

# Effect of continuous jejunal perfusion of elemental and complex nutritional solutions on pancreatic enzyme secretion in human subjects<sup>1</sup>

N. VIDON, P. HECKETSWEILER, J. BUTEL, AND J. J. BERNIER

With the technical assistance of Mrs M. Rongier, A. Evrard and J. Rouchette

From the Unité de Recherches sur la Physiopathologie de la Digestion, INSERM U. 54, Hôpital Saint-Lazare, Paris, France

**SUMMARY** Pancreatic secretion of lipase and chymotrypsin in response to elemental diets and a crushed food homogenate was studied in normal subjects. The solutions were infused at constant flow rates at the ligament of Treitz with polyethylene glycol as a nonabsorbable marker. A triple lumen tube was used, enabling collection of secretions at 35 and 70 cm from the infusion point. The results show that a crushed food homogenate has a greater stimulative effect on pancreatic enzyme secretion than the elemental solutions and that this can be directly related to its greater nitrogen content. The osmolality of the infused solutions does not appear to be important. The relative merits of the solutions tested and total parental nutrition in reducing pancreatic enzyme secretion are discussed.

Some authorities claim that pancreatic enzyme secretion is lower with an elemental solution. This observation is based on clinical findings (McArdle *et al.*, 1972; Ragins *et al.*, 1973; Voitk *et al.*, 1973; Young *et al.*, 1975) and experimental studies performed on laboratory animals (Bounous *et al.*, 1967; Brown *et al.*, 1970; Ragins *et al.*, 1973). This contrasts with physiological studies which demonstrate that the pancreatic enzyme secretion appears as a response to duodenal or jejunal aminoacids perfusion (Ertan *et al.*, 1971).

The purpose of this study was to compare secretion in healthy subjects during continuous jejunal perfusion of either elemental solutions or a crushed food homogenate. The results confirm that an elemental diet has a stimulatory effect upon the human pancreas.

## Methods

### MATERIALS

#### *Elemental solution A*

Vivonex (Eaton Laboratories). This contained: 1-

<sup>1</sup>This work was supported by grant No. 73 5 129 12 from the Institut National de la Santé et de la Recherche Médicale.

Received for publication 30 September 1977

aminoacids 21 g/l; glucose and oligosaccharides 227 g/l; lipids derived from cartham oil 1.5 g/l; mineral salts: sodium 42 mmol/l; potassium 29 mmol/l; vitamins and trace elements. The solution had a calorific value of 1 KCal/ml and an osmolality of 620 mOsmol/kg.

#### *Elemental solution B*

This was a 50% dilution of solution A.

It provided, therefore, 1/2 KCal/ml and had an osmolality of 280 mOsmol/kg.

#### *Crushed food homogenate*

Realmartyl (Sopharga Laboratories). This contained chicken meat, egg yolk powder, soya flour, glucose, saccharose, maltose and dextrine maltose, corn and wheat oils. Its composition was as follows: proteins 43 g/l; sugars 134 g/l; lipids 29 g/l; sodium 50 mmol/l; potassium 29 mmol/l. It had a calorific value of 1 KCal/ml and the osmolality was 450 mOsmol/kg.

## Procedure

Seventeen healthy subjects, between the ages of 18 and 30 years who had no clinical evidence of small bowel disease, were studied. Each swallowed a triple lumen tube (Vidor *et al.*, 1977).

**Study 1**

Eight subjects were perfused with elemental solution A at 1 ml, 2 ml, and 3 ml/mn and the crushed food homogenate at 2 ml/mn.

**Study 2**

Nine subjects were perfused with elemental solution A at 1 ml and 2 ml/mn and elemental solution B at 2 ml and 4 ml/mn. Thus, by adjusting the flow rates, infusion of a fixed calorific value was maintained.

The distal end of the infusion tube was passed to the level of the ligament of Treitz (and its position checked by screening). After a three hour equilibration period, three samples were collected 70 cm below the infusion point and three others 35 cm below it.

