LETTERS TO THE EDITOR

Hepatitis E acquired in the UK

We can confirm the finding of McCrudden *et al* (*Gut* 2000;**46**:732–3), that acute infection with hepatitis E virus (HEV) can be acquired in the UK. A 61 year old man presented in March 1999 after a two week illness with fever, malaise, and nausea, followed by cholestatic jaundice and a palpable spleen. Results of tests included alkaline phosphatase 277 IU/l, alanine aminotransferase 2118 IU/l, bilirubin 244 umol/l and INR 1.7. He had no risk factors for liver disease and did not swim in the sea. He had not travelled outside the UK for four years and had never been to an area where hepatitis E was endemic. Serology was negative for acute markers of hepatitis A and EBV and for any evidence of hepatitis B or CMV. Clinical recovery was uneventful and four months later, liver function tests had returned to normal. Serum was taken from the patient at presentation and at one, two, three, and eight months. All specimens were examined by enzyme immunoassay for total anti HEV antibody (HEVEIA, Abbott, Maidenhead, Berks, UK) and IgM anti HEV antibody (HEV IgM ELISA, Genelabs Diagnostics PTE Ltd, Singapore). The first sample was positive in the total and IgM anti HEV antibodies. Over the following months the IgM reactivity waned and then became negative while the total antibody test remained positive. Blood samples from close contacts (including a friend who had been to India four years earlier) were tested at eight months and were all negative for total anti HEV antibody.

We believe that our patient too had UK community acquired hepatitis E, although the source of his infection remains unknown. One possibility is consumption of imported food contaminated with HEV. This mechanism has been responsible for cases of hepatitis A.[1] It is difficult to identify a particular imported food as the source of our patient's infection as his dietary habits were not unusual and had not changed. Another hypothesis is that HEV may be a zoonotic infection. HEV has been demonstrated in pigs in several countries, including the US.[2] Two human HEV cases acquired in the US involved a virus similar to porcine strains of HEV.[3] Furthermore, pig handlers in China and Thailand have high rates of HEV seropositivity.[2] Serological evidence of HEV infection has also been found in wild rats in the US.[4]

Our patient reported no contact with rats or pigs but we are arranging for HEV genetic sequencing to be performed on his serum samples. We recommend that HEV serology should be more commonly applied to blood specimens from patients with acute hepatitis of obscure cause. Few laboratories in the UK test routinely for HEV and those centres that do test are usually referred specimens only from patients with a history of travel to an area where HEV is endemic. Unless more indigenous cases are detected and followed up epidemiologically, the origin of such infection will remain obscure.

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Acid suppression and upper GI cancer diagnosis

EDITOR,—Bramble *et al*[1] have recently suggested that the long recognised lack of impact of open access gastroscopy on the detection of earlier upper GI cancer[2 3] may be due in part to the masking of cancer by prior acid suppressive therapy. This is based on a higher rate of undiagnosed cancer at index gastroscopy in their group of patients who had received acid suppressive therapy within the six months before that gastroscopy. They conclude that clinical guidelines and endoscopy waiting times should take account of this. However, there are some serious flaws in their case series which preclude the drawing of such conclusions.

Firstly, their study is retrospective. Without prospective randomisation, one cannot ensure that their two groups are comparable. The patients who were not prescribed antisecretory therapy are more likely to have had symptoms or signs suggesting underlying cancer. Because such symptoms occur in more advanced cancer, the cancer is not surprisingly more likely to be readily detectable. By contrast, the group who were treated with antisecretory medication are more likely to have uncomplicated dyspepsia and thus less advanced and less readily diagnosable tumours at the time initially investigated. Were the two groups comparable with respect to sinister symptoms at the time of presentation?

Secondly, they appear to assume that the early discovery of cancer in their non-treated group was worthwhile—that is, the cancer was treatable. However, they do not report any data for tumour stage for either group, which presumably must have been readily accessible from case note review. Were the two groups comparable for stage of tumour at the time of diagnosis? Their argument will only hold up if those who did not receive antisecretory medication were detected at an earlier stage of tumour progression.In summary, this case note review reinforces the need for a strong evidence base from which conclusions which dictate major changes in clinical practice with huge resource implications should be made. Unfortunately, this report does not provide evidence to justify the conclusions made.

