LETTERS TO THE EDITOR

Postprandial mesenteric blood flow

SIR,—We read with interest the study by Sieber *et al*[1] in which they used Doppler ultrasound to measure superior mesenteric arterial blood flow in response to liquid test meals given orally and intraduodenally (with and without atropine), and the additional effects of the infusion of combinations of cholecystokinin octapeptide 8, secretin, gastrin 17, and glucagon. We would like to raise several points.

(1) The authors used a 3 MHz Doppler flowmeter. Wavelength considerations with this frequency probe dictate that the best AP spatial resolution of the diameter measuring cursor is ±1 mm (a best 'guess' of 0·5 mm can sometimes be made). The authors, however, have quoted superior mesenteric artery diameter readings to two decimal points and claim to be able to show increases in the diameter of between 5 and 26% after food intake. Furthermore, it is not clear whether an AP and lateral cross sectional diameter reading or a single longitudinal AP diameter reading was taken (in which case the superior mesenteric artery was assumed to be circular). It would have been better if the authors had quoted the mean and the range of the diameter reading.

(2) The quoted increase in superior mesenteric arterial blood flow in response to the oral test meal (180–360% above basal) is far greater than previous reports.[2–5] It is not clear from the data whether the same subjects were studied on all occasions and compared – a total of nine subjects was enrolled in the study but data are only shown for six. If the same six subjects were not examined on each occasion, direct comparisons between experiments are less reliable. This is further compounded by the clear differences in basal mean (SEM) flow rates between the experiments (data not all shown) of 443 (38) ml/minute before the oral test meal and 520 (56) ml/minute before the intraduodenal test meal. What is the day to day coefficient of variation for the technique in their hands? Were all observations performed by one operator?

(3) The authors state that they infused glucagon, cholecystokinin octapeptide 8, secretin, and gastrin in doses designed to simulate postprandial circulating concentrations. No data, however, are presented to support this, and the authors cannot therefore be sure that physiological concentrations of these hormones were achieved. Furthermore, the dose of glucagon used (500 ng/kg/hour or 8·33 ng/kg/minute) is a supraphysiological dose[6–10] and would result in plasma concentrations much greater than those normally circulating postprandially. A dose of less than 3 ng/kg/minute would have been more appropriate. We cannot therefore agree with the authors' contention that the hormones 'are unlikely to be involved as blood borne hormones' in mediating splanchinic vasodilation on the data presented but agree with the hypothesis.

We have recently shown (unpublished data) that fasting superior mesenteric arterial blood flow in six subjects measured by Doppler ultrasound decreases during physiological infusions of glucagon. A 1 ng/kg/minute infusion produced no detectable rise in basal glucagon concentrations (mean (SEM) basal glucagon values 144 (15) ng/l: after 30 minutes 1 ng/kg/minute glucagon infusion resulted in a value of 129 (80) ng/l) and a 3 ng/kg/minute glucagon infusion raised values to 214 (37) ng/l. Mean (SEM) fasting blood flow fell from 678 (97) ml/minute to 549 (88) ml/minute after 30 minutes of 1 ng/kg/minute glucagon infusion and to 453 (63) ml/minute after 20 minutes of a 3 ng/kg/minute infusion. There were no associated changes in cardiac output, stroke volume, blood pressure, pulse, or peripheral vascular resistance. This suggests that glucagon is a selective splanchnic vasoconstrictor at physiological concentrations and, indeed, is not involved in mediating the postprandial hyperaemia observed in previous studies. It is noteworthy, however, that Lee *et al*[11] using indocyanine dye clearance methods showed that supraphysiological infusions of 10 and 20 ng/kg/minute glucagon caused no systemic haemodynamic or total hepatic blood flow changes in a group of cirrhotic subjects. Azygous blood flow, however (and hence superior mesenteric blood flow), rose significantly in those with well compensated cirrhosis, suggesting that at supraphysiological doses (similar to those used by Sieber *et al*[1]) glucagon may be a splanchnic vasodilator.

(4) The authors state that blood pressure and pulse were monitored throughout the experiments but apart from incomplete data for the intraduodenal test meal with and without atropine, they present no evidence of blood pressure or pulse rate changes in response to any of their meals or infusion experiments. The pulse and blood pressure response to meals varies with both the age of the subject[12] and meal composition,[13] and these data should have been included or discussed in the current study.

(5) Atropine was shown to attenuate the postprandial hyperaemic response to the meal, suggesting that the cholinergic nervous system has a role in this change. The mechanism for the postprandial response is, however, likely to be multifactorial and may also involve β adrenergic[14] and peptidergic mechanisms. Neurotensin,[15] vasoactive intestinal polypeptide,[16] and calcitonin gene related peptide[17] are known to be powerful splanchnic vasodilators and may also be involved in postprandial splanchnic vasodilation.

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Reply

SIR,—Dr Wells raises important points about our recent publication,[1] especially about the methodology used to assess superior mesenteric artery blood flow (SMABF). Several comments need clarification, however, and we would like to reply in the same order as given in the letter:

(1) We used a 3·5 MHz sector scanner for diameter measurements (and not a 3 MHz Doppler flowmeter as stated in the letter). This sector probe was combined with a pulsed Doppler flow meter (3·0 MHz). Diameters were presented as mean (SEM) cm units. The statement that we were reporting two decimal points is therefore rather misleading.

In our experience, the superior mesenteric artery has a circular anatomy which is an advantage compared with the portal vein where the determination of the cross sectional area of the vessel is complicated by an ellipsoid vessel shape.

(2) We are puzzled by the statement that the increases in postprandial SMABF reported in our paper were far higher than in the published reports: similar increases have been reported by others[2–4] with comparable meals and caloric loads. On the other hand, the reports cited by Dr Wells are hardly comparable.

