of the carbohydrate side chains. Thus, we feel that data obtained using different methods should be compared very cautiously. In our hands, the use of formalin fixed tissues has given the most reproducible results.

As far as the persistence of changes in lectin binding pattern after gluten free diet, Barresi *et al* provide very interesting and exciting results. We agree that further studies on this matter are still needed, as the patients studied by Barresi after 12 months of gluten free diet still showed partial villous atrophy. The persistence of changes observed by Barresi *et al* in these patients might in fact reflect the incompleteness of recovery rather than the expression of a primary defect.

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Gastroenterologists and nutritional support

SIR,—At the inaugural committee meeting of the Small Bowel/Nutrition Section of the British Society of Gastroenterology in September 1988 it was agreed that a survey should be undertaken to assess the degree of influence and/or participation of BSG members on the practice of clinical nutrition support in the United Kingdom. A brief questionnaire was circulated to 1500 BSG members in December 1988. All replies until June 1989 were collected and analysed; 168 completed questionnaires were returned – a response rate of 11·2%. The breakdown of occupation of respondents is listed in the Table.

TABLE *Completed questionnaires*

Respondents (n)	*Occupation/status*
68	Consultant physicians
36	Consultant surgeons
25	Consultant gastroenterologists
9	Senior registrars (medicine/gastroenterology)
7	Consultant paediatric gastroenterologists
4	Professors of medicine
4	Senior lecturers/readers (surgery)
4	Consultant paediatrician
3	Professors of surgery
3	Senior lecturers (medicine)
2	Senior registrars (surgery)
1	Professor of child health
1	Professor of paediatric gastroenterology
1	Senior lecturer (child health)

Ninety per cent of repondents were responsible for decision making for enteral nutrition of their own patients, but only 45% were responsible for decision making concerning total parenteral nutrition for their own patients. Eighty nine per cent of respondents were also responsible for enteral nutrition support of other clinicians' patients, dropping to only 29% for total parenteral nutrition. Some form of mutrition team or advisory group was available to 39% of respondents, and 7% were in charge of those teams. Six per cent of respondents had access to a team which solely advised on total parenteral nutrition. Three respondents said that nutrition teams were in the process of being 'set-up'. If a nutrition support team was not available (61%), over half respondents stated that 'no-one specific' was responsible for providing nutritional support or that there was 'variable' responsibility. Thirty per cent stated that nutrition support advice was given by the patients' own clinical team, 6·5% had advice provided by dietitians, 5% by consultant anaesthetists, and 3% by pharmacists.

In summary, most of the respondents admitted to some involvement with nutrition support – predominantly enteral. A minority of BSG members were involved with decisions for total parenteral nutrition, even with their own patients. Less than half of the BSG membership had access to nutrition teams. The poor response rate for the questionnaire of 11·2% can be compared with a response rate of 73·4% for a much more detailed and complex questionnaire sent to district dietitians.[1]

The results of this small survey suggest that members of the BSG play a very minor role in decision making for nutritional support. This is perhaps surprising considering the frequency with which gastroenterological patients (both medical and surgical) require nutritional support. It is to be hoped that the formation of the Small Bowel/Nutrition Section of the BSG will stimulate greater interest and participation of gastroenterologists in the practice of nutritional support as so many gastrointestinal diseases are associated with nutritional problems.

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Randomised, double blind comparison of omeprazole and cimetidine in the treatment of symptomatic gastric ulcer

SIR,—We have read with interest the recent article by Bates *et al* (*Gut* 1989; **30**: 1323–8) but we wish to comment on the presentation of the results. Indeed in several Figures of this article (Figs 3, 4, and 5) the per cent of patients is given without the absolute values being stated in either the text or on the figures. We feel that by so doing valuable information might be 'lost', such as, how many patients on cimetidine took no antacids, etc.

It is also stated that more patients on cimetidine than on omeprazole took antacids and it might be interesting to know in what amount and at what time antacids were taken, as this could interfere with biodisposibility of cimetidine.[1].

