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Reply

EDITOR.—We appreciate Professor Bortolotti's comments by our article. Our study showed that therapeutic doses of ranitidine, famotidine, and omeprazole, which suppress gastric acid secretion, affect both gastric motility and gastric emptying. Each agent delayed gastric emptying despite an increase in postprandial antral contractility as assessed using antral manometry, electrogastrography, and dynamic antral scintigraphy. Interestingly, these agents also stimulated antral phase III migrating motor complexes in the fasting state. In this letter, we address some of the comments raised by Professor Bortolotti.

The study was designed primarily to assess the effects of histamine type II receptor antagonists (H_2 RA) on postprandial gastric emptying. We also simultaneously recorded electrogastrography, antroduodenal manometry, and dynamic antral scintigraphy to determine the mechanisms of altered gastric emptying. The study design included a 30 minute period to observe the effects of the gastric acid suppressants on fasting gastric motility to use as appropriate reference values for the postprandial effects. We agree that the 30 minute periods were relatively short to study the fasting period fully, with its 90 minute recurrent fasting migrating motor complexes. As our study was a four way cross over study, the effects of gastric acid suppression were compared, not only with the time periods before the administration of the study drug, but also with appropriate placebo controlled arms in the same subject. Omeprazole was given orally as there is not an intravenous form in the United States. The effects of omeprazole were compared only with the placebo arm. Professor Bortolotti notes that our findings have been confirmed by several other investigators.

Our study was designed to see whether the cholinergic properties of ranitidine seen *in vitro*¹ could be seen *in vivo*. We compared the effects of ranitidine, an H_2 RA with cholinergic activity, with famotidine, an H_2 RA with little cholinergic activity, and with omeprazole, a proton pump inhibitor with no known cholinergic activity. We found that the effects of the gastric acid suppressants (ranitidine, famotidine, and omeprazole) were all similar, suggesting the effects seen were due to gastric acid suppression, rather than to selective properties of ranitidine. With the results of our studies, further investigation of the mechanism of gastric acid suppression on gastric motility can be undertaken. Professor Bortolotti suggests a study on plasma motilin concentrations after the administration of these drugs. We would also suggest measuring serum gastrin and somatostatin concen-

trations as these are also affected by gastric acid suppression and might mediate some of the gastric motor effects seen with gastric acid suppressants. Finally, one would want to monitor gastric pH during the study to help determine the degree of acid suppression with each of these agents. These points are addressed in the discussion section of our manuscript.

We thank Professor Bortolotti for his comments and the chance to address them. Professor Bortolotti has made many contributions to the relationship between gastric acid suppression and gastric motility, not only in normal subjects as our study, but also in gastric pathophysiology such as duodenal ulcer, gastric ulcer, and non-ulcer dyspepsia.

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Faecal elastase 1 in chronic pancreatitis

EDITOR.—I read with interest the recent paper by Lankisch *et al* (*Gut* 1998;42:551-4). The authors studied faecal elastase 1 and faecal chymotrypsin in 30 patients with chronic pancreatitis and concluded that the estimation of faecal elastase 1 is not helpful in diagnosing mild and moderate exocrine pancreatic insufficiency and that this enzyme is not superior to faecal chymotrypsin in the diagnosis of exocrine pancreatic insufficiency. As various studies have already been published on this subject, I believe that it is useful to report the results of these studies, mainly because they clearly show that Lankisch *et al*'s conclusions cannot be substantiated. Domínguez-Muñoz and colleagues,¹ in 20 patients with chronic pancreatitis (six mild, four moderate and 10 severe), found that the sensitivity of faecal elastase 1 was 0%, 100% and 100%, and that of faecal chymotrypsin 0%, 75% and 70%, in the three groups, respectively. Glasbrenner and colleagues² studied 63 patients with chronic pancreatitis (19 mild, 14 moderate and 30 severe) and found that faecal elastase 1 had a sensitivity of 47%, 79% and 100%, and faecal chymotrypsin a sensitivity of 32%, 36% and 63%, respectively. Löser *et al*,³ in 44 patients with chronic pancreatitis (eight mild, 14 moderate and 22 severe), found that faecal elastase 1 had a sensitivity of 63%, 100% and 100%, and faecal chymotrypsin a sensitivity of 25%, 50% and 86%, respectively. Finally, in 44 patients with chronic pancreatitis (nine mild, 13 moderate and 22 severe) we found⁴ a sensitivity of 22%, 77% and 100% for faecal elastase 1, and of 11%, 54% and 77% for faecal chymotrypsin. In the four studies combined, 171 patients with chronic pancreatitis were studied and the sensitivity of faecal elastase 1 was 38%, 87% and 100% in mild ($n=42$), moderate ($n=45$) and severe ($n=84$) chronic pancreatitis, respectively, whereas the sensitivity of faecal chymotrypsin was considerably lower, at 21%, 49% and 74% respectively. Based on these numbers, I believe that it can be clearly stated that faecal elastase 1 has a good sensitivity in patients with moderate and severe pancreatic insufficiency and that it is clearly superior to faecal chymotrypsin in the diagnosis of exocrine pancreatic insufficiency. Lankisch *et al*'s conclusion may

have resulted from the small number of patients included in their study.

