PostScript

LETTERS

If you have a burning desire to respond to a paper published in *Gut*, why not make use of our "rapid response" option?

Log onto our website (www.gutjnl.com), find the paper that interests you, and send your response via email by clicking on the "eLetters" option in the box at the top right hand corner.

Providing it isn't libellous or obscene, it will be posted within seven days. You can retrieve it by clicking on "read eLetters" on our homepage.

The editors will decide as before whether to also publish it in a future paper issue.

Terlipressin and arterial blood volume after paracentesis for tense ascites in cirrhosis

Moreau *et al* described the use of terlipressin, a vasopressin analogue, in ameliorating the reduction in effective arterial blood volume which can occur after paracentesis for tense ascites in cirrhosis (*Gut* 2002;**50**:90–4).

The article states that the first 1 mg intravenous bolus dose of terlipressin was given at the onset of paracentesis. Previous work has shown that infusion of vasopressin in a haemodynamically stable circulation can lead to reduced cardiac performance and coronary blood flow.[1] Moreover, a sustained pressor response can occur in cirrhotic patients, with reduction in heart rate, cardiac output, hepatic blood flow, and pressor effects also on the pulmonary circulation.[2]

Although the authors state no episodes of arterial hypertension occurred in the terlipressin group and that there were no observed changes between pre- and post-treatment electrocardiograms (ECGs), it is not clear whether invasive continuous arterial pressure monitoring was employed in this study or whether continuous ECG readings were taken. Without this level of observation it is difficult to exclude the occurrence of transient asymptomatic episodes of cardiac ischaemia.

Exclusion of patients with a history of cardiac disease, cardiac failure, renal disease, and diabetes mellitus may render the conclusions of this pilot study, and those of any subsequent randomised controlled trials with the same exclusion criteria, difficult to interpret and apply. One may argue that it is these subgroups of patients with comorbid factors who are most likely to suffer the deleterious consequences of a reduction in effective arterial blood volume of any duration or magnitude.

G Singh Ranger
St George's Hospital Medical School, Blackshaw Road, London SW17 OQT, UK; gsinghranger@yahoo.co.uk

References

1 **Ericsson BF**. Effect of vasopressin on the distribution of cardiac output and organ blood flow in the anaesthetised dog. *Acta Chir Scand* 1971:**137**:729–38.
2 **Moreau R**, Hadengue A, Soupison T, *et al*. Abnormal pressor response to vasopressin in patients with cirrhosis: evidence for impaired buffering mechanisms. *Hepatology* 1990:**12**:7–12.

Cardiac response to exercise in cirrhosis

Reading the excellent article on the cardiac response to exercise in cirrhosis (*Gut* 2001;**49**:268–75), I was surprised that patients without ascites were labelled "preascitic". The implication is that these are patients have not as yet developed ascites, presumably because their disease is less advanced than in those patients with ascites.

It is well known that many patients with cirrhosis will never develop ascites, regardless of the severity of other sequelae of portal hypertension that have developed or will ultimately develop. This is certainly borne out by my experience at a busy liver transplant centre. I would respectfully suggest that these patients be instead called simply "cirrhotic patients without ascites".

R H Wachsberg
Professor of Radiology, UMDNJ-University Hospital, 150 Bergen Street, Room C-320, Newark, NJ, USA; wachbrh@umdnj.edu