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Reply

SIR,—Dr Plas raises some interesting points relating to our recent paper. In the text, we stated that diary card data were available for 80–83% of randomised patients, and Figures 4 and 5 relate to this subset of the 105 patients randomised to omeprazole and 92 to cimetidine. Over the first 14 days of the trial, significantly fewer patients receiving omeprazole took antacids compared with those receiving ranitidine ($p=0·001$). At day 14 seven of 74 patients receiving omeprazole and 27/70 receiving cimetidine also took antacids. From days 2–14, the total antacid consumption in the omeprazole group was 597 tablets and in the cimetidine group 885 tablets ($p=0·01$). Patients recorded their daily antacid consumption but not the time at which they took these tablets. A single tablet of the antacid used in our study has a neutralising capacity of 13 mmol HCl, compared with 156 mmol HCl used in the study quoted by Dr Plas; moreover, in our study, the antacid did not contain aluminium. In normal practice, patients take antacids prn and we feel that our study was a fair reflection of this, and therefore of the relative efficacies of omeprazole and cimetidine.

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CREST syndrome: nodular regenerative hyperplasia of the liver and primary biliary cirrhosis an overlap syndrome?

SIR,—We have read with interest the paper by Mc Mahon *et al* about an association between nodular regenerative hyperplasia of the liver, CREST syndrome and primary biliary cirrhosis.[1] We should like to make the following comments. First, the authors state that their report is the third recorded case of association between CREST syndrome and nodular regenerative hyperplasia of the liver; in our opinion they have failed to quote two other previous reports concerning this association.[2,3] Moreover, the paper by Hauftova *et al*[3] was actually the first report of an association between CREST syndrome, nodular regenerative hyperplasia of the liver and primary biliary cirrhosis. Second, we consider that the diagnosis of primary biliary cirrhosis in the report of McMahon *et al* is based on insufficient data to establish the usual diagnosis criteria of primary biliary cirrhosis. The authors argued that increased seric IgM concentration, cholestasis, and decrease in bromosulphthalein clearance which were observed in their patient, favoured the diagnosis of primary biliary cirrhosis. Increase in serum IgM concentration, however, is found in a variety of systemic diseases association with nodular regenerative hyperplasia of the liver[4,5] and was also observed in our patient (personnal communication).[2] Raised alkaline phosphatase activity is noted in 67% cases of nodular regenerative hyperplasia of the liver.[6] A decrease in bromosulphthalein clearance is of no value in the presence of cholestasis and has been reported in patients with nodular

regenerative hyperplasia of the liver exhibiting mild increase in alkaline phosphatase activity.[6] In the report of McMahon *et al*[1] there were no histological features consistent with primary biliary cirrhosis. Moreover it is well documented that nodular regenerative hyperplasia of the liver can be misdiagnosed by needle biopsy,[4 5] but this is not the case for primary biliary cirrhosis. Third, the presence of an antimitochondrial antibody is good evidence of primary biliary cirrhosis, especially when its titre is >1/500.[7 8] The titre of these antibodies, however, was not mentioned in the report discussed. Moreover, antimitochondrial antibodies can be found in sclerodermia[9 11] and in other collagenous disorders even in the absence of associated chronic liver disease. Antimitochondrial antibody is found in 18-27% of these patients with scleroderma even though only 3·4% of these patients had evidence of primary biliary cirrhosis.[11] Finally, McMahon and colleagues have reported a new case of association between CREST syndrome and nodular regenerative hyperplasia of the liver, the basis of which was the positivity of an antimitochondiral antibody.

It is concluded for the reasons already discussed that an overlap syndrome between CREST syndrome nodular regenerative hyperplasia of the liver and primary biliary cirrhosis has not been fully demonstrated.

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Reply

SIR,—We are pleased to note the interest expressed in our paper by Cadranel and colleagues, and are grateful to them for drawing attention to our omission of two further cases, the first reporting the association of nodular regenerative hyperplasia of the liver and CREST syndrome in a letter to *Presse Medicale*[1] and the second describing the association of CREST, nodular regenerative hyperplasia of the liver, and primary biliary cirrhosis in the Czechoslovakian literature.[2] The purpose of our paper however, was to highlight the features of overlap between the syndromes of nodular regenerative hyperplasia of the liver, CREST and primary biliary cirrhosis rather than to report an association or coincidental occurrence of the three conditions.

