LETTERS TO THE EDITOR

Cereal fibre and rectal epithelial cell proliferation: a possible link with duodenal ulceration

EDITOR,—It is interesting that Macrae *et al* (*Gut* 1997;41:239-45) found that unprocessed wheat bran had a greater effect than processed bran or oat bran on the reduction of labelled cells in the top two fifths of rectal epithelial crypts. There is evidence that wheat bran may have effects on other mucosal surfaces, particularly that of the duodenum. The prevalence of duodenal ulceration is lower in India in the unrefined wheat eating areas of the Punjab than in the polished rice eating areas of the South.¹⁻³ Our experimental work on several animal models has shown that wheat bran is protective against peptic ulceration and that this protection is linked with its lipid content.^{4,5} The evidence so far suggests that this effect may be related to a unique combination of lipids in certain cereal fibres and not to a particular type of fibre.

F I TOVEY
M HOBBSLEY

Department of Surgery,
University College London Medical School,
67-73 Riding House Street,
London W1P 7LD, UK

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"Golf ball liver": a cause of chronic hepatitis?

EDITOR,—A 23 year old man was referred to the outpatient clinic in view of persistently abnormal liver function tests for five years. In 1992, he had a gastrointestinal illness manifest by abdominal pain, diarrhoea and vomiting which lasted intermittently for one month. At that time, investigations by his general practitioner revealed that his liver function tests were abnormal: alkaline phosphatase (ALP) 408 U/l, aspartate aminotransferase (AST) 383 IU/l, alanine aminotransferase (ALT) 922 U/l, γ -glutamyl transferase (GGT) 147 IU/l. Viral serology for hepatitis A and B and a Paul-Bunnell test were negative. His symptoms resolved, but his liver function tests did not return to normal.

He was referred to the medical outpatient clinic in 1997 because of the development of further symptoms: episodic abdominal pain, diarrhoea, itch, and fatigue. His urine was noted to be dark and his faeces was pale. Alcohol consumption was moderate and confined to social occasions. He had no history of recent foreign travel, substance or drug misuse. He had no contacts with jaundice and no previous blood transfusions.

Liver function tests were persistently abnormal at that time: ALP 622 U/l, AST 86 IU/l, ALT 193 U/l, GGT 555 IU/l. Other investigations including full blood analysis, erythrocyte sedimentation rate, coagulation screen, urea and electrolytes, serum ferritin, serum copper, and alpha-1-antitrypsin were normal. Analysis of plasma proteins revealed albumin 45 g/l, globulin 37 g/l, total protein 82 g/l. IgG (30.3 g/l) and IgM (4.65 g/l) were raised. Titres of antinuclear antibody (IgG 1:20) and anti-smooth muscle antibody (IgG 1:40) were low. Viral serology for hepatitis A, B and C and Epstein-Barr and cytomegalovirus were negative. Abdominal ultrasound revealed an enlarged spleen, which was not palpable, and normal liver architecture.

Percutaneous liver biopsy revealed nodules separated by fibrous bands and a moderately dense mononuclear cell infiltrate within the portal tracts and fibrous bands, composed mainly of lymphocytes. The bile ducts were well preserved. There was moderately active lymphocytic piecemeal necrosis. Stains for Wilson's disease and alpha-1-antitrypsin deficiency were carried out and were negative. The appearances suggested chronic hepatitis progressing to cirrhosis.

This young man has been a very keen amateur golfer for many years and licks his golf balls during every round. All investigations as indicated above have failed to reveal a specific cause for his chronic hepatitis and cirrhosis. In view of the recent case report (*Gut* 1997;40:687-8) relating acute hepatitis to inadvertent ingestion of 2,4-D, it is proposed that ingestion of this substance by golfers may also lead to chronic hepatitis and even cirrhosis as in the case of this young man with no other apparent cause for his liver disease. The results of abstinence from licking his golf balls are eagerly anticipated.

S JOHNSTON
G MCCUSKER
T J TOBINSON

Craigavon Area Hospital Group HSS Trust,
68 Lurgan Road,
Portadown,
Craigavon BT63 5QQ, UK

Reply

EDITOR,—We were interested to read the letter by Johnston *et al*, further to our report in the July issue, which appears to document a case of chronic active hepatitis possibly caused by the patient's habit of licking his golf balls. It appears that the habit of golf ball licking is certainly not confined to Ireland and appears, at least anecdotally, to be a relatively common practice. Given this widespread practice and the now documented ability of 2,4-D to cause an acute hepatitis, it is certainly within the realms of possibility that a chronic hepatitis may also result from chronic exposure to 2,4-D.

However, the case reported by Johnston *et al* requires some clarification. It would be helpful to know whether any eosinophils were seen on the liver biopsy sample, and if not readily seen on straightforward stains then possibly monoclonal markers such as EG1 or EG2 could be used. This is of importance as if chronic golf ball liver exists then it raises the question of whether it is a toxic phenomenon or a chronic allergic/hypersensitivity process.

It would also be of interest to know whether the authors documented that 2,4-D was actually being spread on the patient's golf course. How long had the patient been licking his golf balls prior to the initial illness in 1992,

and had the chemicals used on the patient's golf course changed in or around this time. Was there any temporal relation between the patient's symptoms and the times of heaviest concentration of 2,4-D on the golf course or the frequency of this patient's golfing excursions? We await with interest any further developments.

C LEONARD

Division of Pulmonary & Critical Care Medicine,
Stanford University Medical Center,
Stanford, CA 94305, USA

C M BURKE

Department of Respiratory Medicine,
James Connolly Memorial Hospital,
Dublin 15, Ireland

C O'KEANE

Department of Histopathology,
Mater Misericordiae Hospital,
Eccles Street, Dublin, Ireland

J S DOYLE

Professor of Medicine - Emeritus,
Beaumont Hospital,
Dublin, Ireland

Mesalazine as a maintenance treatment in Crohn's disease

EDITOR,—We read with interest the occasional viewpoint by Sahmoud and Mary (*Gut* 1997;40:284-5). As is too often the case in such reviews, the authors have failed to identify all of the relevant literature pertinent to the topic: the maintenance of remission or prevention of recurrence of Crohn's disease. For example, with regard to azathioprine, rather than two trials of treatment, actually six trials (including the NCCDS Parts I and II) have been published. The results were summarised recently in a meta-analysis.¹ This systematic review concluded that the common odds ratio for maintaining remission for azathioprine treated patients was 2.3 (95 confidence interval (CI) 1.8 to 2.9) and that there was a relation between the cumulative dose of azathioprine prescribed and the response. Azathioprine should be considered an option for maintenance treatment.

The authors have also selectively reviewed the literature with regard to mesalazine. Turning to the postoperative population, a large North American trial² which identified a benefit for mesalazine for prevention of recurrence has been ignored, as well as trials which used endoscopic recurrence as a surrogate end point.³ A second systematic review, published in the same year as that of Messori *et al* reached similar conclusions and has been updated recently.⁴ Patients who received mesalazine were more likely to remain in remission compared with those on placebo. The relative risk of relapse was 0.63 (95% CI 0.50 to 0.79) for patients receiving mesalazine as compared with placebo.

We agree with the authors that additional studies are required and that differences in patient selection provides a likely explanation for differences in response. Identification of patients at higher risk of relapse could result in more cost effective treatment. Results have been conflicting with regard to clinical attributes of disease activity. While recognising that an analysis based on individual patient data might provide additional insight, the lack of consistent biological markers for high risk of recurrence (for example, permeability studies) in previous studies might make the approach irrelevant.

The issue as to whether or not to initiate maintenance treatment with either mesala-