Authors' reply

We thank Dr Wachsberg for his comments and apologise for not making ourselves clear. In contrast with cirrhotic patients without ascites, who may well have had ascites and used diuretics sometime in the past, preascites is a well characterised stage in the natural history of cirrhosis. It occurs early in the continuum of cirrhosis. Such patients have never had ascites nor required the use of diuretics, and yet they show evidence of abnormal renal handling of sodium. They maintain sodium balance while on a diet of 100 mmol/day sodium[1] but retain sodium when given an acute sodium load such as 200 mmol/day sodium for one week[2] or when challenged with an intravenous saline load.[3] However, these patients can eventually come to sodium balance, after an intake of 200 mmol/day sodium[4] but at the expense of an increase in total and central blood volume,[5] together with suppression of renin-angiotensin-aldosterone and sympathetic activities in the supine position.[6] The assumption of the erect posture leads to activation of these hormonal systems[7] which are responsible for the subtle sodium retention in these patients. Preascites is further characterised by increased dopaminergic activity,[8] a possible consequence of the expanded intravascular volume, and elevated plasma nitric oxide levels,[9] which partly contributes to the glomerular hyperfiltration observed in these patients.[9 10] Finally, preascitic patients also have increased muscle sympathetic nervous activity[11] although the significance of this is not clear at present. Thus the preascitic cirrhotic patient is not simply a cirrhotic patient without ascites but rather the syndrome of preascites is a syndrome with well defined characteristics. While many patients in Dr Wachsberg's busy liver transplant unit may not have ascites, and they may well be receiving their liver transplant for reasons other than ascites, they certainly cannot be confused with preascitic cirrhotic patients.

F Wong, L Blendis
Department of Gastroenterology and Hepatology, Toronto General Hospital, Toronto, Canada

Correspondence to: Dr F Wong; florence.wong@utoronto.ca

References

1 **Warner LC**, Campbell PJ, Morali GA, *et al*. The response of atrial natriuretic factor and sodium excretion to dietary sodium challenges in patients with chronic liver disease. *Hepatology* 1990;**12**:460–6.
2 **Wong F**, Liu P, Allidina Y, *et al*. Pattern of sodium handling and its consequences in pre-ascitic cirrhosis. *Gastroenterology* 1995;**108**:1820–7.
3 **Wong F**, Massie D, Hsu P, *et al*. The renal response to a saline load in well compensated alcoholic cirrhosis. *Hepatology* 1994;**20**:873–81.
4 **Wong F**, Liu P, Blendis L. Sodium homeostasis with chronic sodium loading in preascitic cirrhosis. *Gut* 2001;**49**:847–51.
5 **Wong F**, Liu P, Tobe S, *et al*. Central blood volume in cirrhosis: measurement by radionuclide angiography. *Hepatology* 1994;**19**:312–21.
6 **Bernardi M**, Trevisani F, Santini C, *et al*. Aldosterone related blood volume expansion in cirrhosis before and after the early phase of ascites formation. *Gut* 1983;**24**:761–6.
7 **Bernardi M**, Di Marco C, Trevisani F, *et al*. Renal sodium retention during upright posture in preascitic cirrhosis. *Gastroenterology* 1993;**105**:188–93.
8 **Sansoe G**, Ferrari A, Baraldi E, *et al*. Endogenous dopaminergic activity in Child-Pugh A cirrhosis: potential role in renal sodium handling and in the maintenance of clinical compensation. *Eur J Clin Invest* 1998;**28**:131–7.
9 **Sansoe G**, Silvano S, Mengozzi G, *et al*. Systemic nitric oxide production and renal function in non-azotemic human cirrhosis: a reappraisal. *Am J Gastroenterol* 2002 (in press).
10 **Wong F**, Massie D, Colman J, *et al*. Glomerular hyperfiltration in patients with well compensated alcoholic cirrhosis. *Gastroenterology* 1993;**104**:884–9.
11 **Pozzi M**, Grassi G, Redaelli E, *et al*. Patterns of regional sympathetic nerve traffic in preascitic and ascitic cirrhosis. *Hepatology* 2001;**34**:1113–18.

Aetiology of extrahepatic portal vein thrombosis

I read with interest the article by Janssen *et al* (Gut 2001;**49**:720–4) regarding the aetiology and determinants of survival of extrahepatic portal vein thrombosis (EPVT). Among others, this retrospective study investigated the systemic risk factors for EPVT. We would like to add hyperhomocysteinaemia as a relatively new, not yet mentioned, risk factor.[1–3] This is illustrated by a recent case in our clinic.

