Correspondence

SIR,

Balldin and colleagues\(^1\) reported an increase of serum total amylase activity in cigarette smokers, but their results failed to be confirmed by Nasrallah et al.\(^2\).

We have evaluated serum total amylase activity, isoamylase fractions by electrophoretical method and salivary \(\alpha\)-amylase activity in 70 subjects, aged 30–65, divided as follows: group S consisted of 30 subjects who had smoked cigarettes for three to 20 years and at time of study smoked more than 20 cigarettes/day; group N consisted of 40 non-cigarette smokers who served as reference group.

No subject used had a history of alcohol abuse or of gastroenterological disease. The Table indicates that there is no difference in the fasting levels of total amylase and pancreatic isoamylase in the two groups considered.

<table>
<thead>
<tr>
<th></th>
<th>Group S (32)</th>
<th>Group N (40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total amylase</td>
<td>236.69±11.18</td>
<td>293.40±18.19</td>
</tr>
<tr>
<td>Type P</td>
<td>111.56±9.02</td>
<td>120.84±8.66</td>
</tr>
<tr>
<td>Type S</td>
<td>125.13±6.02</td>
<td>172.56±12.73</td>
</tr>
<tr>
<td>Salivary amylase</td>
<td>274.3±16.05</td>
<td>437.5±32.62</td>
</tr>
</tbody>
</table>

All results are shown as M ± SEM (units/l). Saliva diluted 1/1000.

It may be observed that cigarette smokers exhibit a reduction in serum type S isoamylase that correlates well with the significant reduction of salivary amylase activity. Several studies reported that tobacco smoke contains agents with cytotoxic or carcinogenic effects on the exocrine pancreas,\(^3,4\) but little is known about the effect of tobacco smoke on salivary glands.

From our results it could be argued that chronic cigarette smoke may exert a toxic effect on salivary glands, by acting through a local effect or a neurovascular reflex. In any event, the real impact of findings linking cigarette smoking with abnormalities in salivary amylase activity should be further investigated.

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References


In vitro determination of small intestinal permeability

SIR.—We were interested to read the recent paper by Drs Bjarnason and Peters (Gut 1984; 25: 145–50) describing their in vitro technique for showing abnormalities of intestinal permeability in coeliac disease. While we agree with the authors that the results they present do not confirm a reduced intestinal permeability to small hydrophilic molecules, we believe this is a result of their selection of probe molecules, and does not provide evidence that such a reduction of permeability does not occur. The three molecules used in this work are all considerably larger than probe molecules such as mannitol, monosaccharides and low molecular weight polyethylene glycols, for which there is indisputable evidence of reduced absorption in coeliac disease.\(^1,4\) The inverse relationship between molecular weight and intestinal permeability to molecules with a molecular weight between 340 and 5200 daltons shown by Bjarnason and Peters confirms our own observations in an animal model,\(^5\) although we believe that molecular volume is a more appropriate parameter to relate to intestinal permeability than molecular weight. We have also found that there is a different inverse relationship for smaller molecules with a molecular volume between 130 and \(230 \times 10^{-2}\) nm,\(^3,5\) suggesting that such small molecules are absorbed via a different pathway from which EDTA, cyanocobalamin and inulin would be excluded by their physical size, and we believe it is this pathway which becomes less permeable in coeliac disease.

The major advantage of tests of intestinal permeability based on the simultaneous administration of two molecules is the contrasting changes in their absorption that occur in coeliac disease, reducing the influence of extraneous factors such as gastrointestinal transit time and renal function on the test result\(^6\) and increasing the sensitivity and specificity of the test.\(^7\) Thus we cannot agree that the
choice of probe molecules used in tests such as the cellulose/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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References


6 Cobden I. MD Thesis. University of Newcastle-on-Tyne.


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 communications1-4 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(ethylene-glycol) 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 hydrophilic 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 cellulose 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 al5 have indeed shown that 5 g mannitol decreases the absorption of the monosaccharide, Rhamnose 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...
In vitro determination of small intestinal permeability.

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