CORRESPONDENCE

Readers are encouraged to write letters to the editor concerning articles that have been published in GASTROENTEROLOGY. Short, general comments are also considered, but use of the Correspondence section for publication of original data in preliminary form is not encouraged. Letters should be typewritten double-spaced and submitted in triplicate.

Hepatitis G Virus in Intravenous Immunoglobulin

Dear Sir:

Healey et al. conducted a comprehensive study of an acute hepatitis outbreak in patients receiving a particular batch of Gammagard intravenous (IV) immunoglobulin (Ig)¹ and attributed the cause to hepatitis C virus (HCV) that was not completely inactivated. A routine follow-up of liver function tests in all IV Ig recipients is therefore recommended.

Two additional points are worthy of discussion. First, is there any cotransmission of other hepatitis viruses by this batch of contaminated IV Ig? Most imminently, the recently identified hepatitis G virus/GB virus—C virus (HGV or GBV-C)^{2,3} should be examined. HGV can be transmitted by transfusion³; however, it has never been screened in blood donors. With a viremia rate of about 1%–2% among healthy, volunteer blood donors in Western countries,² the plasma pool for IV Ig preparation must contain a substantial amount of HGV. It is estimated that about 15,000 individual donations from several thousand donors contribute to the plasma pool to produce a single batch of IV Ig, in which at least 100 U of blood contain HGV. In comparison, as the blood donors are screened by a well-established anti-HCV assay that only fails in identifying a small portion of seronegative HCV-carrying donors (<5%), in the plasma pool, the number of units still containing HCV should be <5 U. Therefore, in this inadequately inactivated IV Ig lot, HGV, because of a much heavier load than that of HCV, more likely also escaped the inactivation process, remains viable, and is transmitted to the recipients.

The second point is the contribution of HGV infection in the patients with hepatitis receiving this batch of IV Ig. The clinical picture of HGV infection is far from clear.^{2,4} In our prospective study of posttransfusion hepatitis, HGV was shown to cause little or very mild hepatitis in the majority of infected recipients.⁵ On the other hand, serious hepatitis to the extent of fulminant hepatitis has been reported in Japan.⁶ HGV infection in IV Ig recipients, most of whom are immunocompromised, might lead to significant morbidity and merits thorough investigation. If IV Ig-transmitted HGV is confirmed, a phylogenetic tree analysis of these viruses is also interesting. In contrast to that of IV Ig-transmitted HCV, the analysis would very likely reveal heterogeneous origins of the HGV infection because of more HGV-carrying donors in the plasma pool. This information should be useful in understanding the risk of HGV infection in the contaminated IV Ig and in further defining the role of this new virus in causing human hepatitis.

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2. Simons JN, Leary TP, Dawson GJ, Pilot-Matias TJ, Muerhoff AS, Schlauder GG, Desai SM, Mushahwar IK. Isolation of novel virus-like sequences associated with human hepatitis. 1995;1:564–569.
3. Linnen J, Wages J, Zhang-Keck ZY, et al. Molecular cloning and disease association of hepatitis G virus: a transfusion transmissible agent. Science 1996;271:505–510.
4. Zuckerman AJ. The new GB hepatitis viruses. Lancet 1995;345:1453–1454.
5. Wang JT, Tsai FC, Lee CJ, Chen PJ, Sheu JC, Wang TH, Chen DS. A prospective study of transfusion-transmitted GB virus C infection: similar frequency but different clinical presentation compared with hepatitis C virus. Blood (in press).
6. Yoshida M, Okamoto H, Mishiro S. Detection of the GBV-C hepatitis virus genome in serum from patients with fulminant hepatitis of unknown aetiology. Lancet 1995;346:1131–1132.

Reply. We agree with Chen et al. that cotransmission of other hepatitis viruses should be considered. During the initial outbreak, coinfection with other hepatotropic viruses (hepatitis A and B viruses, Epstein–Barr virus, and cytomegalovirus) was excluded. More particularly, our collaborators, Jarvis et al.,¹ have examined batches of Gammagard IV Ig and serum from recipients of the HCV-contaminated batch of Gammagard for the presence of HGV. Six of six batches tested, including the contaminated batch (93F21AB11B) of Gammagard, were positive for HGV. However, HGV has not been detected in any U.K. recipients of this contaminated batch tested (14 of 14 serum samples from 3 to 6 months after exposure). These data suggest that if HGV transmission occurred in these patients, it was not associated with chronic infection or clinical episodes of hepatitis. However, the exact interaction between the immune response to repeated inoculation with HGV RNA and the subsequent HCV outbreak cannot be known. It is possible that such responses to HGV, which shares considerable homology to HCV, may contribute to the severity of acute HCV infection in immunodeficient patients found in both this and previous outbreaks of HCV.^{2,3}

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1. Healey CJ, Sabharwal NK, Daub J, Davidson F, Yap PL, Fleming KA, Chapman RWG, Simmonds P, Chapel H. Outbreak of acute hepatitis C following the use of anti-HCV virus—screened intravenous immunoglobulin therapy. Gastroenterology 1996;110:1120–1126.

1. Jarvis LM, McOmish F, Hanley JP, Yap PL, Ludlam CA, Simmonds P. Low transmission rate of hepatitis G virus/GBV-C to haemophiliacs and other recipients of plasma products. *Lancet* 1996 (in press).
2. Bjoro K, Froland S, Yun Z, Samdal HH, Haaland T. Hepatitis C infection in patients with primary hypogammaglobulinemia after treatment with contaminated immune globulin. *N Engl J Med* 1994; 331:1607–1611.
3. Healey CJ, Watson J, Durrige M, Snowdon N, Christie J, Wong S, Read S, Kurtz J, Fleming KA, Chapel H, Chapman RWG. Treatment of acute hepatitis C with alpha interferon in agammaglobulinemia—the UK Maggard outbreak (abstr). *Gastroenterology* 1995;108:A1082.

