The most surprising thing about *Helicobacter pylori* is its site of residence—within the stomach. Failure of early reports of the presence of spiral gastric organisms to evoke much interest was probably due to a general reluctance to view the stomach as a habitat for micro-organisms because of the extreme acidity of its lumen. Marshall and Warren’s ‘discovery’ in 1982 changed that, and now, within 18 years of the cultivation of a microaerophilic flagellated spiral organism from the human stomach, *H. pylori* is not only regarded as the commonest chronic bacterial infection of mankind, but also the principal cause of duodenal ulcer disease and an important factor in the pathogenesis of gastric cancer.

The ability of *H. pylori* to survive and thrive in the stomach is due to several factors. The organism is motile and can penetrate the gastric mucus to reach the epithelial surface. It also secretes urease, which hydrolyses urea to carbon dioxide and ammonia, thereby allowing it to surround itself with an alkaline micro-environment, facilitating survival in an acid milieu. This property has been exploited as a diagnostic tool in the CLO test and the urea breath test.

The presence of *H. pylori* at the gastric mucosal surface causes profound changes in gastric physiology which vary at different stages of colonization. Transient hypochlorhydria lasting for up to several months is well described in individual cases of acute *H. pylori* infection. There have also been reports of ‘spontaneous hypochlorhydria’ in association with the development of gastritis, and of ‘epidemic hypochlorhydria’ in association with *H. pylori*. Together with volunteer experiments these lend support to the view that a transient increase in gastric pH follows acute *H. pylori* infection.

Thereafter, chronic infection exerts variable effects on gastric acid secretion. In some, the gastritis is confined to the antral region of the stomach and stimulates increased release of gastrin from the antral G cells, which in turn stimulates the healthy uninfamed mucosa of the body region of the stomach to secrete excess amounts of acid, which may result in duodenal ulceration. In others the gastritis involves the body of the stomach and leads to atrophy, impairing its ability to secrete acid. Patients with an atrophic body-involving gastritis and hypochlorhydria have an increased risk of gastric cancer.

*H. pylori* is very common in the developing world, where it is associated with childhood diarrhoeal disease, undernutrition and growth faltering. It has been proposed that the loss of the gastric acid barrier during acute *H. pylori* infection could permit the passage of other potentially enteropathic micro-organisms into the small intestine, leading to an enteropathy, diarrhoea and malnutrition, resulting in growth failure. In parts of the developing world, the infection is extremely common from an early age. High adult seropositivity rates are related to overcrowded and unsanitary childhood living conditions, and poor hygiene and domestic services are associated with an enhanced risk of infection. Cross-infection has been demonstrated by DNA fingerprinting methods, and the seroprevalence of *H. pylori* infection is significantly higher in spouses of patients with a duodenal ulcer than in controls. However there is no evidence of a link between *H. pylori* infection and the number of sexual partners, which suggests that spread between adults is not easy. Person-to-person transmission is thought to be by the faecal-oral or oral-oral routes, although the relative importance of each remains unclear.

Four research groups have studied the correlation between infection with hepatitis A and *H. pylori* in an attempt to answer this question. Two contradictory Italian studies found evidence for and against a common mode of transmission. A community-based study from the UK concluded that the case for faecal-oral transmission of *H. pylori* was not proven, and that other modes of transmission should be considered. However, a study of hospital staff in the USA reported a significant correlation between the seroprevalence of *H. pylori* and hepatitis A, suggesting that faecal-oral transmission was likely. Further supportive evidence for faecal-oral spread comes from a study showing that employees in institutions caring for intellectually disabled patients have a higher incidence of *H. pylori* infection than the general population. Oral to oral spread has been
suggested from the isolation of *H. pylori* from dental plaque and from saliva. Polymerase chain reaction (PCR) analysis of saliva from patients with proven *H. pylori* infection has demonstrated *H. pylori*-specific DNA but not conclusively shown it to be the same strain as that in the stomach. Moreover, dentists do not appear to be at increased risk of *H. pylori*. 

Culture of *H. pylori* in the stools of Gambian infants suggests that the physiology of the gastrointestinal tract in early life may favour faecal-oral transmission. The shorter intestinal transit rate of children, and the association of acute infection with hypochlorhydria, may permit the passage of *H. pylori* through the large bowel and excretion of viable micro-organisms in the stool. Support for the hypothesis that hypochlorhydria is an important factor in determining whether *H. pylori* can be cultured from faeces comes from experiments in ferrets colonized with *H. mustelae*, which induces histopathological changes in the stomach comparable to those seen in gastric *H. pylori* colonization in man. The rate of isolation of the micro-organism from the stool of infected animals was significantly increased when they were rendered hypochlorhydric.

