In conclusion, the value of clinical ultrasound is widely underestimated both by clinicians, family practitioners, and radiologists as well. Clinical ultrasound deserves a more widespread use than in departments of radiology alone because of its beneficial effects on patient care, the ease, speed, and safety of decision making and its capability for conserving scarce financial and manpower resources.

L GREINER
Medical Clinic A – Gastroenterology,
Klinikum Wuppertal, University Witten/Herdecke,
Heusnerstr 40, D-42283 Wuppertal, Germany

Reply

EDITOR,—Professor Greiner is right to extol the virtues and simplicity of sonography as a first line imaging investigation in patients with gastrointestinal and abdominal disease and he is equally correct to point out that these values are not universally appreciated. In many countries, particularly the USA, sonography is less widely used, with the consequence that comparatively costly investigations such as endoscopy and magnetic resonance imaging or those involving ionising radiation, such as computed tomography are more liberally used in preference. In the UK however, gastroenterologists and surgeons appreciate the benefits of simple sonography and already understand most of the issues.

There are four questions of practical importance raised by Professor Greiner's letter. Who should do ultrasound? What are the costs? Is the Volkswagen as good as the Rolls Royce, and what training is necessary?

Many radiologists would disagree with me, but I do not feel that it matters who undertakes sonography, as long as they are properly trained and continue to learn by a process of audit and CME activity.

Costs are difficult to evaluate precisely, but the capital and revenue implications of a larger number of less frequently used ultrasound machines, are probably greater than those for a smaller number of centrally available, but heavily used machines. This is particularly so in view of the comparatively short life of an ultrasound machine, consequent upon rapidly advancing ultrasound technology. Most British hospitals tend to run a central endoscopy unit, used by physicians, surgeons, radiologists, and general practitioners, appreciating that a fragmented service is more costly. This is no less likely to be so for ultrasound than it is for endoscopy.

I cannot agree with Professor Greiner that the cheaper Volkswagen machine is as effective as the Rolls Royce machine. There are no hard data on this and a true comparison would have to take into account the cost of missed diagnoses and misdiagnoses that occur as a consequence of the equipment alone. Certainly radiologists appreciate that the sophisticated high specification machines give greater versatility and confidence to the examiner. Perhaps the real analogy between the Volkswagen and the Rolls Royce is not to ask which gets from A to B better, but to ask which you would rather have around you in difficult circumstances when there is the potential for danger or disaster.

Finally, Professor Greiner does not tackle the requirements for training at all. How do we define training for non-radiologists undertaking sonography? How do they know they are adequately trained and more importantly, how does the patient know that

they are adequately trained? Just as in endoscopy, the patient may well not be interested in whether the examiner is a physician, surgeon, nurse, sonographer, radiologist or general practitioner, as long as the examiner is properly trained and provides a safe, accurate service. Again, just as with endoscopy, I believe that it is the provision of acceptable training guidelines, which is the most crucial aspect of this debate and which will dictate the quality of ultrasound services.

D F MARTIN
Department of Radiology,
Withington Hospital, Nell Lane,
West Didsbury, Manchester M20 2LR

Diverticular disease

EDITOR,—The aetiology of non-infectious colitis may be difficult to ascertain as mucosal biopsy specimens do not consistently demonstrate diagnostic features.^{1,2} Shepherd provided a timely and comprehensive review of such inflammatory changes associated with diverticular disease (*Gut* 1996; 38: 801–2), highlighting the diversity of the inflammatory processes and providing an insight into the pathogenesis of ulcerative colitis. However in our experience diverticular disease presenting as a chronic continuous colitis is unusual.

We recently reviewed the case notes of all patients with a histological diagnosis of chronic non-specific proctocolitis made between 1985 and 1990 at our hospital. Of the 42 patients initially diagnosed 14 were subsequently shown to have ulcerative colitis. Twenty one patients had non-specific proctocolitis on repeat biopsies and the colitis in these patients, who were predominantly young women (18 women mean age 43), ran a prolonged (average five years) but mild course. Only continuous colitis was observed. Just two patients with colitis had concomitant diverticular disease and, in contrast with other studies,³ neither rectal sparing nor progression to ulcerative colitis was observed. The remaining patients had clinically distinct diagnoses such as radiation colitis.

We conclude that although diverticular disease associated colitis is a recognised entity, in our clinical practice its occurrence is rare constituting just two cases over a five year period. We accept that some diagnoses of ulcerative colitis or Crohn's colitis may be incorrect, none the less the association with diverticular disease appears unusual. Our finding that persistent non-specific proctocolitis predominated in women of reproductive age may suggest a distinct disease and warrants further investigation. However our report is limited to both sample size and duration of follow up; these deficiencies are currently being addressed.