Although we agree that the biochemical abnormalities reported in our patient may be seen in nodular regenerative hyperplasia of the liver, the combination of results is, in our experience, typical of primary biliary cirrhosis. In our unit, which has a special interest in primary biliary cirrhosis, 96% of patients have had a raised serum IgM, 94% a raised serum alkaline phosphatase and 70% a severely depressed BSP-K_2 (50% of whom have a normal serum bilirubin as did this patient at the time of testing). Cadranel *et al* correctly state that decreased bromosulphthalein clearance has been reported in patients with nodular regenerative hyperplasia of the liver.[4] We have however, used a more detailed analysis of bromosulphthalein kinetics and shown a severe impairment in hepatic excretory function (BSP-K_2) in our patient, which to our knowledge has not previously been reported in nodular regenerative hyperplasia of the liver.[4] The mechanisms leading to a raised serum alkaline phosphatase concentration in liver disease are complex but in primary biliary cirrhosis are thought to be related to damage to the bile duct system, which can be recognised easily morphologically.[5] The mechanism of raised serum alkaline phosphatase in nodular regenerative hyperplasia of the liver, however, is unknown because the bile ducts appear normal at light microscopy. Our observation of reduced hepatic excretory capacity suggests that the raised alkaline phosphatase in nodular regenerative hyperplasia of the liver may be the result of an abnormality in the bile duct apparatus, presumably at the ultrastructural level.

The interpretation of the antimitochondrial antibody testing is more complex than outlined in the paper. Serum was negative by immunofluorescence and a sample was referred to Professor Berg's laboratory in Tubingen, FRG. The initial results by ELISA showed the presence of anti-M2 antibodies of IgM (1 in 220) and IgG (1 in 320) type in addition to anti-M4 antibody of low activity, which have been stated to be characteristic of primary biliary cirrhosis.[6] Further analysis by Western blotting, however, showed that these antibodies were of the recently described 'naturally occurring type' and this is what we reported in the paper.[7] Although these antibodies have been described in the sera of families and contacts of primary biliary cirrhosis patients, sera of some patients have shown the presence of primary biliary cirrhosis specific and non-primary biliary cirrhosis specific determinants in parallel.[8] This raises the difficult question of the specificity and interpretation of anti-mitochondinal antibody testing with increasing scientific sophistication, and further studies on the relationship between these antibodies and primary biliary cirrhosis are awaited.

We do not claim in the paper that the patient reported had primary biliary cirrhosis as the histological features were those of nodular regenerative hyperplasia of the liver alone. The letter from Cadranel *et al* however, invites comment on the wider issue of the criteria for the diagnosis of primary biliary cirrhosis and what should be accepted as the gold standard. First, the clinical presentation of the disease can vary from the asymptomatic to the classical picture of pruritus followed by progressive jaundice but incorporates a subgroup of patients who develop severe portal hypertension and do not become jaundiced.[9] Second, it is well recognised that up to 20% of cases in major series have a negative antimitochondrial antibody by conventional methods[10]. Third, antimitochondrial antibody positive patients with otherwise normal liver function tests have recently been shown to have histological features of primary biliary cirrhosis.[11] Finally, histological diagnosis of primary biliary cirrhosis may be extremely difficult in the absence of the florid duct lesion and may be mimicked by other conditions such as chronic active hepatitis, sarcoidosis, and lymphoma.[12] On this last point, we would disagree with Cadranel *et al* and suggest that primary biliary cirrhosis can be misdiagnosed on needle biopsy.

In summary, we feel that the conclusion of our paper remains valid. The association of CREST syndrome with primary biliary cirrhosis is well recognised, the association of CREST with nodular regenerative hyperplasia of the liver is further strengthened by our report, and nodular hyperplasia of the liver has recently been shown as a cause of portal hypertension in early stage primary biliary cirrhosis. Our case brings together the clinical features of CREST syndrome, the histological features of nodular regenerative hyperplasia of the liver, and the biochemical and serological features of primary biliary cirrhosis, and highlights the overlap between these three syndromes.

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