same amount. These data suggest that the decreased energy intake of children with chronic renal insufficiency is a related but not causal factor in their reduced growth velocity.

Attempts to increase the energy intake over that recommended for age by dietary supplementation were defeated in those children with normal intakes. Despite Caloreen contributing a mean of 19% of their daily energy requirements their total energy intakes increased only 3%—that is, they merely reduced their intake of other substances. We therefore cannot say whether successful supplementation would have led to catch-up growth or merely an increase in weight.

For the healthy child the caloric cost of growth is probably only 10% of the total energy intake, the remainder being divided between the metabolic rate and physical activity. Ashworth,¹⁴ studying malnourished children with a prolonged reduction in energy intake, showed only a slight reduction in basal metabolic rate, while physical activity and growth were compromised to a greater extent. This may also have occurred in the children we studied, but physical activity is difficult to assess. Several mothers stated, however, that their children's wellbeing and activity improved while they were receiving energy supplements. Energy supplements may therefore be of some benefit in children with moderate to severe degrees of renal insufficiency.

Normally 10-15% of the total energy intake of British children consists of protein¹⁵; the mean percentage in our patients was 11%. Six of the 11 children receiving supplements reduced their protein intake over the ensuing year, and in all 11 children there was a decrease in the percentage of energy obtained from protein. This observed reduction in protein intake may be related to the absence of observed growth acceleration or may be merely a reflection of appetite depression due to an extra carbohydrate intake. Since extra energy from Caloreen was not used for catch-up growth, however, dietary nitrogen intake may have been selectively reduced to limit its excretion by malfunctioning kidneys.

When renal disease dates from infancy—a time of maximal growth velocity—impaired function may result in reduced growth and permanent stunting.² Since this may well result from a reduced energy intake, supplementation must be started in the first few months of life if it is to prevent growth retardation. As we have already emphasised,¹⁵ it is important that chronic renal insufficiency should be diagnosed early and that management of children with this condition should be improved. Only then can the role of energy supplementation be properly assessed.

This work was supported by project grant No G972/143/C from the Medical Research Council.

References

- ¹ Guthrie, L G, *Lancet*, 1897, **2**, 585.
- ² Betts, P R, and Magrath, G, *British Medical Journal*, 1974, **2**, 189.
- ³ Chantler, C, and Holliday, M A, *Clinical Nephrology*, 1973, **1**, 230.
- ⁴ Simmons, J M, et al, *New England Journal of Medicine*, 1971, **285**, 653.
- ⁵ Chantler, C, et al, Paper read at Paediatric Research Society, October, 1973.
- ⁶ Marshall, W A, *Archives of Disease in Childhood*, 1971, **46**, 414.
- ⁷ Glasgow, E F, Moncreiff, M W, and White, R H R, *British Medical Journal*, 1970, **2**, 687.
- ⁸ Chantler, C, and Barratt, T M, *Archives of Disease in Childhood*, 1972, **47**, 613.
- ⁹ Tanner, J M, et al, *Archives of Disease in Childhood*, 1971, **46**, 745.
- ¹⁰ Tanner, J M, Whitehouse, R M, and Takaishi, M, *Archives of Disease in Childhood*, 1966, **41**, 454.
- ¹¹ Greulich, W W, and Pyle, S I, *Radiographic Atlas of Skeletal Development of Hand and Wrist*, 2nd edn. California, Stanford University Press, 1959.
- ¹² Tanner, J M, *Growth at Adolescence*. Oxford, Blackwell Scientific, 1962.
- ¹³ Department of Health and Social Security, *Recommended Intakes of Nutrients for the United Kingdom*. London, HMSO, 1969.
- ¹⁴ Ashworth, A, *British Journal of Nutrition*, 1968, **22**, 341.
- ¹⁵ Betts, P R, and White, R H R, *Nephron*, 1976, **16**, 325.

(Accepted 15 December 1976)

Inhibition of gastric secretion in treatment of pancreatic insufficiency.

J H B SAUNDERS, S DRUMMOND, K G WORMSLEY

British Medical Journal, 1977, **1**, 418-419

Summary

The content of pancreatic enzymes in the duodenum was studied in two patients with pancreatic achylia after a standard meal supplemented with commercial pancreatic extract. Gastric transit of the enzymes, with appearance of near-normal amounts in the duodenal contents, occurred only after inhibition of gastric secretion and buffering of residual gastric acid with antacids. Gastric inhibition and neutralisation of acid are therefore necessary for the satisfactory treatment of patients with pancreatic exocrine insufficiency but normal gastric function.

University Department of Therapeutics, Ninewells Hospital, Dundee DD2 1UB

J H B SAUNDERS, MB, MRCP, medical registrar
S DRUMMOND, BSC, research assistant
K G WORMSLEY, DSC, FRCP, consultant physician

Introduction

The destruction of pancreatic enzymes by gastric acid and pepsin is the most important of the factors that vitiate the satisfactory treatment of pancreatic exocrine insufficiency with supplements of pancreatic extracts by mouth.¹ We have therefore studied the effects on the gastric transit of enzymes in such an extract, given with a meal, of inhibiting gastric secretion with the H₂-receptor-blocking drug metiamide.

Materials and methods

Two patients with chronic pancreatitis and pancreatic achylia, confirmed by lack of pancreatic response to stimulation with secretin and cholecystokinin,² gave informed consent to each study. After an overnight fast a multilumen tube was sited with its tip in the distal duodenum. A liquid meal containing protein 16.7 g/l (Casilan) and starch 56.7 g/l was given by mouth. Gastric and duodenal contents were sampled at intervals of 10 minutes. After 50 minutes each patient received a further, identical meal containing the contents of three capsules of pancreatic extract with previously determined high content of potent pancreatic enzymes.³

Each patient then began treatment with a total of 1 g metiamide daily. On the day of the test the last dose was given 90 minutes before

the same set of two meals as above. In a further test, during treatment with metiamide, the patients received an antacid (30 ml magnesium trisilicate mixture (BNF) or 1.5 g sodium bicarbonate) together with the meal and pancreatic extract.