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Reply

Gillen and McColl correctly point out the problems of a retrospective study and we do state in the article that we were unsure as to why some patients had been prescribed antisecretory therapy while others had not. We feel it might be difficult to justify a prospective study on ethical grounds when the consequences of missing just one cancer would be enormous in the context of a clinical trial, not to mention any medicolegal implications. To a large extent, the argument about advanced cancer patients having different symptoms is irrelevant if patients with ulcer like symptoms are being missed when the diagnosis is really "ulcer cancer". As Gillen and McColl suggest, these patients are less likely to have advanced disease but surely this is precisely the group we should be diagnosing as early as possible (and hence at the first gastroscopy). If "symptomatic treatment" turns out to be healing treatment, masking the true diagnosis, this is a cause for serious concern. The extent to which proton pump inhibitors might do this is even more worrying.

With regard to their second point, there is ample evidence in the literature that the stage at which gastric cancer is diagnosed affects five year survival and very early disease is curable.[1] In our health district the vast majority of gastric cancers are beyond stage II, and the point of our paper was to highlight the fact that a significant number of patients had previously been investigated and told they had benign disease. The patients reasonably expect that their prognosis would have been better if they had been diagnosed six months or one year earlier. As 87% of our patients do not have early stage disease[2] and the authors do not operate on patients, the outcome of surgery was not the prime focus of the paper. We know that very few will be cured by surgery. The only effective way of improving outcome is to diagnose the condition earlier and the crucial question is whether this is achievable in the UK.

Finally, we are not proposing any changes which would have "huge resource implications" or result in "major changes in clinical practice". Our message is that proton pump inhibitors should not be prescribed to patients with dyspepsia over the age of 45 years without a gastroscopy. It follows, therefore, that patients should not have to wait an unnecessarily long time for this simple investigation. Is a randomised, controlled trial

really needed to confirm that this is good clinical practice?

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Re-epithelialisation of Barrett's oesophagus

EDITOR,—We were interested to read the case report by Van Laethem and colleagues of a carcinoma arising under a re-epithelialised segment of Barrett's oesophagus (*Gut* 2000;**46**:574–577). This raises issues in the debate over ablation of Barrett's epithelium. There has been interest in ablating the columnar epithelium to encourage squamous regrowth which may reduce the risk of progression to adenocarcinoma. However, there have been numerous reports of buried glands under the regenerated mucosa.[1–3]

While we accept that columnar glands may persist under the squamous epithelium and that this may represent a continuing carcinoma risk, this is difficult to quantify. Indeed, this is the first report of such a malignant change. It may be that as any buried glands are no longer exposed to potential carcinogens in the form of acid or bile reflux, the risk is reduced. Although the ultimate aim of treatment is to eliminate the risk of potential malignant change, any means of reducing such risk, for example by diminution of the volume of metaplastic tissue, would be worthwhile. This whole issue needs further evaluation by appropriately designed clinical trials.[4]

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Outcome of lamivudine resistant hepatitis B virus infection in liver transplant recipients in Singapore

EDITOR,—We read with interest the article by Mutimer and colleagues (*Gut* 2000;**46**:107–113). The Birmingham group described the clinical course of four liver transplant patients who developed graft infection with lamivudine resistant virus. Lamivudine resistant hepatitis B developed after a mean duration of nine months (range 8–11) after the transplant. Liver function abnormalities occurred at a mean duration of six months (range 3–12) after the emergence of lamivudine resistant virus and three of the four patients died 5–20 months later. The authors concluded that the lamivudine resistant phenotype can cause severe graft damage.

In our liver transplant centre, 12 patients with chronic hepatitis B (four with hepatocellular carcinoma) underwent liver transplantation over a five year period. All were given lamivudine before and after transplant. Lamivudine resistant hepatitis B developed in six of the nine survivors at a mean duration of 60 weeks (range 1–127) after liver transplant. Apart from weaning off immunosuppression aggressively, no further antiviral treatment was added. All six had normal liver function at their last follow up (mean 28, range 0–123 weeks after emergence of lamivudine resistant virus).

Contrary to what the Birmingham group experienced, all of our patients with lamivudine resistant virus were well, with no evidence of graft dysfunction. Long term outcome of such patients remains unknown and it may be premature to conclude that the lamivudine resistant phenotype causes severe graft damage.

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Gastric cancer in patients with benign dyspepsia

EDITOR,—There is an ongoing debate regarding the value of endoscopy in younger patients presenting with dyspepsia. One important consideration is the likelihood of detecting an underlying cancer which might be cured by early treatment. The large retrospective study by Breslin and colleagues in the January issue of *Gut* (*Gut* 2000;**46**:93–97) indicates that underlying cancer will be diagnosed in about 1 in 1000 patients presenting with uncomplicated dyspepsia under 45 years of age. However, the calculated 95% confidence intervals for this are wide (1 in 2963 to 1 in 300).

