found a median delay of 17 weeks from the onset of symptoms to a definitive histological diagnosis in patients with gastric cancer. Use of an open access endoscopy service reduced this delay. There was no correlation between the delay in diagnosis and tumour stage or the success of potentially curative resection. The prognosis for gastric cancer is poor. To detect early gastric cancer, patients should be examined before the onset of dyspeptic symptoms. Fortunately, gastric cancer is rare in the Western world and epidemiological studies have shown that the incidence of and mortality from gastric cancer have decreased considerably. Screening people for gastric cancer before the onset of symptoms is therefore not feasible. Early detection of gastric cancer is not yet possible, and focusing attention on patients with a history of serious gastrointestinal symptoms may be of little value.

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1 van Weel C. Validating long term morbidity recording. *J Epidemiol Community Health* 1995;49(suppl 1):29-32.

2 Martin IG, Young S, Sue-Ling H, et al. Delays in the diagnosis of oesophagogastric cancer: a consecutive case series. *BMJ* 1997;314:467-71.

Reply

EDITOR,—The points raised by Laheij and colleagues are relevant to the debate regarding the late diagnosis of gastric cancer in Western Europe. Their figure of 39% consulting their general practitioner over a mean time period of 12 years is not far away from our figure of 30% investigated for symptoms in the 13 years leading up to diagnosis. We are not suggesting that all of these patients had gastric cancer at the initial time of presentation, but many almost certainly did (most of those investigated in the last four years—a "miss" rate of 1 in 6). There are two important points to note. Firstly, general practitioners may not think of the correct diagnosis because of previous (reassuring) investigations with the result that the diagnosis is delayed by years not months. Secondly, and related to the first point, general practitioners will prescribe powerful acid suppression for patients with a previous ulcer history which will result in resolution of symptoms and a further delay in diagnosis. This raises the question when do general practitioners re-refer a patient for gastroscopy when previous investigations showed no pathology or benign disease? It is also important to remember that early gastric cancer has "benign" symptoms and so it is effectively too late when the patient has lost weight or become anaemic.

We disagree that gastric cancer cannot be diagnosed earlier and progress will only be made if we alter current practice to include investigating patients "at risk" before starting

antisecretory therapy and lowering the threshold for re-investigating patients who may have a history of dyspepsia. Screening is not feasible and we are not proposing such a policy. However within current practice we feel that there is room for improvement in the diagnosis of this disease which is not uncommon, representing the fourth commonest cancer in men in the UK.

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The genetics of ulcerative colitis based on one Swede

EDITOR,—I was interested to read the review on the role of inherited factors in inflammatory bowel disease by Satsangi *et al* (*Gut* 1997;40:572-4), but dismayed by the evidence provided. They claim that twin pairs provided strong evidence for genetic predisposition and that the most pertinent was that reported by Tysk *et al* using data from the Swedish Twin Registry.¹ However, the claim for ulcerative colitis rests on a single twin of the 50 000 registered. The probands were identified as hospitalised cases in Sweden. The 50 pairs of twins where one twin had suspected ulcerative colitis were whittled down to 36 pairs: 16 monozygotic and 20 dizygotic or of unknown zygosity. No hospitalised pairs were found. Twins of probands were interviewed and the occurrence of any gastrointestinal complaint was thoroughly discussed in order not to miss a mild non-hospitalised case. In spite of this approach only one twin of a proband could be claimed as a case of ulcerative colitis and he was one of the monozygotic group. This pair had only distal ulcerative colitis. From this one twin a heritability coefficient of 0.53 was calculated (with 95% confidence interval 0.24 to 0.82) and not 0.24 to 1.0 as stated by Satsangi *et al*. Thus, the 53% heritability claimed in both papers is based on one man with mild ulcerative colitis. The definition of his disease differed from that in the probands and the authors admit to deficiencies in their selection procedure. Tysk *et al* also admit that the prevalence of ulcerative colitis in the twins differs from that of the general population in Stockholm (mostly singletons). Twin studies cannot inform about disease in singletons if the prevalences are not the same. As the mean observation period was almost 20 years, it is unlikely that many more healthy twins will develop ulcerative colitis.¹ With 94% discordance in monozygotic twins, it is difficult to accept that most ulcerative colitis is inherited in either twins or singletons.

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1 Tysk C, Lindberg E, Jarnerot G, et al. Ulcerative colitis and Crohn's disease in an unselected population of monozygotic and dizygotic twins. A study of heritability and the influence of smoking. *Gut* 1988;29:990-6.

Reply

EDITOR,—We are grateful to Dr Harding for his comments, and we share his reservations regarding interpretation of twin studies in common diseases. Indeed, we have pointed out on a number of occasions that the genetic contribution in ulcerative colitis is less strong than that in Crohn's disease. Nevertheless, the model of disease inheritance which is most consistent with the epidemiological and molecular genetic data currently available is that Crohn's disease and ulcerative colitis are related polygenic disorders. The twin data are supported by epidemiological studies of familial prevalence from Scandinavia, the UK, and the USA. In recent years these epidemiological data have been supplemented by molecular genetic studies from a number of independent investigators. These studies have provided evidence for the presence of a number of genetic determinants of susceptibility and disease behaviour in ulcerative colitis. There is great optimism that these studies will result in an advance in the understanding of the pathogenesis of these common disorders. We strongly agree that both environmental as well as genetic factors are important in the pathogenesis of ulcerative colitis.

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Iron reduction therapy in hepatitis C

EDITOR,—Three papers in the July issue report on the possible association between iron and tissue damage in conditions other than haemochromatosis. Tan *et al* (*Gut* 1997;41:14-18) found that gastric cancer cells are more susceptible to photodynamic therapy when iron is removed. Boucher *et al* (*Gut* 1997;41:115-20) found that treatment of hepatitis C with interferon leads to a decrease in liver iron content. Bacon (*Gut* 1997;41:127-8) briefly commented on the association between iron and hepatitis C, including some evidence that iron depletion may be beneficial in patients who fail to respond to interferon α .

Shortly after Bacon *et al*'s pioneering report in 1993 on iron reduction therapy in hepatitis C,¹ and mainly because of a lack of any other option at the time, we started applying this form of therapy in our growing population of patients who had failed to respond to interferon and who had the unfavourable 1b genotype.

The simplest and cheapest way to reduce body iron stores is repeated drawing of one unit of whole blood (as for haemochromatosis). However, we encountered several unexpected difficulties in our attempts to implement a phlebotomy programme for patients with chronic hepatitis C. A small group of patients are reluctant to undergo repeated phlebotomy because of ethnic or psychological reasons (there is a belief that blood equals life and therefore that blood loss depletes the body of life giving power). A second group cannot tolerate blood loss because of recurrent episodes of faintness and presyncope. These patients need several hours' observation, a chaperone, and sometimes intravenous fluid before they can be discharged home. In a third group venous access is a problem. The