Correspondence

Secretin and pancreatic enzyme secretion

SIR,—We have read with interest the recent paper of Gullo and coworkers¹ suggesting that secretin stimulates pancreatic enzyme secretion in man. Our own results are at variance with the findings of Gullo *et al.* Looking through the literature we have realised that the influence of secretin on human pancreatic enzyme secretion is not well defined. The question as to whether secretin stimulates pancreatic enzyme secretion or not is of basic physiological importance as this finding could challenge current regulatory concepts. In this review of the literature we have only included the results in man in which either pure natural or synthetic secretin preparations have been used and in which basal pancreatic enzyme secretion was measured.

Domschke and coworkers² evaluated the effects of increasing doses of synthetic secretin on pure pancreatic juice collected by endoscopic cannulation and failed to detect any significant effect on pancreatic enzyme output. Chey *et al* and Niederau and coworkers have reported in different papers^{3–6} that secretin does not significantly stimulate pancreatic enzyme secretion (duodenal intubation technique, marker perfusion to correct for jejunal volume loss).

In our own hands, secretin over a full range of doses (0.012–1 CU/kg/h) produced small increases of trypsin output which were not significantly different from basal values.⁷ The results of another unpublished study are given in the Table. In this study six healthy volunteers received secretin in a dose of 1 CU/kg/h for 60 min after a basal collection period of 60 min. Pancreatic secretory response was assessed by duodenal intubation and a marker perfusion technique. Again secretin did neither stimulate trypsin nor protein outputs over basal.

Table Pancreatic secretory response to 1 CU/kg/h of synthetic secretin infused over 60 min. Data are mean $\pm$ SEM, n=6

	Bicarb output mmol/15 min	Trypsin output KIU/15 min	Protein output mg/15 min
Basal	0.13 $\pm$ 0.03	198 $\pm$ 60	9.5 $\pm$ 1.8
1 CU/kg/h	11.50 $\pm$ 0.90	176 $\pm$ 29	11.8 $\pm$ 0.8

Summarising these results we can only come to the conclusion that most evidence so far available favours the hypothesis that secretin does not stimulate pancreatic enzyme secretion over basal

values. We do not have an explanation for the differing results of Gullo and coworkers, but the selection of patients who had been operated at the papilla of Vater only a few days before the experiments might have influenced the outcome of the study, a fact that has been pointed out by the authors already.^{1,8} Moreover, the possibility that the catheter lying in the Wirsung's canal for several days may have affected the pancreatic secretory response to secretin cannot be excluded, as it has been shown that long catheters lying in the pancreatic duct can disturb the secretory response.⁹ We were surprised that the authors chose lipase as an indicator of pancreatic enzyme secretion, an enzyme the assay of which is known to pose methodological problems.

In conclusion, most evidence favours the hypothesis that secretin does not stimulate pancreatic enzyme secretion in man.

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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 study¹ (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^{2,3} 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*⁴ (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.¹ 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*⁴ 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 μ l 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 μ l

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.^{5,6} 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.¹ Similar findings have been reported by Wormsley² 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 others⁸) 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 Wormsley² and our own,¹ show that secretin does,