Each sample, once collected, was placed immediately on ice and the following were estimated on each: pH; osmolality; polyethylene glycol concentration by the Hydén method (1956) to give information about the flow rate at each sampling point; lipase activity estimated by the Marchis-Mouren method (Marchis-Mouren *et al.*, 1959); chymotrypsin activity by the method of Figarella *et al.* (1965); nitrogen by the Kjeldahl method.

**Results**

The results of study 1 are shown in Table 1. These indicate that pancreatic secretion of lipase and chymotrypsin varies directly with the infusion rate of undiluted Vivonex. However, for the same calorific

Table 1 *Vivonex, solution A, at different flow rates, and Realmentyl: enzymatic secretions*

	(cm)	<i>Vivonex solution A</i>			<i>Realmentyl</i>	<i>Correlation</i> Enzyme / <i>Vivonex</i> secretion / flow rate
		1 ml/mn	2 ml/mn	3 ml/mn	2 ml/mn	
CHT secretion	35	198 ± 29	207 ± 32	251 ± 26	351 ± 52	P < 0,30
UI/mn	70	127 ± 21	198 ± 31	282 ± 44	328 ± 58	P < 0,01
Lipase secretion	35	501 ± 191	664 ± 86	1552 ± 417	1908 ± 323	P < 0,02
UI/mn	70	145 ± 58	386 ± 98	1098 ± 314	1477 ± 198	P < 0,01

Values are means ± SEM.

Table 2 *Vivonex, solution A, at different flow rates, and Realmentyl: nitrogenous load*

	<i>Vivonex solution A</i>			<i>Realmentyl</i>
	1 ml/mn	2 ml/mn	3 ml/mn	2 ml/mn
Nitrogenous load (mg/mn)	3.39 ± 0.05	6.60 ± 0.12	10.17 ± 0.16	13.89 ± 0.30

Values are means ± SEM.

Table 3 *Vivonex solutions A and B: enzymatic secretions*

	(cm)	1 KCal/mn		2 KCal/mn	
		<i>Solution A</i> 1 ml/mn	<i>Solution B</i> 2 ml/mn	<i>Solution A</i> 2 ml/mn	<i>Solution B</i> 4 ml/mn
CHT secretion	35	210 ± 49	178 ± 48*	312 ± 64	701 ± 37*
UI/mn	70	136 ± 30	130 ± 19*	187 ± 35	279 ± 24*
Lipase secretion	35	385 ± 80	457 ± 125*	789 ± 142	716 ± 152*
UI/mn	70	289 ± 42	243 ± 70*	475 ± 112	387 ± 66*

Values are means ± SEM.

\*Comparison with solution A: not significant.

Table 4 *Vivonex, solution A, at different flow rates, and Realmentyl: enzymatic concentrations*

	(cm)	<i>Vivonex solution A</i>			<i>Realmentyl</i>
		1 ml/mn	2 ml/mn	3 ml/mn	2 ml/mn
Concentration CHT	35	70 ± 12	53 ± 7	41 ± 4	86 ± 11
UI/ml	70	80 ± 17	60 ± 7	52 ± 8	92 ± 9
Concentration Lipase	35	213 ± 82	174 ± 21	251 ± 69	483 ± 80
UI/ml	70	91 ± 34	116 ± 26	207 ± 63	437 ± 67

Values are means ± SEM.

