Letters


Ménetrier’s disease

EDITOR.—We read with interest the case report by Bayerdorffer et al showing that Helicobacter pylori is a potential cause of Ménetrier’s disease (Gut 1994; 35: 701–4). The findings in their patient showed clearly that H pylori gastritis can present as hypotrophic gastritis combined with protein loss and that eradication of the H pylori infection can lead to rapid disappearance of hypotrophy and restoration of normal gastric mucosa. We disagree, however, with the authors’ presumption that Ménetrier’s disease and hypertrophic gastropathy are synonymous. There are many reasons for believing that equating the two terms is ill advised. (1) A variety of conditions can cause enlarged gastric folds. In addition to the true ‘hyperplastic gastric pathologies’ Ménetrier’s disease and Zollinger–Ellison syndrome, a variety of conditions, e.g. oesophageal varices and post-gastrectomy, can also be associated with enlarged gastric folds. (2) Increased gastric protein loss can be found occasionally in many disorders that are associated with enlarged gastric folds, but protein loss is not a universal feature of any of these disorders. It is typically lacking in Zollinger–Ellison syndrome, and its reported occurrence in Ménetrier’s disease is variable. (3) Criteria for Ménetrier’s disease are based on different conditions associated with sarcoidosis, allergic (eosinophilic) gastritis, and Cronkhite–Canada syndrome. (4) The concept that massive foveal hyperplasia is a definitive feature of Ménetrier’s disease is greatly strengthened by studies showing that there is an accompanying change in the distribution and activity of transforming growth factor α in the gastric mucosa in Ménetrier’s disease. In addition, the experimental induction of an excess of transforming growth factor α in transgenic mice results in similar mucosal cell hyperplasia. (5) It is highly probable that ‘hypertrophic hypersecretory gastropathy’ (Schindler’s disease), another distinctive entity that is sometimes mistakenly designated as Ménetrier’s disease, is probably a manifestation of H pylori gastritis with large folds. We urge authors and editors not to use the term Ménetrier’s disease as a generic designation when reporting for any of the above-mentioned diseases associated with enlarged rugae. The eponym should be limited to those rare cases that fulfil Ménetrier’s original description of massive foveal hyperplasia without gastritis. This approach is essential from a nosologic and patient treatment standpoint if the varied aetiologies and resulting treatment implications of hypertrophic gastropathy are to be properly understood. Bayerdorffer et al would have preferred to see it termed simply H pylori associated hypertrrophic gastritis.
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EDITORS,—We agree with Hendrix and Yardley that Helicobacter pylori infection with hypertrophic gastric folds and a protein loss syndrome should in future be termed merely 'H. pylori induced hypertrophic gastropathy' and not Menetrier's disease; and further, that on detection of hypertrophic gastric folds a search should be carried out for other possible infectious causes or underlying diseases with hypertrophic folds, or both. In the past, this has not been done, either in case reports or reviews of large numbers of cases of Menetrier's disease. In particular, most publications failed to evaluate inflammatory infiltration as an exclusion criterion for Menetrier's disease. Thus, for example, Schindler described Menetrier's disease in his article on 'hypertrophic glandular gastritis', and Scharschmidt in his review, expressly emphasised that 'round cell infiltration of the lamina propria was also frequently noted and was very prominent in some cases' of Menetrier's disease.

The suggestion that only massive foveolar hyperplasia or hypertrophy of the corpus gastritis should be termed Menetrier's disease, was made comparatively late by Appelman, but was often ignored. The cases of Menetrier's disease reported from the Mayo Clinic were, for example, accepted as 'true' Menetrier's disease when 'a hypertrophic gastropathy with hypoproteinemia' presented. Indeed, in the first synopsis of 43 patients, 'a systematic histologic study of the gastric mucosa' was even deliberately not undertaken. In the latest review of the Mayo Clinic cases, it was then shown that a comparatively large percentage of these patients had a 'lymphocytic gastritis', also with loss of protein, that recall that the former 'gastritis en nappe' has more recently been shown to be a special form of lymphocytic gastritis, and that this gastritis can also include appreciable foveal hyperplasia and also takes into account the fact that Menetrier made reference to 'polyanodenomes gastriques', which he further subdivided into 'polyanodenomes polypeux' and 'polyanodenomes en nappes', there are justifiable doubts as to whether Menetrier's disease as such ever was an individual entity in the first place.

