LETTERS TO THE EDITOR

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 exquisitely 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 after resection than in the tissue sample collected just before resection, indicating substantial RNA degradation and suggesting that it would not be possible to detect viral RNA sequences with any high sensitivity. Further, the authors themselves note that postoperative resection causes RNA degradation and suggest that only RNA samples that are immediately frozen can be useful for detecting viral RNA sequences. In conclusion, we believe that the negative results reported by Haga et al cannot be considered as evidence against the presence of measles virus RNA in intestinal tissue. However, the authors’ methodology is flawed, and their results do not provide evidence against the presence of measles virus RNA in intestinal tissue.

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Reply

EDITOR,—Dr Smith claims that there remains a flaw in the condition of intestinal tissue used to detect measles virus. It is partially acceptable that RNA degeneration occurs by ischaemia after surgery. Even so we need to use the resected specimen because the positive in situ hybridisation for measles was observed principally in the submucosa and serosa by Wakefield et al. It is important to seek measles viruses in various areas throughout the thickness of the intestine. To avoid the risk of failing to detect the measles virus in such a small sample as a biopsy specimen, the resected specimen must be more useful.

Furthermore, it is impossible to freeze the intestinal specimens in such a short time as 45 seconds after resection. Concerning the ischaemic time of the specimens, some reports describe that generally measles virus is detectable if the autopsy time is less than six hours in the brain tissues of patients with subacute sclerosing panencephalitis (SSPE) by in situ hybridisation. Under ~70°C, even after 20 years of storage, most cases of SSPE provide positive results for measles virus by nested reverse transcription polymerase chain reaction (RT-PCR).

As a positive control in our study, the brain tissue of a SSPE patient had three hours of autolysis time and three years of storage time under ~80°C. Even in paraflned embedded specimens, measles virus is detectable for immunohistochemical staining, in situ hybridisation, and RT-PCR. Generally, nested RT-PCR provides much higher sensitivity to detect viruses compared with immunohistochemical staining, electron microscopy, and in situ hybridisation. 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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Oesophageal hypersensitivity

EDITOR,—We reply to the claims of Chadwick and Wakefield. As Lund et al described, one virion contains well in excess of 100,000 nucleocapsid proteins, each of which contains a segment of viral RNA. Although viruses do not contain sequences that provide a mechanism to prevent annealing of the viral RNA, they do contain sequences that provide the highest sensitivity out of many 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 ambulatory 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 fraction of patients the pH probe was positioned by the pH step up method, which is known to inaccurately 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 differs considerably among patients. As meal composition and timing were not standardised and severity of symptoms not assessed (for example, by visual analogue scales) it is difficult to consider a given pH monitoring as providing evidence for oesophageal hypersensitivity.

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