N P MICHELL
G CHUNG-FAYE
D B TRASH
Manor Hospital,
Moat Road,
Walsall WS2 9PS

1 Nottegham B, Salomez JL, Gower-Rousseau C, Marti R, Lemahieu M, Nuttens MC, *et al.* What is the prognosis in unclassified colitis? Results of a cohort study of 104 patients in the Northern-Pas-de-Calais Region. *Gastroenterol Clin Biol* 1993; 17: 811–5.

2 Le Berre N, Heresbach D, Kerbaol M, Culet S, Bretagne JF, Chaperon J, *et al.* Histological discrimination of idiopathic inflammatory bowel disease from other types of colitis. *J Clin Pathol* 1995; 48: 749–53.

3 Makapugay LM, Dean PJ. Diverticular-disease associated chronic colitis. *Am J Surg Pathol* 1996; 20: 94–102.

Reply

EDITOR,—I entirely concur with the sentiments by Michell *et al* with regard to the difficulties of biopsy diagnosis in so called non-infectious colitis. I also accept that diffuse chronic inflammatory pathology associated with diverticular disease is a rare condition, as my leading article indicated. Focal luminal inflammation is more common in diverticular disease¹ but is still rare giving the overall prevalence of diverticular disease in the population. I was interested in their series that not only reports the comparative rarity of diffuse 'diverticular colitis' but also seems to identify an interesting subgroup of patients, particularly young women, with prolonged but mild 'inflammatory bowel disease'. As they indicate, this series of patients requires further investigation as to whether it represents a distinct disease entity.

N A SHEPHERD
Department of Histopathology,
Gloucestershire Royal Hospital,
Great Western Road,
Gloucester GL1 3NN

1 Gore S, Shepherd NA, Wilkinson SP. Endoscopic crescentic fold disease of the sigmoid colon: the clinical and histopathological spectrum of a distinctive endoscopic appearance. *Int J Colorect Dis* 1992; 7: 76–81.

Helicobacter pylori and duodenogastric reflux

EDITOR,—The paper by Ladas *et al* (*Gut* 1996; 38: 15–8) considers a very interesting theme, however it has some important methodological drawbacks, which in my opinion may affect the results. Firstly, a one hour assessment of duodenogastric reflux (DGR) seems inappropriate. A 24 hour monitoring is needed to quantify the exposure time of the mucosa to the refluxate. This is true because, although duodenogastric reflux physiologically occurs during 24 hours in normal subjects,^{1,2} 18 of 29 (62.1%) subjects included in this study and, more importantly, eight of 18 (44.4%) of those who were considered more prone to reflux (*H pylori* positive subjects) were shown to be devoid of duodenogastric reflux. Secondly, the *H pylori* positive and *H pylori* negative series of subjects hardly seem comparable (44.4% DU, 44.4% NUD, 11.1% oesophagitis in the *H pylori* positive and 18.2% DU, 81.8% NUD in the *H pylori* negative group). These different illnesses are certainly capable of affecting duodenogastric reflux differently, independently from *H pylori* status! Thirdly, post-treatment assessment of duodenogastric reflux (despite the inadequate method) in the three subjects, who had pre-treatment reflux and were not successfully cured of *H pylori*, would have been interesting. Reflux persistence after eradication failure could have represented a good counterproof and would have strengthened the datum of eradication associated reflux disappearance, which was obtained in only six subjects! Unfortunately this was not done.

Therefore, the paper provides enough evidence for the conclusion that '*H pylori* may survive the noxious effect of bile reflux in the

intact stomach', but this is well known and obvious because duodenogastric reflux is a physiological event, which takes place in all the subjects as well as in all the *H. pylori* positive ones. In contrast, in my opinion, because of these *methodological* reasons the statement that 'data suggest that *H. pylori* may induce DGR' is apodictical and needs to be proved by examining wider series and using more adequate methods.

P BECHI
Istituto Clinica Chirurgica,
V.le Morgagni, 85,
50134 Florence, Italy

- 1 Keane FB, Dimagno EP, Malagelada JR. Duodenogastric reflux in humans: its relationship to fasting antroduodenal motility and gastric, pancreatic and biliary secretion. *Gastroenterology* 1981; **81**: 726–31.
- 2 Schindlbeck NE, Heinrich C, Stellaard F, Paumgartner G, Müller-Lissner SA. Healthy controls have as much bile reflux as gastric ulcer patients. *Gut* 1987; **28**: 1577–83.