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Reply

EDITOR.—We are grateful for the interest Professor Gullo has taken in our recently published paper. He disagrees with one of our conclusions, namely that the estimation of faecal elastase 1 is not distinctly superior to the usual faecal chymotrypsin estimation.

His disagreement is based on four different studies which he has combined for meta-analysis. We doubt whether these four studies may be used for a meta-analysis as faecal elastase 1 was studied using a variety of different methods. In Glasbrenner *et al*'s study¹ the faecal elastase test was done in patients in whom the diagnosis of chronic pancreatitis was based on endoscopic retrograde cholangiopancreatography (ERCP), and in the study by Domínguez-Muñoz and colleagues² the diagnosis was based on ERCP and computed tomography. Löser and colleagues³ tested, as we did, against the secretin-pancreozymin test, which is the gold standard for testing exocrine pancreatic function.^{4,5} The tests which Professor Gullo used are presently unknown as his study has yet to appear in print.

The upper limit of normal for a faecal chymotrypsin test is 3 U/g stool. Concentrations between 3 and 6 U/g stool usually raise a suspicion of exocrine pancreatic insufficiency. In our study, both concentrations were used. It would be interesting to know what the results of the other studies¹⁻³ would have been if they had used the upper level of normalcy. However, even if a correct analysis was to undermine in a larger number of patients our modest conclusion that faecal elastase 1 is not distinctly superior to the faecal chymotrypsin estimation, the criticism does not concern the main message of our paper.

We concluded that faecal elastase 1 is particularly helpful in detecting severe exocrine pancreatic insufficiency. Several studies, including ours, have shown that the severe form may be detected with a sensitivity of between 73 and 100%.^{1-3,6-8} However, a similar conclusion can be reached about various other indirect pancreatic function tests.^{4,5}

We concluded that the test was not helpful in the mild to moderate form where the sensitivity was 40% and 33%. This is in agreement with other studies scoring a sensitivity from 0 to 47%.^{1,2,8} for the mild form of chronic pancreatitis or exocrine pancreatic insufficiency. Only Löser and colleagues³ claim a sensitivity of 63% for mild and 100% for moderate cases. It should be noted that in these groups the incidence of patients with

diabetes mellitus was 25% and 50%, which is unusually high and may indicate that these patients had more severe exocrine pancreatic insufficiency than believed. Furthermore, this group used bicarbonate output rather than bicarbonate concentration plus enzyme output for grading exocrine pancreatic insufficiency. In our experience, about a quarter of patients with abnormal bicarbonate concentration still have a normal bicarbonate output, and some of Löser *et al.*'s patients may have belonged to a more severe group according to our grading system. If they had used our system, they probably would have obtained a lower sensitivity for faecal elastase 1 in their moderate group.

Additionally, the specificity of the test for differentiating steatorrhoea of pancreatic and non-pancreatic origin is not sufficient as most patients with non-pancreatic malabsorption had false positive results in one study.⁶ The test may also show falsely low results in patients with diarrhoea and requires lyophilisation of stool samples, but even then very low concentrations of elastase 1 can be found, yielding indecisive information in most cases.⁹

Thus, the two major problems for the clinician—that is, the diagnosis of mild exocrine pancreatic insufficiency/chronic pancreatitis and differentiating pancreatic steatorrhoea/diarrhoea from non-pancreatic steatorrhoea/diarrhoea, cannot be solved with this new, and certainly not cheap, faecal enzyme test, and that was the key message of our paper.

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221; illustrated; £66.00.) Dordrecht: Kluwer Academic Publishers, 1997. ISBN 0-7923-8722-8.

I have yet to attend a Falk Symposium but it seems likely to be an agreeable experience. The ability to consider the big questions of biomedical science in a multidisciplinary setting is not to be missed. Perhaps if I write a good review I might be invited to the next one!

Symposium 91 considers two very important gastrointestinal problems which none the less make slightly strange bedfellows. The inside of the dust jacket, but not the cover, revealed that this was a Paediatric Symposium. This was a relief, as I was about to return it to the editor. Of the 168 pages devoted to review articles on inflammatory bowel disease (IBD), only 10 are dedicated to children. There is only one chapter on abdominal pain devoted to surgical aspects, followed by 27 poster abstracts on paediatric IBD and abdominal pain.