Abnormal Intestinal Motility in Irritable Bowel Syndrome

Dear Sir:

We read with interest the paper on jejunal sensorimotor dysfunction in irritable bowel syndrome (IBS) by Evans et al.¹ They concluded that abnormal postprandial jejunal motor activity is related to jejunal mechanoreceptor hypersensitivity. In their study, which compared 11 patients with diarrhea-predominant IBS with 25 healthy controls, abnormal phase 2 and phase 3 activities were found in 73% and 64% of patients, respectively. Postprandial motor activity was abnormal in 36% after an 800-kcal meal and in 100% after a 400-kcal meal.

In a recent study, we analyzed 24-hour ambulatory jejunal manometry in 35 patients with diarrhea-predominant IBS and 50 healthy controls.^{2,3} Abnormal motility, defined as at least one motility variable out of the range of controls, was found in only 43% of patients, with an abnormal postprandial motility after a 600-kcal meal present in only 14%. Abnormalities in the fasting state were disturbed aboral migration of phase 3 (6%), prolonged irregular burst activity (3%), increased duration of clustered activity (23%), and increased contraction amplitude (23%) and increased proportion of aborally propagated contractions (3%) during phase 2. In the postprandial state, an increased percentage of propagated contractions was the only abnormal finding.

The results obtained by Evans et al.¹ are obviously discrepant to several previous studies,^{4–6} including our own data. Besides different study conditions (patient selection, ambulatory vs. stationary recordings, and standardized food intake vs. self-selection of meals) and the heterogeneity of the IBS, we feel that another reason to explain these differences might be the size of the patient and control group.

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1. Evans PR, Bennett EJ, Bak JT, Tennant CC, Kellow JE. Jejunal sensorimotor dysfunction in irritable bowel syndrome: clinical and psychological features. *Gastroenterology* 1996;110:393–404.
2. Schmidt T, Hackelsberger N, Leitel G, Widmer R, Meisel C, Pfeiffer A, Kaess H. Is small bowel motility abnormal in the irritable bowel syndrome (abstr)? *Gastroenterology* 1995;108:A605.
3. Schmidt T, Hackelsberger N, Widmer R, Meisel C, Pfeiffer A, Kaess H. Ambulatory 24-hour jejunal motility in diarrhea-predominant irritable bowel syndrome. *Scand J Gastroenterol* 1996;31:581–589.
4. Kellow JE, Phillips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology* 1987; 92:1885–1893.
5. Kellow JE, Gill RC, Wingate DL. Prolonged ambulant recordings of

small bowel motility demonstrate abnormalities in the irritable bowel syndrome. *Gastroenterology* 1990;98:1208–1218.

6. Gorard DA, Libby GW, Farthing MJG. Ambulatory small intestinal motility in diarrhoea predominant irritable bowel syndrome. *Gut* 1994;35:203–210.

Reply. We thank Schmidt et al. for their interest in our recent paper.¹ They refer specifically to the 11 patients with diarrhea-predominant IBS in our sample of 24 patients with IBS and discuss the rates of small bowel motility abnormalities that we found in this subgroup.

The main thrust of our paper was to evaluate the relationships between enteric hypersensitivity, dysmotility, and psychosocial factors in IBS; thus, we did not present detailed data on the specific type of abnormalities observed in each of our subgroups. Apart from their own study,² the studies to which Schmidt et al. refer^{3–5} cannot be compared directly with our recent study because of differences in experimental protocols and data analysis. In particular, only between-group comparisons of parameters were undertaken in these latter studies, and rates of abnormality were not determined. Moreover, postprandial recordings were not obtained in one of these studies,⁵ and, in the other two studies,^{3,4} postprandial motility was not analyzed quantitatively. The test meals also differed between our study and that of Schmidt et al.² In regard to the study of Schmidt et al.,² it is likely that the small bowel motor parameters that were analyzed differed from those evaluated in our study. It is not stated which parameters were analyzed in their study and whether, for example, motility indices or the presence of phase 3–like activity during the fed pattern were determined. We observed alterations in these latter parameters postprandially in our patient group. We acknowledge that larger control groups may result in wider “normal ranges”; however, in determining rates of abnormality based on one or more parameters outside a control range, the results are clearly also dependent on the number and type of parameters evaluated. This in turn may be dependent on the type of computer-assisted analysis used.

Overall, because of the variations in study methodology and data analysis, we cannot agree that the results obtained in our recent study are “obviously discrepant” to those of earlier studies. Finally, and perhaps most importantly, in addition to the problems of patient heterogeneity in IBS, as outlined by Schmidt et al., it is clear that until the methodology and analysis of human small bowel motility recordings can be standardized between centers, differences will continue to be apparent.

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2. Schmidt T, Hackelsberger N, Widmer R, Meisel C, Pfeiffer A, Kaess H. Ambulatory 24 hour jejunal motility in diarrhea-predominant irritable bowel syndrome. *Scand J Gastroenterol* (in press).
3. Kellow JE, Phillips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology* 1987; 92:1885–1893.
4. Kellow JE, Gill RC, Wingate DL. Prolonged ambulant recordings of