A 54 year old woman was hospitalised because of worsening of upper abdominal pain which started two weeks before admission and was continuously present. Her personal and family history for thromboembolic processes was uneventful and she did not smoke. She did not use vitamin supplements. One day prior to admission she was

using the progesterone norethisterone (Primolut N) because of vaginal blood loss.

Combined portal-splenic vein thrombosis was diagnosed using colour Doppler ultrasonography and computed tomography. There were already some venous collaterals in the hilar area of the liver; hence the thrombosis would have been present for at least several weeks.

After investigations for thrombophilias were carried out, intravenous heparin and oral anticoagulant therapy were started and the patient improved.

The patient was found to be heterozygous for the prothrombin gene G20210A mutation and for the methyltetrahydrofolate reductase mutation. Mild hyperhomocysteinaemia (fasting/six hour post methionine load values 18/91 µmol/l) was also detected. Plasma vitamin B_6, B_{12}, and folate levels were normal. The patient is currently on lifelong oral anticoagulation therapy and has not yet started to use vitamin supplements.

Mild hyperhomocysteinaemia is a hypercoagulability risk factor for the development of EPVT which, at the time of the study of Janssen *et al*, had not been recognised as a prothrombotic factor. The association of hyperhomocysteinaemia and prothrombin gene mutation in EPVT has been documented only once in the literature. It is still unclear if the association is additive or synergistic for the development of thrombosis.[1] We would like to recommend determination of homocysteine levels in patients with idiopathic EPVT as vitamin B_6 and folate supplementation is a cheap and safe therapy in preventing deleterious vascular complications.

B W M Spanier, J Frederiks
Department of Internal Medicine, Spaarne Ziekenhuis Heemstede, Händellaan 2, 2102 CW Heemstede, the Netherlands

Correspondence to: B W M Spanier; b.w.mspanier@freeler.nl

References

1 **Silingardi M**, Ghirarduzzi A, Galimberti D, *et al*. Mesenteric-portal vein thrombosis in a patient with hyperhomocysteinemia and heterozygous for 20210A prothrombin allele. *Thromb Haemost* 2000;**84**:358–9.
2 **Marie I**, Levesque H, Lecam-Duchez V, *et al*. Mesenteric venous thrombosis revealing both factor II G20212A mutation and hyperhomocysteinemia related to pernicious anemia. *Gastroenterology* 2000;**118**:237–8.
3 **Audemar F**, Denis B, Blaison G, *et al*. Left branch portal vein thrombosis associated with hyperhomocysteinemia. *Gastroenterol Clin Biol* 1999;**23**:1388–91.

Author's reply

Spanier and Frederiks describe the role of diagnosing hyperhomocysteinaemia in a patient with portal vein thrombosis. Their case not only illustrates the potential importance of hyperhomocysteinaemia but also the concurrence of multiple risk factors in portal vein thrombosis.[1 2] Two inherited thrombotic risk factors (methylenetetrahydrofolate and prothrombin gene G20210A mutation) predisposed the patient to a thrombotic event which became clinically manifest after the recent start of progesterone.

There is clear evidence that hyperhomocysteinaemia is an independent risk factor for cardiovascular diseases. Hyperhomocysteinaemia can be diagnosed by genetic testing for the methylenetetrahydrofolate mutation and by measurement of increased plasma homocysteine levels, both fasting and after loading with methionine. The pathophysiological mechanism of homocysteine induced vascular disease is not well understood. It is even unclear whether homocysteine itself or a related metabolite or cofactor is primarily responsible for the thrombogenic effects of hyperhomocysteinaemia in vivo.