The first chapter is by Wakefield of the Royal Free Group, expanding on the popular and still controversial theme of measles and IBD. The symposium occurred in March 1996 and inevitably we miss out on his latest proposed links with autism and non-specific ileocolitis. A further hypothesis is proposed by Okabe, based on impaired natural killing and antibody dependent cell mediated cytotoxicity, with viruses, again, as a possible target. The second chapter (Brandtzaeg, Haraldsen, and Rugtveit) presents a more conventional hypothesis based on failure of immune exclusion. Amongst the inevitable plethora of abbreviations there are gems such as the use of interleukin 10 enema in IBD. Wallace and Bell suggest an alternative method of controlling inflammation by preventing white cells from adhering to the endothelium.

A chapter by Fujihashi and 13 others on mucosal immunity is of greater interest to vaccinologists rather than to gastroenterologists. The following chapter by Hollander and only five others covers the fascinating area of animals that lack specific cytokines and that develop chronic IBD but only in the presence of gut flora. An impressively fruitful area for research and potential interventions.

In the first chapter of the clinical section, Seidman and Deslandres have written a salutary chapter highlighting the most of the mistakes that I have made in the management of paediatric IBD. It should be required reading for paediatric gastroenterologists.

In the treatment section, Behrens points out that there have been no randomised, controlled clinical trials of 5-amino salicylic or sulphasalazine in children. The same applies to slow release budesonide, reviewed by Scholmerich. This section concludes with two chapters by Hadziselimovic and Emmons, and Sumer on interferon α as therapy and all give it a warm welcome.

Finally, the surgical contribution by Herzog on chronic abdominal pain in children is inherently interesting, but it avoids the 95% of children in whom abdominal pain has no cause.

Of the 27 abstracts (one in German) *Helicobacter pylori* was a popular subject. Of seven abstracts, four related to abdominal pain. There were richer pickings for abdominal pain in 10 abstracts in this section.

Hence abdominal pain has been short changed compared with IBD in this volume, reflecting the research activity, relative sever-

ity but not the frequency of the two conditions. In retrospect, it might have been more sensible to concentrate on paediatric IBD. Because of this bias, and the excellent chapters on IBD, this volume would appeal to gastroenterologists of the adult type. Let's hope that the price comes down when we move to a single currency.

D C A CANDY

Helicobacter Infection. Edited by Farthing MJG, Patchett SE. (Pp 263; illustrated; £45.00.) London: Royal Society of Medicine Press, 1998. ISBN 1-85315-342-7.

Helicobacter pylori is my favourite animal, but even allowing for that I found this monograph (because that is what it really is) a real page turner. If one is honest about it, few medical texts are actually enjoyable to read and ploughing through the so called literature can be hard work. Many books contain a lot of useful facts, but the prose can be turgid and laden with clichés. This issue of the British Medical Bulletin is a shining exception to the rule. Attractively produced by the Royal Society of Medicine Press, it sits easily in the hand and for a paltry £45 the 28 authors will take you on a fascinating and enlightening tour of the *H pylori* scene. On the way you will visit basic science, epidemiology, the clinical conditions associated (or not, as the case may be) with *H pylori* infection, diagnosis, treatment and management strategies, paediatrics and non-gastrointestinal effects of *H pylori* infection, and the possible development of a vaccine. The tour ends with a debate on the important topic of cost effectiveness of eradication therapy.

The planning committee was chaired by the Editor of *Gut* (Professor Michael Farthing), assisted by Dr Duncan Bell, Dr Jean Crabtree, Professor David Forman and Dr Stephen Patchett, and they have done an excellent job. Remarkably, for a multi-author text, there are no overlaps between the chapters and the scientific editors (Farthing and Patchett) must have worked very hard to have achieved an impressive uniformity of style. All the contributions are of a high standard, all are written by internationally recognised experts in the respective fields and deal authoritatively with their topics. The bibliographies include papers published up to 1998.

Does the book contain everything one needs to know about *H pylori* in 1998? Pretty nearly, but not quite—no one is perfect. To allow myself a few minor quibbles: perhaps the relation of *H pylori* to gastro-oesophageal reflux disease and the post eradication symptoms in patients with duodenal ulcer, could have been discussed.

Who should read this volume? As everyone knows, there has been a veritable explosion of publications on the various aspects of *H pylori*, but do we really need another monograph on it? If it reaches the standard achieved by *Helicobacter Infection*, the answer is a resounding yes. For the committed helicobacterites *Helicobacter Infection* provides an excellent refresher course and will stimulate those who are casting about for interesting hypotheses to test and grant application to write. Clinical research workers and hospital clinicians will find helpful discussions and even some answers, to the many dilemmas and uncertainties that still bedevil the management of *H pylori* infection. One is tempted to say that this text is required reading for the

BOOK REVIEWS

Inflammatory Bowel Diseases and Chronic Recurrent Abdominal Pain. Edited by Hadziselimovic F, Herzog B. (Pp