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