In our study on risk factors and determinants of survival for portal vein thrombosis, we did not investigate hyperhomocysteinaemia. As mentioned by Spanier and Frederiks, this relates primarily to the fact that in most of our patients hyperhomocysteinaemia was not recognised as an established thrombogenic risk factor at the time of diagnosis. Furthermore, many patients exhibited comorbidity or concurrent risk factors for portal vein thrombosis, which may lead to poor nutritional status and therefore interfere with plasma homocysteine measurement. These factors include the presence of liver cirrhosis, malignancy, and infections.[3] Although testing for the point mutation (C677T) in the methylenetetrahydrofolate reductase gene avoids the problem of acquired hyperhomocysteinaemia, this genetic defect by itself does not appear to be a significant independent risk factor for atherothrombotic disease.[4] From a therapeutic viewpoint, testing for hyperhomocysteinaemia is interesting, also for portal vein thrombosis, because vitamin supplementation (with folic acid, pyridoxine, and vitamin B_{12}) is generally effective in reducing homocysteine concentrations. However, it is not known if this therapy confers a risk for either extensive splanchnic thrombosis or other thrombotic manifestations which can develop in patients with portal vein thrombosis.[5] Ongoing prospective controlled trials are investigating the potential beneficial effect of homocysteine lowering treatment on cardiovascular morbidity and mortality in subjects with hyperhomocysteinaemia. Before advocating widespread screening for hyperhomocysteinaemia in patients with portal vein thrombosis, it would be preferable to have a better understanding of the clinical efficacy of these therapeutic interventions.

H L A Janssen
Department of Gastroenterology and Hepatology, University Hospital Rotterdam, Dr Molewaterplein 40, 3015 GA Rotterdam, the Netherlands; devlaming@mdl.azr.nl

References

1 **Denninger MH**, Chait Y, Casadevall N, *et al*. Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. *Hepatology* 2000;**31**:587–91.
2 **Janssen HL**, Meinardi JR, Vleggaar FP, *et al*. Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd-Chiari syndrome and portal vein thrombosis: results of a case-control study. *Blood* 2000;**96**:2364–8.
3 **Ferre N**, Gomez F, Camps J, *et al*. Plasma homocysteine concentrations in patients with liver cirrhosis. *Clin Chem* 2002;**48**:183–5.
4 **Deloughery TG**, Evans A, Sadeghi A, *et al*. Common mutation in methylenetetrahydrofolate reductase. Correlation with homocysteine metabolism and late-onset vascular disease. *Circulation* 1996;**94**:3074–8.
5 **Condat B**, Pessione F, Hillaire S, *et al*. Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy. *Gastroenterology* 2001;**120**:490–7.

Rifampicin and treatment of cholestatic pruritus

Prince *et al* described three patients with primary biliary cirrhosis who developed hepatotoxicity when given rifampicin to treat their cholestatic pruritus (*Gut* 2002;**50**:436–9). They describe the use of rifampicin as "secondline" treatment of cholestatic pruritus. Firstline therapy is generally considered to be cholestyramine, a bile acid sequestrant. Use of this agent is frequently unsatisfactory because of gastrointestinal side effects, especially constipation. I am writing to summarise new evidence that retention of endogenous bile acids causes cholestatic pruritus, and to call attention to a recent abstract indicating that colesevalem, a new bile acid sequestrant, appears to be more potent than cholestyramine and does not induce constipation.

The view that bile acid retention causes pruritus is a very old one. Varco[1] in 1947 noted that biliary drainage reduced pruritus in patients with extrahepatic biliary obstruction and that when bile was fed to patients, their pruritus returned. Huet and colleagues[2] reported that biliary drainage improved cholestatic pruritus in patients with intrahepatic cholestasis. Administration of cholestyramine, an anion exchange resin with a strong affinity for bile acids, improved pruritus[3] as did passage of plasma over charcoal or anion exchange resins.[4] More recently, extracorporeal albumin dialysis, a procedure that removes bile acids, has been shown to diminish cholestatic pruritus.[5] In all of these procedures, retained substances in addition to bile acids could have been removed at the same time so that cause and effect relationships were uncertain.

Partial biliary diversion is effective in treating cholestatic pruritus. A likely explanation for the efficacy of this surgical procedure is that it reduces the load of bile acids to the ileal transport system and thence to the liver, resulting in less retention of bile acids. In an important study, Hollands *et al* reported that ileal bypass was effective in treating cholestatic pruritus.[6] The ileal transport system is considered to solely transport bile acids. Thus this report in the surgical literature provided unequivocal evidence for bile acids being related directly or indirectly to cholestatic pruritus.