However, only two research groups have so far claimed to culture *H. pylori* from stool, and they did not genotype the isolate. Many new species of *Helicobacter* have been described over the last 5 years, which can be grouped into urease-positive and -negative species, and by site of isolation. The group of urease-positive *Helicobacter* spp. found in the bowel includes organisms such as *H. pullorum* and *H. canis*, raising the possibility that the organism isolated in The Gambia was a urease-positive enteric *Helicobacter* other than *H. pylori*.

Although it has proved difficult to culture the organism from stool, extensive indirect evidence suggests that the organism, or parts of it, can be found there. PCR amplification of *H. pylori* DNA is an extremely sensitive method of detection, but inhibitory substances in the stool hinder attempts to extract and amplify DNA. In one study of patients with proven gastric *H. pylori* infection, PCR successfully detected the 16S rRNA gene in 90% of faecal samples. However others have failed to achieve such high detection rates. A primer based on the 16S rRNA gene may lack the specificity needed to identify *H. pylori*, because this gene is conserved across a number of bacterial species. The combination of PCR and restriction fragment length polymorphism analysis of the amplified DNA provides for specific identification of *H. pylori* and for typing of strains. However, PCR for *H. pylori* may not be specific, and cross-reaction with other species of *Helicobacter* could therefore occur.

There are also questions about the form and viability of the organism in the stool. In common with other spiral bacteria such as *Campylobacter* spp., *H. pylori* can exist in both ‘normal’ and coccoid forms. Coccoid forms of *H. pylori* were described soon after its discovery, predominate in older cultures and cannot be subcultured in vitro. They may represent a viable but non-culturable form analogous to spores formed by other bacteria, and it may be in this form that *H. pylori* is excreted and survives in the environment. The rate of formation of the coccoid form in the stomach may be related to local nitric oxide production, but little is known about factors that trigger transformation during passage through the gut. It remains uncertain whether these forms of *H. pylori* are viable and revert to cultivable forms, or whether they represent a nonviable degenerative phase. Outside the stomach, the morphology, metabolism and growth behaviour of *H. pylori* changes, and this may be most evident when *H. pylori* passes in the faeces to an aerobic environment.

Recent development of a stool antigen test (Premier Platinum HpSA; Meridian Diagnostics, Cincinnati, USA) supports the view that *H. pylori* is excreted in the faeces. The ELISA uses a polyclonal anti-*H. pylori* capture antibody, and the manufacturer claims a sensitivity of 90% and specificity of 100% compared with endoscopic identification of *H. pylori*. The kit detects *H. pylori* antigen, but this may just be a product of digestion of the organism residing in the stomach. Therefore, other than two reports of culture from the stool, there is little evidence that *H. pylori* survives in the colon. The origin of DNA amplified by PCR from the stool is not known, because it has not been typed and compared with *H. pylori* DNA from the stomach.

Many micro-organisms that colonize or infect the upper gastrointestinal tract may also be isolated from the stool. The colon is the habitat of a vast and diverse microflora, many of which take part in fermentative and other metabolic activities. Ingested micro-organisms that pass through the gut may be excreted unchanged (such as *Salmonella* and *Shigella*), chronically colonize a part of the gastrointestinal tract (such as *Giardia*), or reside in the large bowel and/or be excreted in forms other than in which they were ingested (such as *Entamoeba*). It should not come as a complete surprise, therefore, to find evidence of *H. pylori* in the colon, though it could be present in the stool largely in a non-cultivable (coccoid) form.

Detection of *H. pylori* antigens in the stool will drive researchers with new determination to culture the organism from faeces, and to try to characterize the form in which it exists in, or passes through the large bowel. It is possible that failure of attempts to repeat the culture of *H. pylori* from stool are because the organism does not usually survive.
passage through the gastrointestinal tract, except when intestinal transit is rapid and there is hypochlorhydria. It may be that the antigen test is merely detecting antigen material from dead and partially digested bacteria from the stomach.

The principal questions raised by the detection of *H. pylori* antigens in the stool are: where in the gastrointestinal tract does *H. pylori* reside and how is it transmitted? Are the types and forms of *H. pylori* found in the stomach the same as those in the stool and oral cavity, and does eradication of gastric infection also eliminate the organisms from these sites? If the answer to the second question is yes, then the stool antigen test could eclipse the urea breath test as a non-invasive screening test for *H. pylori* colonization, and facilitate epidemiological studies of its mode of transmission.

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**References**