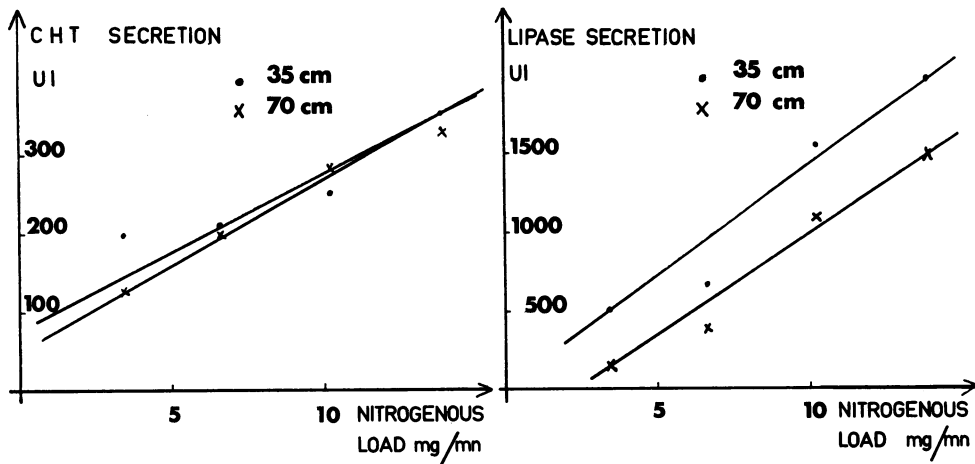


Fig. 1 Relationship between enzymatic secretion and nitrogenous load. (Vivonex, solution A, at different flow rates, and Realmentyl.)

value, enzyme flow rate was greater with the crushed food homogenate than with Vivonex.

When nitrogenous load is considered (Table 2), the enzyme secretion is seen to be directly related to it (Fig. 1).

The results of study 2 are seen in Table 3. There is no significant difference between enzyme secretion with either diluted or undiluted Vivonex when the calorific value is kept constant. Lipase concentration appears to be lower at 70 cm from the infusion point than at 35 cm for both Vivonex and Realmentyl. However, chymotrypsin concentration was nearly the same at both levels (Table 4). Flow rates of both enzymes were lower at 70 cm (Table 1, 3).

### Discussion

Our results indicate that pancreatic enzyme secretion occurs in response to jejunal perfusion of both Vivonex and crushed food homogenate. This is in agreement with previous studies in man (Go *et al.*, 1970) and in the dog (Meyer and Grossman, 1972) with intrajejunal administration of aminoacids. The mechanism for this appears to be hormone dependent.

The technique employed to measure the pancreatic secretion tends to underestimate it. There are three reasons for this.

Firstly, the solution is perfused at the ligament of Treitz and it had been shown that the rate of pancreatic enzyme secretion is inversely proportional to the distance from the pylorus of the point of infusion (Konturek *et al.*, 1972).

Secondly, the presence of PEG, at a concentration of 10 g/l diminishes the activity of the lipase

(Vavrinkova and Krongl, 1965) by approximately 20% (personal findings).

Thirdly, analysis of the intestinal liquid collected at points located approximately 55 cm and 85 cm distal from the ampulla of Vater indicated that an inactivation of pancreatic enzymes, notably the lipase (Table 4), had occurred in the intestine. This finding is in accord with the previously published results of Borgström *et al.* (1957) and of Pelot and Grossman (1962). The absorption of water can compensate for this inactivation and maintain the intraluminal concentration (Table 4).

In spite of this underestimation, the enzyme concentrations obtained in the present studies are as high as we would normally expect to obtain in a Lundh test. In our laboratory, after a test meal made up of milk proteins (25 g), corn oil (30 g), and enough water to obtain a 400 ml volume, the normal results are: lipase > 100 UI and CHT > 30 UI (Bozec, 1976).

The results of these studies show that pancreatic enzyme secretion increases with the calorific and nitrogenous loads infused, but that the volume or osmolality of the infused solution do not affect it.

The stimulant effect of lipids could not have been a contributory factor, as the amount infused was small (the highest rate of Vivonex infusion was equivalent to 6 g lipids in 24 hours). Moreover, Go *et al.* (1970) have reported that the addition of lipids in micellar solution to an aminoacids solution does not significantly increase pancreatic enzyme secretion.