In one study,[5] a different technique was employed to quantify SMABF (dye dilution). In a second, a lower caloric load was tested[6] and in the study of Qamar[7] only fasting SMABF was measured.

Nine subjects participated in this study. For all oral food experiments as well as the hormone studies, the same six volunteers were studied. For the experiments involving intraduodenal food application, three additional subjects were

recruited as three volunteers from the first set of experiments were not happy to swallow an intraduodenal tube.

Fluctuations in basal SMABF between different test days do, in our review, reflect acceptable physiological variations. As all determinations were performed by the same investigator (CS), the fluctuations cannot be attributed to an interobserver variability.

(3) We have measured postprandial secretin, cholecystokinin, and gastrin concentrations for many years.[8-10] We did not measure these in the present study, because we felt that the plasma concentrations did not add any new pertinent information. We acknowledge the references stated with regard to glucagon values found postprandially. Even if the glucagon dose employed induced an increase at the upper limit of physiological glucagon concentrations, we still believe that our conclusions are valid and this is underlined by the lack of change in SMABF observed in our study with this dose of glucagon.

We cannot comment on the unpublished data discussed in the letter, as they are not available yet.

In summary, we have presented data on specific mechanisms regulating postprandial mesenteric artery blood flow using the echo-Doppler flowmetry. Quantitative studies of postprandial hyperaemia are important for the understanding of normal physiological processes. We therefore hope that future research by various groups (as the group of Dr Wells) will be able to shed more light into the physiology and pathophysiology of intestinal blood flow regulation.

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Helicobacter pylori infection in healthy people

SIR,—We have recently published the results of an epidemiological study in *Gut* reporting discrepancies between active *Helicobacter pylori* (Hp) infection determined by means of the ^{13}C-urea breath test and the prevalence of anti-Hp antibodies in healthy volunteers. Further developments in serological tests make it necessary to report additional information and to reconsider our conclusions based on the serological data presented in the paper.

A systemic humoral immune response to *H pylori* has been searched for in many studies (including our own) by similar serological tests,[1-5] some of which have become commercially available. They have all in common that whole bacterial cells were primarily used as antigen (acid glycine extracts or sonicated whole cell preparations or formalin treated bacteria). The antigen used in these tests, however, contains flagella proteins that are well known to share antigenicity with flagellae of other bacteria, especially *Campylobacter jejuni*.[6 7] False positive serological test results can therefore not be excluded. Thus new serological tests using purified high molecular outer membrane proteins of *H pylori* and urease as antigens have recently been developed.[8 9] These second generation serological tests may be more specific for *H pylori* infection.

We have investigated the sensitivity and specificity of several different serological tests in a population of patients in whom the presence or absence of *H pylori* infection was unequivocally established. These patients all had upper gastrointestinal tract endoscopy with antral mucosal biopsies that were used for microbiological *H pylori* culture, and a quick urease test (CLO test) and they all underwent a ^{13}C-urea breath test. Sera were used only from patients in whom either all three tests were positive (*H pylori* infection present) or all three tests were negative (infection absent). These latter patients were also questioned about treatment with antibiotics within the past six months and included in the present analysis only if the response was negative. Sera from this population were tested for anti-Hp antibodies with our own enzyme linked immunosorbent assay ELISA and two commercially available, first generation serological tests (anti-Hp IgG EIA Roche, Hoffman-La Roche, Basel, Switzerland, and GAP test IgG, Bio Rad Laboratories, Glattbrugg, Switzerland) and a new second generation serological test that uses a well characterised, highly immunogenic, purified Hp-specific multicomponent antigen preparation free of cross reacting flagella proteins (anti-Hp IgG EIA Roche second generation, Hoffman-La Roche). Sera from 223 patients were tested; 64 patients had *H pylori* infection and 159 did not. The sensitivity and specificity of the four serological tests are shown in the Table.

	Meyer et al[1]	*Roche 1st*	*GAP*	*Roche 2nd*
Sensitivity	100	93	94	97
Specificity	80	85	85 (96)*	93

*If test results were included that reacted slightly or strongly (specificity within parentheses) positive.

Firstly, it is obvious that the three first generation tests react positively in 15–20% of people who have no active *H pylori* infection. If the same people are, however, tested with the second generation test, only 7% have anti-Hp without active infection. The cumulative percentage of patients reacting with either one of the three first generation tests amounted to 29%, resulting in a specificity of only 71%. These findings support the hypothesis that with first generation serological tests in an important fraction of people, anti-Hp antibodies may be due to non-specific binding to the antigen in the test kit rather than to a specific response to *H pylori* infection in the past. While it is still possible that healthy people eventually eliminate *H pylori* spontaneously, this conclusion may not be drawn from our results based on the first generation serological test that was used. Similar caution, however, should be used in the interpretation of virtually all studies that reported *H pylori* prevalence data based on first generation serological tests.[1-5] Epidemiological studies designed to gather information on the prevalence of *H pylori* should preferentially use direct proof of infection rather than serology.

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Medical treatment of bleeding peptic ulcer: old drugs, new regimens

SIR,—Haemorrhage from peptic ulcer is due to the erosion of artery at the ulcer base by the combined digestive actions of acid and pepsin. Platelet plug and clot formation (both factors being pH sensitive) seal the bleeding artery. Dissolution of the clot is the most important factor for peptic ulcer rebleeding.[1] Intragastric acidity prolongs the duration of bleeding[2] as the gastric juice contains fibrinolytic substances[3] and a pH <7 results in inhibition of platelet aggregation and dissolution of the clot.[4] Understandably then, attempts to counteract the acid[5 6] or pepsin[7] or to inhibit fibrinolysis[8] should result in stabilisation of the clot and prevention of rebleeding. Yet to date the efficacy of none of the above mentioned drugs