Reply

EDITOR,—We appreciate the comments raised by Dr P Bechi about our recent publication (*Gut* 1996; **38**: 15–8). We agree that one hour assessment of duodenogastric reflux (DGR) by double labelled scintigraphy may not be the most sensitive method for DGR estimation. However, the use of a nasogastric aspiration tube¹ and perfusion techniques² to measure DGR over several hours are unphysiological. The nasogastric tube may induce DGR and the unpopularity of such experiments preclude the investigation of a proper number of patients. The new method of 24 hour portable DGR monitoring (Bilitec 2000, Synectics) is currently the best method to measure DGR quantitatively^{3–4} in the fasting and postprandial state, during day and night. This technique was not available when we carried out our study, and it is still under investigation and standardisation.^{3,4}

We also agree with the comment that 'normal' subjects have various degrees of DGR, but studies of 'normal' subjects have not discriminated *H. pylori* positive and negative persons.^{1–4} However, it has recently been shown that patients with type B gastritis have a high incidence of DGR.⁵ This study lends support to the results of our experiments, where we have shown that significantly more patients who had DGR were *H. pylori* positive (91 v 44%, $p=0.01$) and that DGR is reduced after successful *H. pylori* eradication. These evidences justify our statement that '*H. pylori* may induce DGR'.

S D LADAS
S A RAPTIS
Gastroenterology Unit,
Second Department of Internal Medicine,
Athens University, Evangelismos Hospital,
Athens, Greece

H MALAMOU
Department of Clinical Microbiology,
Penteli Children's Hospital,
Palia Penteli, Greece

H GIANNOPOULOU
M KESSE-ELIA
Department of Nuclear Medicine,
Evangelismos Hospital, Athens

- 1 Schindlbeck NE, Heinrich C, Stellaard F, Paumgartner G, Wuller-Lissner SA. Healthy controls have as much bile reflux as gastric ulcer patients. *Gut* 1987; **28**: 1577–83.
- 2 Keane FB, Dimagno EP, Malagelada JR. Duodenogastric reflux in humans: its relationship to fasting antroduodenal motility and gastric, pancreatic and biliary secretion. *Gastroenterology* 1981; **81**: 726–31.

- 3 Just RJ, Kuo B, Castell DO. Changes in intra-gastric pH show poor correlation with duodenogastric bile reflux. *Gastroenterology* 1994; **100**: A101.
- 4 Kauer WKH, Ireland AP, Peters JH, Johnson WE, Bremner CG, DeMeester TR. Evaluation of duodenogastric reflux in patients with gastric symptoms utilizing a fiberoptic sensor for bilirubin. *Gastroenterology* 1995; **108**: A122.
- 5 Okamoto E, Haruma K, Fujimura J, Hata, Yamanaka H, Tani H, *et al.* High incidence of duodenogastric reflux in patients with type-B gastritis. *Gastroenterology* 1995; **108**: A661.

Calcium and colorectal epithelial cell proliferation

EDITOR,—There is still much debate whether calcium can prevent colorectal cancer in patients with an increased risk of the development of such tumours. Calcium intervention studies, using epithelial cell proliferation as an intermediate end point, have produced inconsistent results. Most studies have focused only on the effect of calcium on the rectal epithelium. Several open uncontrolled studies^{1–4} have shown a reduction of rectal epithelial cell proliferation during calcium supplementation, but small placebo controlled studies are not as uniform in their conclusions.^{5–8} Recently Weisgerber *et al* (*Gut* 1996; **38**: 396–402) considered this aspect of sample size, as well as the fact that studies were performed with biopsy specimens from the rectum. With respect to the small size of patient populations, two recent studies included much larger numbers of subjects. Bostick *et al*, performed a randomised, double blinded study in sporadic adenoma patients.⁹ Patients received placebo ($n=66$), 1 g calcium/day ($n=64$) or 2 g calcium/day ($n=63$) for six months. Rectal biopsy specimens were obtained at baseline, and at one, two, and six months. In this study no difference in proliferation was observed between the three groups. However, calcium normalised the distribution of proliferating cells in the crypts, which is supposedly beneficial with respect to cancer risk. Rothstein *et al*¹⁰ published a preliminary report on a very large study in which adenoma patients were randomised to receive 1.2 g calcium ($n=173$) or placebo ($n=160$). Before and after six to nine months supplementation rectal biopsy specimens were taken. Calcium had no effect on proliferation and, in contrast with the previous study, no effect on the distribution of proliferating cells either. With respect to the effect of calcium on proliferation of colonic mucosa, Weisgerber *et al*¹¹ suggested in their recent paper that, apart from one open uncontrolled trial,¹² this had not been studied before. In another open uncontrolled study we unexpectedly observed an increase of proliferation in the sigmoid of adenoma patients after 12 weeks 1.5 g calcium/day.¹³ Weisgerber *et al*¹¹ performed a randomised, double blinded study and did not find any effect of longterm calcium supplementation on sigmoidal cell proliferation. These results confirm to a great extent our recently reported findings in a randomised, double blinded study in 30 first degree relatives of patients with hereditary non-polyposis colorectal cancer.¹⁴ These subjects are known to have an increased epithelial cell proliferation rate,¹⁵ which responded to calcium in two open studies.^{1,2} The subjects received 1.5 g calcium/day or