It seems unlikely also that the carbohydrate fraction was important in this respect, as the crushed food homogenate produced higher enzyme flow rates than

Vivonex, although it contained less glucose and polysaccharides. This, too, is in keeping with the published works of others (Comfort and Osterberg, 1941; Wang and Grossman, 1951; Hong *et al.*, 1961; Go *et al.*, 1970).

Thus, we are led to the conclusion that the nitrogen content of each solution is the major stimulatory factor involved. There is, indeed, a close correlation between the enzymatic output and the nitrogen load. These results confirm the work of Wolfe *et al.* (1975) who, after comparing the effect of duodenal perfusion of phenylalanine (127 mM/l) or of Vivonex (aminoacids 155 mM/l) with the effect of an intravenous perfusion of cholecystokinin, concluded that the stimulatory effect of elementary alimentation upon the pancreas is essentially due to the aminoacids. Our finding also confirms the work of Ekelund and Johansson (1975) who found that the secretion rate of lipase at 12 mg nitrogen/mn was twice as great as at 7 mg/mn and approximated to the maximal stimulation expected in a secretin-pancreozymin test (Schütz *et al.*, 1969). Go *et al.* (1970) found that nitrogen content to be important, but, unlike Ekelund and his co-workers and ourselves, to be maximal at an infusion rate of only 3.4 mg aminoacids/mn (18 mM/l essential and non-essential aminoacids at 10 ml/mn).

With the same technique, we also studied the absorption of nutrients (Vidon *et al.*, 1977). The nitrogen absorption in a jejunal segment of 70 cm is slight. Therefore a high concentration of nitrogen would have to be used. In the case of Vivonex, the nitrogen concentration is relatively low. A higher nitrogen load would in turn bring about an increased pancreatic secretion.

To sum up, the presence of nitrogen in duodenal jejunal lumen provokes a secretion of pancreatic enzymes. This secretion is proportional to the quantity of nitrogen perfused and is probably independent of the form of the perfused nitrogenous substances.

The clinical implication of this finding is that, to reduce significantly the pancreatic secretion during the treatment of pancreatitis or intestinal fistula, parenteral feeding may be the only means of achieving this.

