Measles viral genomic sequences in intestinal tissue

EDITOR,—In a thorough investigation, Haga et al were unable to demonstrate the presence of measles virus RNA in intestinal specimens from patients with inflammatory bowel disease (Gut 1996; 36: 211–5). Although they developed an exquisite sensitive technique, there remains a fundamental flaw in their methodology. They described intestinal tissue postoperative resection times ranging from 20 to 90 minutes. Such prolonged ischaemic times would have reduced the sensitivity of their assay considerably, as substantial RNA degradation would have occurred. MacPherson et al reported a significantly lower yield of RNA in surgical intestinal specimens compared with resection tissue within 15 minutes to 1 hour 45 minutes compared with biopsy specimens frozen within 15 minutes. Further degradation can also occur during prolonged storage at −70°C. The assay may be sufficiently sensitive to detect viruses compared with immunohistochemical staining, electron microscopy, and in situ hybridization. Although the conditions for RNA in the intestine might be different than in brain tissue, the most important strategy to seek measles virus is to choose the method that provides the highest sensitivity. Our methods satisfy these criteria.

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Reply

EDITOR,—We reply to the claims of Chadwick and Wakefield. As Lund et al described one virion contains well in excess of 250 copies of the genome. The virus particle contains several genomes, and one plaque forming unit may not represent one measles viral genome. With regard to the delay between resection and freezing of samples, I have already described the details in the reply to Dr Smith. Although we confirmed the absence of PCR inhibition by spiking the homogenate from 250 mg of control intestinal tissue with 5 pg of RNA from a measles-infected Vero cell culture, the spiking to postoperative control tissue might provide more exact evaluation for RNA degradation, even though the spiking before and after homogenisation might not make so much difference. Fundamentally we think that the most important strategy to detect measles virus is to choose the method that provides the highest sensitivity out of various methods available in the world.

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Oesophageal hypersensitivity

EDITOR,—We would like to comment on the paper by G Shi et al (Gut 1995; 37: 457–64). A statistically significant association of symptoms and reflux episodes was found in 96 patients with normal oesophageal exposure to acid during 24-hour 24-channel single-lead ambulatory oesophageal pH monitoring.

The authors stated that this was consistent with the idea of oesophageal hypersensitivity to acid. This group of patients was very heterogeneous, as 14 of 96 of these patients had reflux oesophagitis, 28 of 96 had hiatal hernia, and 22 of 96 were not endoscoped before pHmetry. Furthermore, in an unspecified number of patients the pH probe was positioned by the pH step up method, which is known to accurately locate the lower oesophageal sphincter in 58% of patients. As reported by Anggiansah et al a placement of the probe at 10 cm instead of 5 cm above the lower oesophageal sphincter accounts for a change in diagnosis in 45% of patients. Furthermore, it is well known that patients often do not tolerate pHmetry and may diminish their food and beverage intake considerably. Underreporting of symptoms is common and severity of symptoms differ considerably among patients. As meal composition and timing were not standardised and severity of symptoms noted (for example, by visual analogue scales) it is difficult to consider a given pH monitoring as significant.
representative and even more to establish hypersensitivity to acid. Thus, these several difficulties in pH monitoring in a heterogenous patient population do, in our opinion, prevent a new classification of oesophageal hypersensitivity to acid. A prospective and standardised study in these patients is needed to better define whether the hypersensitive oesophagus is a distinct clinical entity, or whether pH monitoring underdiagnoses gastro-oesophageal reflux disease.


Reply

EDITOR,—We would like to thank Drs Borovicka and Michetti for their interest in our paper and appreciate their critical comments.

We would not say that our group of patients was 'very heterogeneous'. Indeed, almost all patients studied complained of 'typical' reflux symptoms although they did differ from a pathological point of view, that is presence (and severity) or absence of mucosal lesions. The vast majority of them had a normal oesophageal mucosa, a finding recently reported by Trimble et al2 who studied patients with normal acid exposure and a convincing correlation between symptoms and reflux episodes. Therefore, in this patient population, endoscopy is often meaningless and this is why it was not performed in 23% of our patients.

Our study is a retrospective one with the inherent drawbacks, but it reports data from a large series of consecutive patients from one centre. It is therefore understandable that pH monitoring was performed under different conditions. Some had an oesophageal manometry because of their predominant symptoms (for example, dysphagia or odynophagia) and, in these patients, manometric localisation of lower oesophageal sphincter (LOS) was used for positioning the pH probe. In those with no previous manometry, pH step up was used to localise LOS. Although manometric determination of LOS may be the 'gold standard' to position the pH probe, a close correlation was discovered between the manometrically localised LOS and the sudden pH change occurring when the electrode is moved from the stomach to the oesophagus.3,4 The mean difference found by Klausen et al5 between manometric assessment and pH step up technique was less than 0-5 cm, which is in agreement with our own experience.

There are some physiological reasons to suggest that the type and amount of food ingested during the recording period as well as the degree of physical activity can actually affect the duration and the extent of oesophageal acid exposure.3 In the early studies performed in hospitalised patients and using stationary pHmetry, many authors including ourselves4 recommended to standardise diet and physical activity in the hope of reducing inter and intra-individual variability. Patients were told to avoid acidic beverages and foods to reduce artefacts and risks of confusion with reflux episodes. However, a free diet does not seem to change either the diagnostic value or the reproducibility of the technique.6 In addition, Jamieson et al7 reported that there is no significant difference, with the exception of the number of reflux episodes, between oesophageal pH recordings performed in an inpatient or outpatient environment. To identify the temporal relation between symptoms and reflux episodes, it becomes more and more important to emphasise the many advantages of ambulatory recording in patients engaged in everyday activities with no restriction regarding diet and exercise.8 In contrast, standardisation may unnecessarily affect the patient's regimen and reduce the ability of the test to detect a significant association between symptoms and reflux episodes.9

Although we did not assess the severity of symptoms in our patients, we correlated them with reflux episodes. When one or several symptoms occurred during reflux episodes or within two minutes of their end, and the possibility of this occurrence by chance was excluded by probability calculation, we assumed that refluxed acid had induced symptoms. As total acid exposure was within normal range and reflux episodes were actually shorter and less acidic than in patients with gastro-oesophageal reflux disease, an oesophageal hypersensitivity to acid could reasonably be hypothesised for this subgroup of patients. The presence of low grade oesophagitis in 19% of our patients indicates—as suggested by Heading’s term—that a greater mucosal sensitivity to damage may coexist with increased nicotine exposure in patients with 'acid hypersensitive oesophagus'.

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NOTE

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