Correspondence


Reply
In reply to the letter of Beglinger et al I should like to make the following comments:

(1) First of all, I wish to point out that our study (the first to have investigated in a systematic manner the action of secretin on human pancreatic secretion) was carried out on pure pancreatic juice which without doubt represents the most appropriate means of studying pancreatic secretion. Duodenal juice is a mixture of various digestive secretions which may affect in different ways the composition of pancreatic juice.

(2) There are profound methodological differences between our study and those performed by Beglinger et al, and others cited by them (differences not only in the type of juice used but also in the type of pancreatic stimulation). These differences make a comparison of the results very difficult, and may explain the discrepancies. Moreover, it should be pointed out that the vast majority of the studies they cited were not specifically designed to investigate the action of secretin on the pancreatic enzyme secretion and were not, therefore, detailed examinations of this action.

(3) In their review of papers dealing with the action of secretin on human pancreatic enzyme secretion, Beglinger et al have omitted the papers published by Wormsley et al which show that secretin does stimulate pancreatic enzyme secretion and potentiates CCK-stimulated enzyme secretion in man.

(4) With regard to the work of Domschke et al (the only other study carried out on pure pancreatic juice) the possible reasons for the differences between our results and those they obtained, are already discussed in our paper. In addition, it should be mentioned that if we look at the pattern of the protein concentration in response to secretin, it can be seen that it is similar in both studies. An important difference between the two studies, however, is that in the work of Domschke et al the volume of pancreatic juice increased progressively until the secretin dose of 0.5 clinical units/kg/h and then no further increases occurred despite infusion of higher doses of hormone (maximum flow rate approximated 250 µl per 5 min per kg of body weight). In our study, however, in agreement with the vast majority of literature data, the pancreatic juice flow increased progressively even with the highest doses of secretin, 0.9 and 2.7 clinical units/kg/h (maximum flow rate approximated 350 µl per 5 min per kg of body weight). If we take into account that the increase in protein output in response to secretin was mainly because of the increase in pancreatic juice volume, the above difference could have played an important role in the different results.

(5) Regarding the results given by Beglinger et al in the letter, the comments made in point 2 also apply here. Beglinger et al infused only one dose of secretin and compared the secretin-induced protein output with basal output. It is well known that basal pancreatic secretion undergoes important fluctuations in relation to interdigestive migrating motor complex and that a marked increase of enzyme secretion occurs during phase 2 and early phase 3 of the complex. Because of these marked fluctuations, taking basal secretion as a control secretion in this type of study could be very unreliable. In this connection, it would be of interest to know during which phase of the interdigestive motor complex Beglinger et al began the secretin infusion. We administered increasing doses of secretin (which is probably a more appropriate method for this kind of investigation than a single dose) and we showed progressive increases in protein output. Similar findings have been reported by Wormsley using a similar stimulation method.

(6) We do not feel that the type of patients studied and the presence of the catheter in the Wirsung could have influenced the results. We7 (and others) have shown that pancreatic secretion is depressed in the first two or three days after the operation and then returns to normal. For this reason, we started the studies at least six days after the operation. The fact that values of pancreatic juice flow and bicarbonate secretion found in our study are very close to – if not higher than – those reported by several other investigators in normal individuals, strongly indicates that the functional state of the pancreas in our patients was strictly normal. Finally, the presence of the catheter in the Wirsung may, possibly, depress pancreatic secretion but not increase it.9

(7) It is not strictly true, as Beglinger et al claim, that we chose lipase as an indication of enzyme secretion. In fact, we chose lipase and in addition, also protein secretion. As expected, the behaviour of both lipase and protein was parallel. I also disagree that the assay of lipase used poses methodological problems. This method has been thoroughly validated10 and is in widespread use both clinically and for research purposes.

(8) The only detailed studies specifically designed to investigate the action of secretin on human pancreatic enzyme secretion that is, the study of Wormsley and our own,1 show that secretin does,
in fact, stimulate pancreatic enzyme secretion. Therefore, it would seem that the conclusion drawn by Beglinger et al in their letter reflects mainly a personal view lacking adequate experimental support.

Finally, I would suggest that Beglinger et al study the action of secretin on pure pancreatic juice, using doses and periods of stimulation similar to those used by us. Only then, I believe, can we compare our studies and discuss the action of secretin on human pancreatic enzyme secretion.

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References


In vitro determination of small intestinal permeability

SIR.—Drs Bjarnason and Peters (Gut 1984; 25: 910–11) appear to have misunderstood the purpose of our previous communication which was to point out that the failure of their in vitro studies to show reduced absorption of probe molecules in coeliac disease does not imply that such reduced absorption does not occur, because the molecules they used in their study are not appropriate for this purpose. We would agree that any reduction in absorption may be due to a decrease in mucosal surface area, but as the permeability of the intestine is a composite of several diffusion pathways, of which both the sites and structures responsible for their selective permeability characteristics are unknown, we do not believe that intestinal permeability can be equated with (enterocyte) membrane permeability.

We are unable to accept the criticisms levied at the cellobiose/mannitol test. There is no evidence whatsoever to support the contention that a hypertonic cellobiose/mannitol test solution bypasses the diseased segment of the intestine, or that intestinal transit will affect urinary recovery of probe molecules; indeed, this subject has been studied in some detail and there is no correlation between gastrointestinal transit time and urinary recovery of cellobiose or mannitol,1 and the effect of a hypertonic test solution increases, rather than decreases, the sensitivity of the test system for proximal small intestinal disease.1 Whatever the explanation for the interesting observations by Catt et al,2 these experiments were all performed in isotonic solutions and are perhaps of little relevance to the use of hypertonic test solutions, which induce an increased absorption of disaccharides,3 as opposed to the decrease reported by Catt et al in isotonic solution. We agree that disaccharides may not be the ideal osmotic filler for cellobiose/mannitol test solutions, but have not been able to show any effect of lactase deficiency on probe molecule recovery.1

Finally, we cannot agree with the comments of Bjarnason and Peters on the sensitivity and specificity of the differential sugar absorption tests which have been shown to be valuable in the recognition of small intestinal disease by all those who have reported their findings,4–8 while others have failed to confirm the value of the Sc1-Cr-EDTA absorption test.9 None of the techniques used to show abnormal intestinal permeability has been claimed to be specific for coeliac disease, and none of them are, as is shown by the reports of Bjarnason and his colleagues, of abnormal permeability to Sc1-Cr-EDTA in various circumstances ranging from alcohol ingestion10 to colonic Crohn’s disease.11

The differences between our results and those of