#### References

- Borgström, B., Dahlqvist, A., Lundh, G., and Sjövall, J. (1957). Studies of intestinal digestion and absorption in the human. *Journal of Clinical Investigation*, **36**, 1521-1536.
- Bounous, G., Sutherland, N. G., McArdle, A. H., and Gurd, F. N. (1967). The prophylactic use of an 'elemental' diet in experimental hemorrhagic shock and intestinal ischemia. *Annals of Surgery*, **166**, 312-343.
- Bozec, S. (1976). Comparaison de la réponse enzymatique pancréatique obtenue après stimulation par repas d'épreuve (test de LUNDH) et par administration de secrétine et de céroléine. A propos de 30 observations. MD Thesis: Paris.
- Brown, R. A., Thompson, A. G., McArdle, A. H., and Gurd, F. N. (1970). Alteration of exocrine pancreatic storage enzymes by feeding on an elemental diet: a biochemical and ultra-structural study. *Surgical Forum*, **21**, 391-393.
- Comfort, M. W., and Osterberg, A. E. (1941). Pancreatic secretion in man after administration of different stimulants: a comparative study. *American Journal of Digestive Diseases*, **8**, 337-344.
- Ékelund, K., and Johansson, C. (1975). Output of bilirubin and pancreatic enzymes in response to different liquid test meals in man. *Scandinavian Journal of Gastroenterology*, **10**, 507-511.
- Ertan, A., Brooks, F. P., Ostrow, J. D., Arvan, D. A., Williams, C. N., and Cerda, J. J. (1971). Effect of jejunal aminoacid perfusion and exogenous cholecystokinin on the exocrine pancreatic and biliary secretions in man. *Gastroenterology*, **61**, 686-692.
- Figarella, C., Taulier, J., and Sarles, H. (1965). Dosage de la chymotrypsine et de la trypsine dans le suc duodénal. *Bulletin de la Société de Chimie Biologique*, **47**, 679-686.
- Go, V. L. W., Hofmann, A. F., and Summerskill, W. H. J. (1970). Pancreozymin bioassay in man based on pancreatic enzyme secretion: potency of specific amino acids and other digestive products. *Journal of Clinical Investigation*, **49**, 1558-1564.
- Hong, S. S., Chin, D. S., and Hur, K. B. (1961). Influences of hexamethonium and some dietary factors on human pancreatic and bile secretion. *Journal of Applied Physiology*, **16**, 810-814.
- Hydén, S. (1956). A turbidimetric method for the determination of higher polyethylene-glycols in biological materials. *Kungliga Lantbrukshögskolans. Annaler*, **22**, 139-145.
- Konturek, S. J., Tasler, J., and Obtulowicz, W. (1972). Localization of cholecystokinin release in intestine of the dog. *American Journal of Physiology*, **222**, 16-20.
- McArdle, A. H., Brown, R. A., Echave, V., Rivilis, J., and Thompson, A. G. (1972). Alterations in gastric and pancreatic secretion induced by the feeding of an elemental diet. (Abstract.) *Archives Francaises des Maladies de l'Appareil Digestif*, **61**, 115c.
- Marchis-Mouren, G., Sarda, L., and Desnuelle, P. (1959). Purification of hog pancreatic lipase. *Archives of Biochemistry and Biophysics*, **82**, 309-319.
- Meyer, J. H., and Grossman, M. I. (1972). Comparison of D- and L-phenylalanine as pancreatic stimulants. *American Journal of Physiology*, **222**, 1058-1063.
- Pelot, D., and Grossman, M. I. (1962). Distribution and fate of pancreatic enzymes in small intestine of the rat. *American Journal of Physiology*, **202**, 285-288.
- Ragins, H., Levenson, S. M., Signer, R., Stamford, W., and Seifter, E. (1973). Intrajejunal administration of an elemental diet at neutral pH avoids pancreatic stimulation: studies in dog and man. *American Journal of Surgery*, **126**, 606-614.
- Schütz, H. B., Andersson, S., and Lagerlöf, H. (1969). Pancreatic exocrine secretion in normal subjects studied by continuous infusion of pancreozymin and secretin. *Scandinavian Journal of Gastroenterology*, **4**, 597-602.
- Vavrinkova, H., and Kronidl, A. (1965). Use of polyethylene glycol in investigations of absorption of fat. *Nature*, **208**, 293-294.
- Vidon, N., Hecketsweiler, P., Cortot, A., and Bernier, J. J. (1977). Étude de l'absorption d'une solution nutritive élémentaire sous perfusion jéjunale continue: influence du débit et de la concentration sur l'absorption des nutriments. *Gastroentérologie. Clinique Biologique*, **1**, 257-266.
- Voitk, A., Brown, R. A., Echave, V., McArdle, A. H., Gurd, F. N., and Thompson, A. G. (1973). Use of an

- elemental diet in the treatment of complicated pancreatitis. *American Journal of Surgery*, **125**, 223-227.
- Wang, C. C., and Grossman, M. I. (1951). Physiological determination of release of secretin and pancreozymin from intestine of dogs with transplanted pancreas. *American Journal of Physiology*, **164**, 527-545.
- Wolfe, B. M., Keltner, R. M., and Kaminski, D. L. (1975). The effect of an intraduodenal elemental diet on pancreatic secretion. *Surgery, Gynecology, and Obstetrics*, **140**, 241-245.
- Young, E. A., Heuler, N., Russell, P., and Weser, E. (1975). Comparative nutritional analysis of chemically defined diets. *Gastroenterology*, **69**, 1338-1345.