An important question in considering the significance of this finding is whether the prevalence of cancer in these patients with benign dyspepsia is any different from that in the general population. In our own country, Scotland, the chance of a patient presenting with gastro-oesophageal cancer before the age of 50 is 1 in 909 (ISD Scotland Cancer Surveillance Group Data Request and Analysis Service) and half of those have presented with the cancer within the age band 45–49. Most of these patients will have had the tumour present in their stomach for a considerable time prior to clinical presentation, which would have been detected by screening endoscopy five years earlier. Even allowing for the fact that population based rates of gastro-oesophageal cancer are higher in Scotland than Alberta,[1] this suggests that the prevalence of underlying cancer in patients presenting with uncomplicated dyspepsia may not be different from that in the general population. Consequently, offering endoscopy to patients with simple uncomplicated dyspepsia to detect cancer may merely represent screening of the general population.

There has been a general assumption that a tumour growing in the stomach will produce dyspeptic symptoms. However, there is no evidence for this. Tumours developing in the colon or other parts of the gastrointestinal tract rarely, if ever, cause symptoms until they produce complications such as bleeding or obstruction.

A very small proportion of patients presenting with uncomplicated dyspepsia will have underlying cancers but this finding may be unrelated to their symptoms. Unless uncomplicated dyspepsia is confirmed to be a symptom of underlying malignancy, then one would be as well to recommend offering endoscopy to patients presenting with a sprained ankle in order to pick up underlying gastro-oesophageal cancer.

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BOOK REVIEW

Colonic Microbiota, Nutrition and Health. Edited by G R Gibson, M B Roberfroid (Pp 304; illustrated; £93) The Netherlands: Kluwer Academic Publishers, 1999. ISBN 0412798808.

I was taught as a medical student that the major function of the colon was that of a storage organ. Since then, premises about the colon have evolved and the complexities of colon function is much better understood, as described by Gibson and Roberfroid's multi-authored book *Colonic Microbiota, Nutrition and Health*.

Although the authors state that the purpose of the book is to overview current knowledge of the activities and functions of the gut microflora, the scope goes beyond these boundaries and takes us on an ecological journey into the exciting life of gut microflora and their impact on colon function in health and disease, and the intimate critical relationship between diet, bacteria, and quality of life.

Gastroenterologists are still recovering from the impact that a bacterium, *Helicobacter pylori*, has had on upper gastrointestinal tract pathology. In this context, it is interesting to note that the large bowel is the most heavily colonised part of the gastrointestinal tract yielding up to 10^{12} bacteria per gram of intestinal contents in healthy human subjects. It is a complex ecosystem in which the numerous

and different species of bacteria degrade and ferment substrates that have escaped digestion in the small bowel. Major genera include bacteroides, bifidobacteria, lactobacilli, clostridia, and enterobacteria, and the main products of bacterial fermentation of the substrate that reaches the colon are short chain fatty acids (SCFA) and gases including hydrogen, carbon dioxide, and, in some individuals, methane. The relevance of SCFA, is that they act as a source of energy for intestinal mucosal cells and reduce the pH of colonic contents. One particular SCFA, butyrate, may be important in protecting against colorectal cancer. The relevance of fermentation to human metabolism can be gauged from the fact that the energy equivalent of 15–40 g of carbohydrate is metabolised by the large bowel.

The book outlines the technological revolution that has occurred in understanding the natural microbial world. Molecular biology has invaded gut microbiology, with the limitations of enrichment cultural techniques being integrated into techniques based upon the detection of the genomic DNA or the analysis of rRNA.