The pH and acid (or bicarbonate) content of all samples was measured by automatic titration to pH 7 with 0.05 mol (2 g) sodium hydroxide/l. The following enzymatic activities were measured in the duodenal aspirates: trypsin,⁴ chymotrypsin,⁵ amylase,⁶ and lipase.⁷

Results

After the meal alone and the meal containing pancreatic extract the gastric contents were strongly acid. Metiamide rendered them less acid, with a pH greater than 2 during the response to the meal alone and to the meal containing pancreatic extract. The administration of antacid resulted in gastric contents with a pH above 7 during the response to the meal. The pH of the duodenal aspirate was acid in all studies except those in which metiamide together with antacid was given with the meal (fig 1).

FIG 1—pH and acid or bicarbonate concentration of duodenal contents after meal. Each point represents mean for the two patients. N denotes mean values in normal people at 10-minute intervals after meal alone.
Conversion: SI to traditional units—H⁺: 1 mmol/l=1 mEq/l. HCO₃: 1 mmol/l=1 mEq/l.

FIG 2—Enzymatic activities of duodenal contents after meal. N denotes mean values in normal people after meal alone.

No pancreatic enzymatic activity was detected in response to the meal alone either before or during treatment with metiamide (fig 2). After the administration of pancreatic extract small amounts of trypsin, chymotrypsin, and lipase were detectable for short periods after ingestion of the meal. Considerably more enzymatic activity was detectable in the duodenal aspirate for 30 minutes after taking the meal containing pancreatic extract during treatment with metiamide, and still more pancreatic enzymatic activity was present, for the whole 50 minutes of the test, when antacid was given with the meal in addition to treatment with metiamide. The levels of enzymatic activity attained in the duodenum under the latter circumstances were comparable to those seen in normal people after ingestion of the same meal (fig 2), except that the amounts of lipase were considerably less than normal. This, however, was because the content of lipase in the pancreatic extract was relatively less than the activities of the other three enzymes.

Discussion

The amount of pancreatic enzymatic activity detectable in the duodenal contents after administering potent enzymatically active pancreatic extract with food to patients with pancreatic achylia has been shown by this study to correlate with the degree of gastric secretory activity. Many patients with chronic pancreatitis secrete excessive amounts of gastric juice (our patients had acid secretory responses to pentagastrin of 46.5 37.9 mmol(mEq)/h respectively), and, indeed, many have associated duodenal ulcers.⁸⁻¹⁰ Our results, which show that the pancreatic enzymes of therapeutic pancreatic extracts are inactivated during gastric transit, correspond well with the previously reported finding that, in vitro, pancreatic enzymes are rapidly and irreversibly inactivated by gastric acid and pepsin.¹¹ We have shown that therapeutic suppression of gastric secretion and buffering of the residual gastric acid permits the passage of the orally administered pancreatic enzymes into the small intestine in enzymatically active form. Under these circumstances digestion reverts to normal in patients with pancreatic exocrine insufficiency, with improvement in the malassimilation of food and rapid gain in weight.¹²

Failure of simple pancreatic replacement therapy to result in normal digestion of food has previously almost invariably precluded the satisfactory treatment of the pancreatic insufficiency associated with pancreatic disease.¹ The administration of pancreatic extracts with proved enzymatic potency³ with food during treatment with an H₂-receptor-blocking drug such as cimetidine (which has now replaced metiamide in the production of therapeutic gastric inhibition), together with antacid to buffer the remaining acid of the gastric contents, now permits the satisfactory normalisation of digestion in patients with pancreatic exocrine insufficiency.

KGW gratefully acknowledges a grant from the Scottish Hospital Endowments Trust. The metiamide was kindly supplied by Smith Kline and French Laboratories Ltd, Welwyn Garden City.

References

1 Saunders, J H B, and Wormsley, K G, *Gut*, 1975, **16**, 157.
2 Wormsley, K G, *Scandinavian Journal of Gastroenterology*, 1969, **4**, 623.
3 Drummond, S, et al, *Scottish Medical Journal*. In press.
4 Erlanger, B F, Kokowsky, N, and Cohen, W, *Archives of Biochemistry and Biophysics*, 1961, **95**, 271.
5 Nagel, W, et al, *Hoppe-Seylers Zeitschrift für physiologische Chemie*, 1965, **340**, 1.
6 Bernfeld, P, and Studer-Pecha, H, *Helvetica Chimica Acta*, 1947, **30**, 1904.
7 Desnuelle, P, Constantin, M J, and Baldy, J, *Bulletin de la Société de Chimie Biologique*, 1955, **37**, 285.
8 Leger, L, Kobel, J-J, and Cazes, P, *Archives Françaises des Maladies de l'Appareil Digestif*, 1960, **49**, 727.
9 Fitzgerald, O, et al, *Gut*, 1963, **4**, 193.
10 Dreiling, D A, and Naqvi, M A, *American Journal of Gastroenterology*, 1969, **51**, 193.
11 Heizer, W D, Cleaveland, C R, and Iber, F L, *Johns Hopkins Medical Journal*, 1965, **116**, 261.
12 Thjodleifsson, B, and Wormsley, K G, *Digestion*, 1975, **12**, 134.

(Accepted 10 December 1976)