The only good Helicobacter pylori is a dead Helicobacter pylori

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1 Blaser MJ. Not all Helicobacter pylori strains are created equal: should all be eliminated? Lancet 1997; 349: 1020–22.

Sir—Martin Blaser suggests that microbiologists should better define markers for different H pylori strains associated with adverse clinical outcome and that epidemiologists should better estimate the disease risks in specific populations. Some genetic markers such as the cagA gene are present in about 60% of H pylori strains. The so-called cytotoxic strains are known to be associated with increased risk of peptic ulcer in adults and children,1 and with gastric atrophy and cancer.2 Children are at increased risk of acquiring H pylori infection, and the earlier the acquisition the greater the risk of developing gastric cancer in adulthood.3 A non-invasive, low-cost test to look for specific H pylori antigens is needed. A western blot on saliva samples could be such a test, and we report preliminary data on 40 children who underwent endoscopy for dyspepsia.

On the morning of the endoscopy, we collected a blood sample from each child and 1 mL of saliva (the child spat in a test tube) which was immediately stored at −20°C. Histology (Giemsia) rapid urease test and 14C urea breath test showed H pylori gastritis in 30 children (14 boys, 16 girls, median age 12 [range 5–16] years). We also enrolled ten negative controls of similar age and sex, five not infected with H pylori. Serum samples and saliva were screened by western blotting after sodium dodecyl sulphate-polyacrylamide gel electrophoresis for H pylori-specific antigens with a commercial kit (Helor-WB, Eurospital, Italy). We tested serum samples at a 1/50 dilution and saliva samples either undiluted or at various dilutions (from 1/125 to 1/4) to reach a final volume of 750 μL. The marker for infection with cytotoxic H pylori strains was the presence of a 120 KDa (CagA-associated protein) band. Presence of 25 KDa band (lectin-like adhesin)3 indicated infection with a non-cytotoxic strain.

With these criteria, the sensitivity of the saliva test was 100% and specificity was 90% with only one false-positive test in ten controls. Undiluted saliva samples gave the best results. The bands in serum samples and saliva were similar, although the number of salivary bands was lower. The 120 KDa band was present in saliva and serum in 20 (66%) of the children infected with H pylori, with a prevalence similar to that of another series of Italian children.4

The cagA protein expressed by cagA-positive strains is highly immunogenic and serum antibodies against it can be used to ascertain cagA expression by all H pylori strains that colonise the stomach; the presence of cagA protein in serum and mucosal secretions correlates strongly with ulcer disease and active gastritis. Indeed our patients infected with cytotoxic H pylori strains had the most severe gastritis; histology showed active gastritis—ie, with polymorphonuclear cell infiltration—in 11 of 20 cagA-positive children and in one of ten cagA-negative children (p<0.02, Fishers test).5

The saliva test for detection of antibodies against cagA is useful to identify patients at risk of developing peptic ulcer, gastric carcinoma, or both later in life. Saliva collection has the advantage of being a non-invasive, simple test. Collection is easy for patients and health-care workers and greatly reduces the risk of blood-borne infection.

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Sir.—We agree with Martin Blaser on the need to reserve anti-Helicobacter therapy for the established indications. Another important argument against mass eradication campaigns is the rapid disappearance of H pylori from western countries. In 1994 in the Netherlands, only 9% of children younger than 10 years,1 and 17% of those under 25 years were infected with H pylori. This prevalence could mean that by 2024 it will be under 15% in individuals younger than 45 years. Epidemiological data from other developed countries lend support to this hypothesis.6 It seems unwise to spend manpower and resources on fighting an infection on dubious clinical grounds which is already dying out.

Blaser does not discuss whether or not the different strains of H pylori react to anti-microbials in a similar way. Patients without peptic ulcers may need a different therapeutic approach. Previous studies showed that the cure rate for a given regimen is higher in ulcer patients than in those with functional dyspepsia or gastritis only.7 This difference cannot be explained by compliance alone. We have investigated the importance of the allelic variation in the gene encoding the cytotoxin (VacA).

We isolated DNA from biopsy samples of the stomach from patients who took part in two recent trials.8 H pylori was eradicated in 59% (27/46) of the patients. One patient was excluded. Among 45 patients, VacA genotypes s1/m1, s1/m2, and s2/m2 were detected in 12 (26-6%), 20 (44-4%), and seven (15-5%) patients, respectively. Multiple genotypes were detected in six (13-3%) patients. CagA was present in 28 (62-2%) patients and was strongly associated with the type s1 VacA allele (p=0.007). Patients with peptic ulcers were more frequently positive for cagA and the s1 type VacA allele than patients with functional dyspepsia (p=0.146 and p=0.012, respectively). We found a higher cure rate for the more pathogenic VacA type s1 strains than the VacA type s2 strains (p=0.075). With the allelic variation in the m region of the VacA gene, no relation with cure rate was observed. Because strains from patients with ulcers often grow more rapidly, we postulate that the VacA type s1 strain, which are more commonly associated with ulcer disease, produce more toxin, induce more inflammation, grow more rapidly, and are more easy to eradicate since antibiotics achieve high concentrations in inflamed tissue, whereas bacteria in the growth phase are more readily killed. By contrast, the VacA type s2 strains, which are more often found in functional dyspepsia, produce no toxin, induce less inflammation, grow slowly, and are more difficult to eradicate in vivo. Such strains are usually in a stationary phase and may simply need a longer or a more aggressive treatment than the strains which cause ulcer disease. Most data on Helicobacter treatment are obtained from patients with ulcers, and may not, therefore, apply to functional dyspepsia. Physicians who want to treat individuals without an ulcer should expect lower cure rates than those reported in the published research. In

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the coming years patients with functional dyspepsia could well need treatment for 10–14 days whereas partial ulcers could be treated successfully in just 7 days.

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Disclosing conflicts of interest
Sir—In his commentary on conflicts of interest in clinical research, Richard Horton (April 19, p. 848) lamented that “the research community has become extremely exercised by this issue” and argues against disclosure. Disclosure has its drawbacks but that does not mean it is unnecessary. It is time for the discussion to go beyond disclosure and focus on whether so many scientists should have avoidable conflicting interests in the first place.

Disclosure is only possible when there is a forum for it, such as a publication or oral presentation. When investigators are restrained by industry sponsors from presenting their work, the sponsorship cannot be revealed. Even when studies are published, financial ties of authors are not always disclosed. Krimsky et al found that in 34% of articles in leading biomedical journals with a Massachusetts-based lead author, that author had at least one disclosed financial interest.

A more important reason for actions beyond disclosure stems from a moral obligation. Researchers have an obligation to fellow scientists and to the public to do the best science possible. Professionals are accorded a great deal of trust (and economic and social status) by society, on the understanding that they will strive for excellence and help further the public’s interests above personal ones. Because academic institutions receive large amounts of...