If bile acids are causal agents, and if bile acid depletion improves cholestatic pruritus, then bile acid administration to cholestatic patients should induce pruritus. Ricci *et al* noted that in two of four patients with primary biliary cirrhosis given cholylsarcosine, a non-metabolisable conjugated bile acid analogue, pruritus was induced.[7]

Despite these convincing lines of evidence, recent authors have been sceptical of the role of bile acids in cholestatic pruritus. This scepticism has arisen because of the lack of correlation between plasma bile acid levels and the magnitude of pruritus in some, but not all, studies. However, in my opinion, the lack of correlation between plasma bile acid levels and pruritus does not exclude a causal role for bile acids for three reasons. Firstly, the level of plasma bile acids fluctuates diurnally and the composition of plasma bile acids in cholestasis is quite complex. Secondly, bile acids might act slowly on peripheral or central receptors (or cause the release of substances that act on these receptors) so there could be a long delay between elevated plasma levels and pruritus. Thirdly, endogenous molecules such as opiates could act synergistically with bile acids to induce cholestatic pruritus.

Cholestyramine binds bile acids but is frequently ineffective. The efficiency of cholestyramine binding is quite low because the K_m for the ileal transport system is in the micromolar range, and at this concentration

bile acid binding is relatively weak. Thus the ileal transport system for bile acids acts as a sink to strip the bound bile acids from the resin. A new bile acid binding polymer, colesevalem, was synthesised by GelTex Pharmaceuticals (now Genzyme General) with a much superior binding affinity for bile acids. Colesevalem is a hydrogel that was developed as therapy for hypercholesterolaemia. Berg, in a recent abstract, reported that in eight patients with cholestatic pruritus who had not responded to cholestyramine, colesevalem was effective in five.[8] Colesevalem has an additional advantage over cholestyramine in that colesevalem does not have gastrointestinal side effects.

In their thoughtful case report, Prince *et al* did not note that rifampicin has a striking effect on bile acid metabolism, inducing 6-hydroxylation.[9] It could well be that 6-hydroxy bile acids either do not induce pruritus or are not conserved by the ileal transport system, as compared with endogenous bile acids, or both. Rifampicin is presumed to induce 6-hydroxylation of bile acids via cyp3A, a microsomal enzyme, whose synthesis is induced by the interaction of rifampicin and the nuclear receptor PXR. PXR activation might also induce bile acid sulfation.

If the use of rifampicin is hazardous in cholestatic disease, as suggested by Prince *et al*, then the treatment of cholestatic pruritus should involve a bile acid sequestrant such as colesevalem and/or an opiate antagonist. It would seem desirable to initiate a prospective, placebo controlled, double blind study using state of the art methods for quantifying itching that would compare the efficacy, safety, and convenience of these two agents, alone or in combination, on cholestatic pruritus.

A F Hofmann

Division of Gastroenterology, Department of Medicine, University of California, San Diego 92093-0813, USA; hofmannaf@cs.com

Conflict of interest: Professor Hofmann has served as a paid consultant of GelTex Pharmaceuticals and has received stock options for the purchase of shares in that company.

