choice of probe molecules used in tests such as the cellobiose/mannitol test is inappropriate; rather we would suggest that the three probe molecules used by Bjarnason and Peters, although providing an elegant demonstration of increased permeability to high molecular weight molecules, are inappropriate to show the reduced permeability of the small intestine to small hydrophilic molecules which is characteristic of coeliac disease.

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Reply

SIR,—We are grateful for the opportunity to reply to Drs Hamilton, Cobden, and Axon's letter, which is somewhat misleading, and again indicates their confusion over the concept of permeability and its terminology.

As we have repeatedly emphasised in our communications[1–4] permeability is not synonymous with absorption. By definition, permeability is a solute flux rate across a unit area of membrane in a given time. Absorption, however, is the solute flux in a given time, irrespective of the membrane size. Absorption can therefore be increased or decreased by varying the surface area, while permeability remains unchanged. There are, however, two situations where intestinal surface area does not need to be defined strictly and thus where absorption may be synonymous with permeability, other factors being constant. Firstly, when the possibility of increased permeability across a membrane which is known to have a reduced surface area is being investigated. For this purpose, one uses an essentially non-absorbable test substance, the appearance of which is truly a reflection of increased permeability. Secondly, when decreased permeability occurs where the surface area is increased, one uses a test substance which is completely absorbed under normal circumstances. If reduced absorption is found, decreased permeability is likely, if other factors have been controlled. There is no place for the use of probe molecules such as mannitol which pass the membrane at an intermediate rate, for measuring permeability because the results obtained are clearly open to variable interpretation.

Mannitol, monosaccharides, and poly(ethyleneglycol) 400 are all absorbed to a variable extent in the five to six hours after oral administration. In normal subjects this ranges from 14–24% of the administered dose. In patients with untreated coeliac disease, their absorption is decreased by approximately 60%, but as the surface area is reduced by at least four-fold, these results clearly cannot be interpreted as reduced permeability. The various claims that coeliac disease is characterised by reduced permeability to small hydrophylic molecules therefore remains a fallacy, and will remain so unless the appropriate experiments show otherwise.

Hamilton *et al* clearly do not understand the inappropriateness and limitations of their test substances. Firstly, their test substances are not inert and are in fact administered in quantities which are almost purgative (5 g cellobiose and 2 g mannitol). These doses will therefore hold water within the intestinal lumen to preserve isotonicity, increasing intestinal motility and therefore effectively bypassing the diseased area under study. Catt *et al*[5] have indeed shown that 5 g mannitol decreases the absorption of the monosaccharide, Rhammose by 35%, while that of Lactulose (disaccharide) is decreased by 18%. Secondly, Hamilton *et al* administered the test substances in a hyperosmolar (1500 mmol/l) solution prepared by the addition of 20 g sucrose and 20 g lactose, the choice of sugars being decided by the palatability of the test solution. It is, however, particularly important to omit lactose because it is well known that lactase is the last brush border disaccharidase to recover after gluten withdrawal in patients with coeliac disease. Lactose is therefore hydrolysed to

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only a very limited extent in patients with untreated coeliac disease and only to a limited extent by patients treated for as short a time as three to eight months. The lactose would therefore remain osmotically active in the small intestinal lumen in coeliac patients, decreasing transit time and reducing the absorption of the test substances, while in normal subjects, it is readily hydrolysed and quickly absorbed. Thirdly, these same workers have themselves noted that cellobiose is itself partially hydrolysed and others have presented experimental data that show that the use of mannitol is questionable.[6] These factors may very well explain the apparent discrepancy between our results and theirs.

Drs Hamilton, Cobden, and Axon should be fully aware that the sensitivity of their test is low in comparison with the 51 Cr EDTA absorption test, and with our recently described *in vitro* test. Numerous communications concerning the use of various sugar ratios attests to their lack of specificity.[7–12]

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Books

Coeliac disease By W T Cooke and G K T Holmes. (Pp. 281; illustrated; price not stated) Edinburgh: Churchill Livingstone, 1984.

This book seeks to present gastroenterologists with a comprehensive account of coeliac disease. It gives an admirable description of the condition from the point of view of an experienced clinician who has cared for coeliac patients for nearly half a century. There is a historical introduction, followed by a discussion on definition, then an account of the jejunal mucosa in coeliac disease. Thereafter, the clinical features of the disorder and conditions associated with it are described. The book concludes with a chapter on aetiology.

Not all will agree with the authors when they argue that it is impossible to define coeliac disease, nor with the view that the intestinal mucosa may sometimes be normal on jejunal biopsy. As might be expected, the best sections of the book are those dealing with the clinical features of the condition. There is an exhaustive bibliography, to the extent that whole lines of text are sometimes taken up by reference numbers, which does not make for easy reading. The order of the chapters and their content sometimes display an endearing eccentricity, metabolic bone disease being included in the chapter on clinical presentation rather than with metabolic disturbances and diagnostic investigations.

For the historian, the full story has yet to be told. The historical section deals in great detail with long forgotten contributions to the literature and there is little consideration of the background to Dicke's epoch making discovery. Dicke was a man of remarkable perception. He was working in the

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