A fascinating aspect of the book that concerns and affects all of us are the chapters on food. With the craze of low carbohydrate diets in order to counter obesity that are sweeping the US, it is refreshing to realise the importance of carbohydrates and the concept of functional food. These foods target specific functions in the body in a positive way due to the presence of health enhancing ingredients. Colonic foods are an example of such functional foods that target the large intestine. These are foods that contain an ingredient that does not undergo significant modification during transit through the small intestine, but reach the colon where they are utilised by the resident bacteria producing metabolites that influence the physiological and biochemical processes in a beneficial manner. Dietary fibre is the best known of the "colonic foods" and is divided into soluble and insoluble fibre. Soluble fibers include pectin, guar gum, B glucan, and psyllium and result in modest reductions in blood lipids, affecting the total and LDL cholesterol fractions. Insoluble fibres (cellulose and lignin) are mainly responsible for faecal bulking. Dietary fibre may play a protective role in diverticular disease and colorectal cancer. Other functional foods are the fructans and resistant starch which, in animal models, affect the triglyceride rich fractions. A novel and potentially important approach to prevention and therapy of colonic diseases is the concept of prebiotics and probiotics. The probiotic approach involves adding live microorganisms to the gastrointestinal tract while prebiotics enhance certain components of the existing flora. Probiotics have potential in the prevention and treatment of rotavirus infections, lactose malabsorption, and food allergy. Tentative claims for benefits of prebiotics include reduction in obesity, improved control of non-insulin dependent diabetes, reduction in the risk of atherosclerotic cardiovascular disease, and prophylaxis of acute gastroenteritis.

How does the above affect individuals? It seems that we should include the following foods in our diet: garlic, onions, asparagus, chicory, dandelion, artichokes, soy beans, leeks, Jerusalem artichokes, wheat, bananas, and rye. Quite a tall order!

The authors have made an important contribution to the concept of the local and systemic effects of the colon, and outlined the benefits of a healthy colon and the evolvement of the idea that functional foods have prophylactic and therapeutic properties. A minor criticism is that there is a repetition of ideas in certain chapters. I would highly recommend this excellent work for gastroenterologists as a seminal study. Gastroenterologists, primary care physicians, and nutritionists will find this book a useful guide, but it will also provide a basic understanding for all health workers.

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NOTES

Sir Francis Avery Jones British Society of Gastroenterology Research Award 2001

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2001 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 old or less on 31 December 2000 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 Glasgow in March 2001. Applications (TWENTY COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2000.

British Society of Gastroenterology Hopkins Endoscopy Prize 2001

Applications are invited by the Endoscopy Committee of the British Society of Gastroenterology who will recommend to the Council the recipient of the 2001 Award. Applications (TEN 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.

An applicant need not be a member of the Society. The recipient will be required to deliver a 20 minute lecture at the Annual meeting of the Society in Glasgow in March 2001. Applications (TEN COPIES) should be made to the Endoscopy Section Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2000.

3rd European Federation of Autonomic Societies (EFAS)

The third European Federation of Autonomic Societies (EFAS) meeting in conjunction with the annual meeting of the sections "Autonomic nervous system" of the German Neurological Society, "Diabetes and Nervous System" of the German Neurological Society, and "Autonomic Nervous System" at the University of Erlangen-Nuremberg, Germany, will be held in Erlangen, Germany on 26–28 April 2001. Abstract deadline: 20 December 2000. Further information: Professor Dr M J Hilz, Department of Neurology, University or Erlangen-Nuremberg, Schwabachanlage 6, D-91054 Erlangen, Germany. Tel: +49 0131 8534444; fax: +49 9131 8534328; website: www.neurologie.med.uni-erlangen.de/oeffentliche_Veranstaltungen.htm

Cleveland Clinic Florida's Gastroenterology Update 2001

Cleveland Clinic Florida will be sponsoring a postgraduate course entitled "Gastroenterology Update 2001" to be held on 10–11 February 2001 in Fort Lauderdale, Florida, USA. Further information: Sally Jagelman, Manager of Continuing Medical Education, Cleveland Clinic Florida, 3000 West Cypress Creek Road, Fort Lauderdale, FL 33309, USA. Tel: +1 954 978 5539; fax: +1 954 978 5056; email: jagelms@ccf.org

GI malignancies can be prevented and treated: from the bench to the bedside

This international meeting will be held on 14–17 February 2001 in Jerusalem and the Dead Sea, Israel. Further information: Marilyne Katz, Secretariat, GI Malignancies, Target Tours, PO Box 29041, Tel Aviv 61290, Israel. Tel: +972 3 5175150; fax: +972 3 5175155; email: gi@targetconf.com

Gastroenterology and Endotherapy: XIXth European Workshop

This course, to introduce the experienced gastroenterologist to the growing field of therapeutic endoscopy, will be held on 18–20 June 2001 in Brussels, Belgium. Further information: Mrs Nancy Beauprez, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B-1070 Brussels. Tel: +32 02 555 49 00; fax: +32 02 555 49 01; email: beauprez@ulb.ac.be