References

1 **Varco RL**. Intermittent external biliary drainage for the relief of pruritus in certain chronic disorders of the liver. *Surgery* 1947;**21**:43–5.
2 **Huet PM**, Rautureau M, Dhumeaux D, *et al*. The effects of biliary drainage in cholestatic hepatitis. *Rev Med Chir Mal Foie* 1970;**45**:271–8.
3 **DiPadova C**, Tritapepe R, Rovagnati P, *et al*. Double-blind placebo-controlled clinical trial of microporous cholestyramine in the treatment of intra- and extra-hepatic cholestasis: relationship between itching and serum bile acids. *Methods Find Exp Clin Pharmacol* 1984;**6**:773–6.
4 **Alarabi AA**, Wikstrom B, Loof L, *et al*. Treatment of pruritus in cholestatic jaundice by bilirubin- and bile acid-adsorbing resin column plasma perfusion. *Scand J Gastroenterol* 1992;**27**:223–6.
5 **Stange J**, Hassanein TI, Mehta R, *et al*. The molecular adsorbents recycling system as a liver support system based on albumin dialysis: A summary of preclinical investigations, prospective, randomized, controlled clinical trial, and clinical experience from 19 centers. *Artif Organs* 2002;**26**:103–10.
6 **Hollands CM**, Rivera-Pedrogo FJ, Gonzalez-Vallina R, *et al*. Ileal exclusion for Byler's disease: an alternative surgical approach with promising early results for pruritus. *J Pediatr Surg* 1998;**33**:220–4.
7 **Ricci P**, Hofmann AF, Hagey LR, *et al*. Adjuvant cholysarcosine during ursodeoxycholic acid treament of primary biliary cirrhosis. *Dig Dis Sci* 1998;**43**:1292–5.
8 **Berg CI**. Use of colesevalem hydrochloride (Welchol™ as a novel therapeutic agent for the management of refractory pruritus in chronic liver disease. *Hepatology* 2001;**34**:541.
9 **Wietholz H**, Marschall HU, Sjövall J, *et al*. Stimulation of bile acid 6 alpha-hydroxylation by rifampin. *J Hepatol* 1996;**24**:713–18.

Oats and coeliac disease

We read the study by Janatuinen *et al* (*Gut* 2002;**50**:332–5) with great interest. However, we would like to highlight some concerns.

The initial study[1] included 92 patients randomised to two groups—oats and gluten free diet, 45 and 47 patients respectively—however, these numbers do not correspond to those in figure 1 of their paper.

Patients were verbally consenting volunteers, thus introducing selection bias to compliance. The number of dropouts, especially in the control group, was surprisingly high (41 in total). Were there so many dropouts because of the unpalatability of oats or concerns over their safety? If the latter, then surely this would be greater in the oats group.

It is not clear whether patients were followed up in the interim period between 12 months and five years. It would be important to ascertain objectively whether the oats group were in fact including oats in their diet, as omission would not address their long term safety. Assessment of compliance and food diary are very subjective, introducing bias towards dietary compliance. How was this done? We were surprised to see that one third of the oats group did not in fact take oats at all, so only one third of patients were ingesting oats on a daily basis. The proportion adhering to a gluten free diet was paradoxically greater in the control group. If oats were allowed then this could be interpreted by patients as acceptance of other (gluten containing) foods also. The purity and amount of oats ingested in the first year was regulated but this was not monitored thereafter and contamination of oat products could lead to small bowel architectural changes.

Histological changes in coeliac disease can be subjective but no mention was made as to whether blind reporting was carried out.

Also, no explanation was given for the greater numbers of high values for ARA, AGA, and EMA in both groups at five years. This needs to be quantified and statistically analysed.

The safety of oats in coeliac disease is extremely important. This and other studies have shown that compliance with a strict gluten free diet is difficult, reflecting its uncompromising limitations as well its relative unpalatability. This paper suggests that oats are safe but the small numbers involved could mask subtle differences between the groups which may result in greater morbidity. In order to address this, further larger multicentre trials are required.

R Dor, D J Shanahan

Academic Unit of Medical and Surgical Gastroenterology, Homerton University Hospital, London E9 6SR, UK.

Correspondence to: R Dor; Riaz.dor@homerton.nhs.uk

Reference

1 **Janatuinen EK** , Pikkarainen PH, Kemppainen TA, *et al*. A comparison of diets with and without oats in adults with celiac disease. *N Engl Med J* 1995;**333**:1033–7.

Authors' reply

Dor and Shanahan point out the inconsistency in the number of study patients in the flow chart in figure 1 of our study on oats ingestion by coeliac patients.[1] Indeed, there is an error. The number of patients in the oats group in remission in the original study (*Gut* 2002;**50**:332–5) should be 26 and not 12. The figures given in the text are however correct.