The description 'polyanodenomes polypeux' given by Menetrier himself, did not include macroscopically evident hypertrophic gastric folds, and his histological description fits that of present day 'hyperplastic' polyps, which the drawing of the macroscopic findings in Menetrier's publication also seems to confirm, as it shows multiple polyps in the antrum and corpus, but no hypertrophic folds.

Also, in these polyps — in contrast with the interpretation of Hendrix and Yardley — Menetrier described an inflammatory infiltrate ('inflitré de cellules migratrices'). And also in the case of the 'polyanodenomes en nappes', Menetrier noted 'des phénomènes de gastritis chronique'.

When it is further considered that the histological technological of 1888 was, of necessity, inferior to that of the present day, that the descriptions were based on necropsy and autopsies, and that we now know that 'polyanodenomes en nappes' changes in the corpus and fundus are typical of lymphocytic gastritis, doubts that Menetrier had ever really described an individual entity or that the cases of Menetrier's disease published over the past decades really represented an individual entity, are considerably strengthened.

Our case history was intended merely to draw attention to the fact that when the clinical and endoscopic pictures suggest Menetrier's disease, we should in future give more consideration to the possibility that the described condition points to H. pylori induced gastritis, which can then be cured by eradication of the H. pylori.

Reply

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M STOLTE
Institute of Pathology,
Bayreuth, Germany
E BAYERDORFFER
Medical Department II,
Klinikum Großhadern,
University of Munich,
Germany

Polyethylene glycol (PEG) as a marker of small intestinal permeability

EDITOR,—We were very interested to read the paper by Peeters et al, who in an attempt to standardise intestinal permeability test conditions, have studied the effects of probe solution composition and osmolality on the permeation of 51CrEDTA and PEG 400 (MW 280-634) across the small intestine (Gut 1994; 35: 1404-8). We endorse the need for standardisation in the conduct of small intestinal permeability tests and in a recent investigation of the effects of hydration status on urinary probe recovery in normal subjects we found that fluid hydration had a considerable effect on the recovery of PEG (MW range 280 to 1100). In contrast, mannitol and lactulose recovery were not affected. Peeters et al expressed their results as 51CrEDTA/PEG 400 ratios and found that the permeation of both markers was significantly reduced in the presence of lactulose and mannitol. We wonder whether differences in the hydration status of their subjects might explain their results.

The dependence of PEG permeation on the state of subjects' hydration at the time of the test is just one problem facing those determined to use PEG as a marker of small intestinal permeability. PEG 400 is absorbed in vivo, and this is not necessarily due to other probes of similar molecular weight such as lactulose (MW 342) and the absorption of PEG is reduced in conditions associated with flat mucosa whereas that of lactulose is increased. These anomalies have never been fully explained by the proponents of PEG as a passive permeability marker. In their recent paper, Peeters et al attempt to explain the unusually avid permeation of PEG 400 in comparison with other probes of similar size on the basis of theoretical considerations regarding the long, thin shape of PEG. It has been proposed that PEG has access to absorptive areas inaccessible to other molecules of comparable size because of its shape. However, this theory has not stood up to experimental analysis. Furthermore the concept of PEG as a long, thin molecule does not take into account the fact that effective size of PEG may in fact be much larger because of hydrogen bonding by the available ether oxygen atoms along the backbone of the molecule. Another possible explanation for the avid permeation of PEG across cell walls, because PEG is lipid soluble, it interacts with the phospholipid bilayer of the cell wall. In a recent in vitro study comparing PEG with lactulose in rat intestinal explants we were able to show that PEG 400 (in contrast with other molecules) could traverse lipid barriers with comparative ease.

Another problem with the use of PEG as a marker of intestinal permeability is the wide variability in the recovery of the smallest molecules in a range of PEGs is comparatively delayed in normal subjects, suggesting a slow wash out of these molecules from the extravascular space into the circulation. Given all these problems with regard to the permeation of PEG across the intestine and its subsequent urinary recovery we suggest that the time has probably come for this molecule to finally be abandoned as a marker of passive small intestinal permeability in vivo.

T H IQBAL
M A COX
K A NIXI
B T COOPER
Gastroenterology Unit,
City Hospital NHS Trust,
Dailey Road,
Birmingham B16 2QH