placebo. To elucidate the potential site specific effects of calcium in the colorectum, biopsy specimens were obtained from the rectum, sigmoid, and descending colon, before and after three months. In none of the three parts of the colorectum was a significant effect of calcium on proliferation observed compared with placebo. The only noticeable difference between the two groups was a decrease of proliferation rate in the luminal crypt compartment in the rectum during calcium compared with placebo, a finding similar to that of Bostick *et al*.⁹

In summary, from the randomised, double blinded studies reported, the following conclusions can be drawn: (1) in the rectum calcium supplementation may normalise the abnormal distribution of proliferating cells in the crypt without affecting overall proliferation rate; (2) no appreciable effect of calcium supplementation on proliferation in the sigmoid can be observed, and the same seems to be true for the descending colon. Based on these conclusions considerable doubt should arise on the value of calcium supplementation for the prevention of colorectal cancer in people with an increased risk of this disease.

J H KLEIBEUKER
N H MULDER
A CATS
R VAN DER MEER
E G DE VRIES
Departments of Gastroenterology and
Medical Oncology,
University Hospital Groningen PO Box 30.001,
9700 RB Groningen, and
Netherlands Institute for Dairy Research,
Ede, the Netherlands

- 1 Lipkin M, Newmark H. Effect of added calcium on colonic epithelial-cell proliferation in subjects at high risk for familial colonic cancer. *N Engl J Med* 1985; **313**: 1381–4.
- 2 Lipkin M, Friedman E, Winawer SJ, Newmark H. Colonic epithelial cell proliferation in responders and nonresponders to supplemental dietary calcium. *Cancer Res* 1989; **49**: 248–54.
- 3 Rozen P, Fireman Z, Fine N, Wax Y, Ron E. Oral calcium suppresses increased rectal epithelial proliferation of persons at risk of colorectal cancer. *Gut* 1989; **30**: 650–5.
- 4 Lans JJ, Jaszwski R, Arlow FL, Tureaud J, Luk GD, Majumdar APN. Supplemental calcium suppresses colonic mucosal ornithine decarboxylase activity in elderly patients with adenomatous polyps. *Cancer Res* 1991; **51**: 3416–9.
- 5 Gregoire RC, Stern HS, Yeung KS, Stadler J, Langley S, Furrer R, *et al.* Effect of calcium supplementation on mucosal cell proliferation in high risk patients for colon cancer. *Gut* 1989; **30**: 376–82.
- 6 Wargovich MJ, Isbell G, Shabot M, Winn R, Lanza F, Hochman L, *et al.* Calcium supplementation decreases rectal epithelial cell proliferation in subjects with sporadic adenoma. *Gastroenterology* 1992; **103**: 92–7.
- 7 Barsoum GH, Hendrickse C, Winslet MC, Youngs D, Donovan IA, Neoptolemos JP, *et al.* Reduction of mucosal crypt cell proliferation in patients with colorectal adenomatous polyps by dietary calcium supplementation. *Br J Surg* 1992; **79**: 581–3.
- 8 Bostick RM, Potter JD, Fosdick L, *et al.* Calcium and colorectal epithelial cell proliferation: a preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 1993; **85**: 132–41.
- 9 Bostick RM, Fosdick L, Wood JR, Grambsch P, Grandots GA, Lillemo TJ, *et al.* Calcium and colorectal epithelial cell proliferation in sporadic adenoma patients: a randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 1995; **87**: 1307–15.
- 10 Rothstein RI, Baron JA, Tosteson TD. Effect of calcium supplementation on human rectal mucosal proliferation: a randomized controlled trial. *Gastroenterology* 1995; **108**: A530.
- 11 Weisgerber UM, Boeing H, Owen RW, Waldherr R, Raedtsch R, Waldendorf J. Effect of longterm placebo controlled calcium supplementation on sigmoidal cell proliferation in