Dor and Shanahan also emphasise the total number of dropouts (41) which covers both the original study of 6–12 months[1] as well as the follow up period of five years. They ask whether this could be due to the possible unpalatability of oats. However, the number of dropouts was similar among controls (19) and those consuming oats (22), and there was no evidence that the oats products were unpalatable.[1] Probably the number of dropouts in many cases reflects the lack of motivation to participate, especially in the unpleasant part of the study—that is, gastroscopy to obtain small intestinal biopsies. As expressed in the text, many patients also felt uncertain about the long term safety of oats. Our results show that such fear was not justified.

Patients had no strict follow up visits to the outpatient clinic of the University Hospital during the time period between 12 months and five years. However, they were advised to have regular follow up clinical and laboratory examinations in the local health care centres. Some also had regular visits to the outpatient clinic of Kuopio University Hospital.

As stated in the article, patients had free choice regarding the amount of oats they wished to consume and which they felt convenient. In this respect the study also reports on the reality and usefulness of oat products. Information on the quantity of oats in the diet and the degree of compliance was based on an interview and a questionnaire carried out by a clinical nutritionist.

Dor and Shanahan raise the question of whether patients interpreted the use of oats as comparable with consuming gluten containing foods. They base this on the degree of compliance in our study. Compliance was 71.4% in the oats group and 78.6% among controls. In our opinion this does not justify such a conclusion. As stated in the article, the oats group also consumed a strict gluten free diet but part of their gluten free products were substituted by oats.

After 12 months, patients used oat products from major Finnish mills. These products have been found to be free of contamination. If oats by itself or oat products had any deteriorating effect on the duodenal mucosa or stimulated immune mechanisms, the results in the oats group would have differed from those of controls. This was not the case. The results indicate that oats were well tolerated.

As in our original study (*Gut* 2002;**50**:332–5), histological examinations were carried out blindly by an experienced pathologist.

The values for the various antibody levels were statistically analysed comparing them at the end of the original study and at the five year time point. There were no statistically significant differences between time points or between the oats and control groups. The high values occurred only in a few patients in both the control and oats groups without any significant effect. As stated, those patients showed poor adherence to a gluten free diet.

We do agree with the final conclusion of Dor and Shanahan that larger multicentre trials could be worthwhile. However, to conduct a similar controlled study with larger numbers of patients and continuous frequent control of intake of oats, including multinational purity analyses of freely available oat

supplements, would be an enormous effort. To date, our investigation is the largest controlled randomised study on oats in coeliac patients. Furthermore, it represents the first attempt in showing the long term safety of oats in coeliac patients.

R Julkunen
Gastroenterological Unit, Department of Medicine, Kuopio University Hospital, Kuopio, Finland

M Uusitupa
Department of Clinical Nutrition, University of Kuopio, PO Box 1627 70211, Kuopio, Finland

Correspondence to: M Uusitupa; Matti.Uusitupa@uku.fi

Reference

1 **Janatuinen EK**, Pikkarainen PH, Kemppainen TA, *et al*. A comparison of diets with and without oats in adults with celiac patients. *N Engl J Med* 1995;**333**:1033–7.

NOTICES

Sir Francis Avery Jones BSG Research Award 2003

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2003 Award. Applications (TWENTY COPIES) should include:

- A manuscript (2 A4 pages ONLY) describing the work conducted
- A bibliography of relevant personal publications
- An outline of the proposed content of the lecture, including title
- A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

Entrants must be 40 years or less on 31 December 2002 but need not be a member of the Society. The recipient will be required to deliver a 30 minute lecture at the Annual meeting of the Society in Birmingham in March 2003. Applications (TWENTY COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2002.

Broad Medical Research Program—Inflammatory Bowel Disease Grants

Funds for inflammatory bowel disease (IBD) research are available immediately from the Broad Medical Research Program of The Eli and Edythe L Broad Foundation for innovative projects regarding etiology, therapy, or prevention. Grants totalling approximately US$100,000 per year are available for basic or clinical projects. Larger erquests may be considered. Initial letter of interest (no submission deadline), simple application, rapid (60 day) peer review, and funding. Criteria for funding includes new ideas or directions, scientific excellence, and originality. Early exploratory projects, scientists not currently working in IBD, and/or interdisciplinary efforts are encouraged. Further information: Marciana Poland, Research Administrator, Broad Medical Research Program, 10900 Wilshire Blvd., 12th Floor, Los Angeles, CA 90024-6532, USA. Tel: +1 310 954 5091; email: info@broadmedical.org; website: www-.broadmedical.org

3rd Nutrition and Health Conference

This will be held on 29–30 November 2002 in London, UK. This year's topics include cancer prevention, cancer treatment, hot topics for coronary heart disease and diet, brain nutrition, gut nutrition, and a diet and lifestyle intervention session. Further information: Nutrition and Health Conference, 16 Brownlow Court, Lyttleton Road, London N2 0EA; tel: +44 (0)208 455 6570; fax: +44 (0)208 455 2126; email: admin@nutritionand health.co.uk; website: www.nutritionandhealth.co.uk

17th International Workshop on Therapeutic Endoscopy

This will be held on 3–5 December 2002 in Hong Kong. Further information: Professor SC Sydney Chung, Endoscopy Centre, Prince of Wales Hospital, Shatin, NT, Hong Kong. Tel: +852 2632 2233; fax: +852 2635 0075; email: info@hksde.org

Advances in the Inflammatory Bowel Diseases

This conference will take place on 6–7 December 2002 in New York, USA. Further information: Heather Drew, Imedex, 70 Technology Drive, Alpharetta, GA 30005-3969, USA. Tel: +1 770 751 7332; fax: +1 770 751 7334; email: h.drew@imedex.com; website: www.imedex.com

15th European Intensive Course (SMIER) Digestive Endoscopy

This course will take place on 16–17 December 2002 in Strasbourg, France. Further information: Michele Centonze Conseil, 6 bis Rue des Cendriers, 75020 Paris, France. Tel: +33 1 44 62 68 80; fax: +33 1 43 49 68 58.

The Future of Gastro-entero-hepato-pancreatology is bright

This Academic Farewell Symposium of Guido NJ Tytgat will be held on 12 December 2002 in Amsterdam, the Netherlands. Deadline for registration is 1 November 2002 (no registration fee) and registration should be done via email to: j.goedkop@amc.uva.nl.

Cancer of Oesophagus and Gastric Cardia: from Gene to Cure

This conference will be held on 13–15 December 2002 in Amsterdam, The Netherlands. Further information: European Cancer Centre, PO Box 9236, NL 1006 AE Amsterdam, The Netherlands. Tel: +31 (0)20 346 2547; fax: +31 (0)20 346 2525; email: ecc@ikca.nl

The Sheila Sherlock Memorial Symposium

Dame Sheila Sherlock, who died earlier this year, was responsible for creating hepatology at the Royal Free Hospital, London. This memorial symposium will take place on 26–28 January 2003 at the Royal Free Hospital, London, UK. Further information: Terri Dolan, Royal Free and University College Medical School, Royal Free Campus, Centre for Hepatology, Upper 3rd Floor, Rowland Hill Street, London NW3 3PF, UK. Tel: +44 (0)207 433 2851; email: t.dolan@rfc.ucl.ac.uk

3rd Chester International Inflammatory Bowel Disease Meeting

This meeting will be held on 10–11 February 2003 in Chester, UK. An international programme includes speakers from the USA, France, Italy, and the UK, and will cover clinical problems, pathogenesis, medical and surgical treatment. Registration details and programme from: Professor Jonathan Rhodes, Department of Medicine, University of Liverpool, Daulby Street, Liverpool L69 3GA, UK. Tel: +44 (0)151 706 3558; fax: +44 (0)151 706 5832; email: rhodesjm@liverpool.ac.uk