# Nutrizym as a Pancreatic Enzyme Replacement

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## SUMMARY

**Twenty courses of Nutrizym or placebo were administered to patients with steatorrhoea due to pancreatic insufficiency. Stool fat excretion fell significantly in all patients while on Nutrizym ($P<0,001$). On placebo, a mean (±SD) of 27,6 ± 18,3 g/24 h of fat was excreted in the stools. On Nutrizym a mean of 12,4 ±9,9 g/24 h of fat was excreted. All patients felt subjectively better and weight loss was arrested.**


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A double-blind therapeutic trial was carried out to assess the efficacy of a powerful enzyme replacement therapy in patients with proved pancreatic insufficiency. All patients had increased stool fats. Nutrizym contains a greater content of trypsin, lipase and amylase than plain pancreatin, and has in addition two other advantages over other enzyme replacements, namely ox bile and peptidases.[1]

## METHOD

Twenty patients (17 male) with pancreatic insufficiency and steatorrhoea were studied. Eighteen patients had ethanol-induced chronic pancreatitis; 1 had an impacted gallstone in a pouch at the ampulla of Vater; and 1 patient had a carcinoma of the pancreas. Ages ranged from 22 to 65 years (mean 42,9, SD ± 10,6 years).

Forty courses of therapy were given in a double-blind randomised cross-over fashion, consisting of Nutrizym (E. Merck) 3 tablets *t.d.s.* for 4 weeks, or placebo at the same dosage. Twelve patients received placebo first, and 8 patients received Nutrizym first.

Fifteen patients had pancreatic function tests after intubation, with secretin (Jorpes) 1 unit/kg intravenously followed 1 hour later by CCK-pancreozymin (Jorpes) 1,5 units/kg intravenously,[2] with measurements of volume, amylase[3] and bicarbonate (van Slyke's method). Five patients had pancreatitis demonstrated at laparotomy. All patients had their faecal fat excretion[4] measured over 72 hours during the last week of each course of Nutrizym or placebo therapy.

## RESULTS

### Pancreatic Function Tests

All 15 patients tested had abnormal pancreatic function tests (Table I). The mean total volume in 80 min (± SD) was 81 ± 44,6 ml. The mean bicarbonate in the 20 - 60 min collection after secretion (± SD) (S2) was 45,1 ± 27,2 mEq/litre. The mean amylase in the first 20 min collection after CCK-PZ (± SD) (PZ) was 1,4 ± 1,3 μU/ml. Normal values for 40 control subjects were: mean total volume 156,6 ± 36,6 ml ($P<0,001$); mean bicarbonate 83,6 ± 30,4 mEq/litre ($P<0,001$) and amylase in PZ collection 9,9 ± 4,6 μU/ml ($P<0,001$) ($P^-$ values refer to differences from the 20 patients with bicarbonate in S2 collection).

TABLE I. PANCREATIC FUNCTION

| | 15 trial patients with pancreatic insufficiency (M ± SD) | 40 control subjects (M ± SD) |
|---|---|---|
| **Total volume (ml)** | **81,0 ± 44,6** | **156,6 ± 36,6** |
| **S2*$HCO_3^-$ (mEq/L)** | **45,1 ± 27,2** | **81,1 ± 25,9** |
| **CCK-PZ† amylase (μU/ml)** | **1,4 ± 1,3** | **9,9 ± 4,6** |

Tube test secretin 1 U/kg intravenously; CCK-PZ† 1,5 U/kg intravenously 1 h later.
* Secretin 2nd sample (20 to 60 min collection):
† Cholecystokinin-pancreozymin.

### Stool Fat Excretion

While on placebo, mean (± SD) stool fat excretion in the 20 trial patients was 27,6 ± 18,3 g/24 h. The lowest stool fat excretion in any patient was 6,9 g/24 h. While on Nutrizym mean faecal fat excretion was 12,4 ± 9,9 g/24 h. The reduction of stool fats while on Nutrizym was highly significant when analysed by paired *t*-tests ($P<0,001$). Half the patients excreted less than 7 g/24 h while on Nutrizym, and the remaining 10 showed significant reductions.

### Clinical Findings

All patients on Nutrizym reported an improvement in their stools. Three patients became constipated. When the amount of Nutrizym was reduced, constipation disappeared, and patients were able to 'titrate' the dose of Nutrizym on some occasions. The daily dose of 3 tablets *t.d.s.* was only required in severe pancreatic insufficiency, and could be reduced to 1 tablet *t.d.s.* in some patients.

## DISCUSSION

Nutrizym contains an inner core of pancreatic enzyme, containing 2 500 units trypsin, 8 100 units lipase and 18 000 units amylase.[1] This is approximately double the

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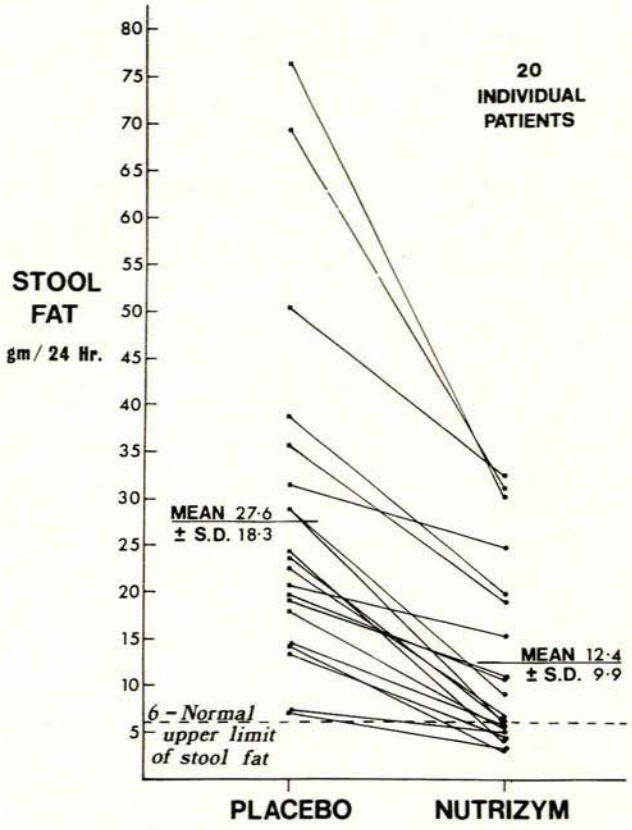


**Fig. 1. Stool fat excretion in 20 trial patients.**

value of Pancrex V Forte.[5] The core is enteric-coated. Surrounding this is a shell of bromelains—a mixture of proteolytic enzymes derived from the stem of the pineapple. The bromelain shell has been shown to produce a significant increase in protein digestion.[1] Nutrizym, therefore, offers a unique 'two-stage' combination of activities. The proteolytic enzymes in the bromelain shell are released in the stomach and initiate protein digestion. The enteric-coated core then passes into the small intestine where the ox bile and pancreatin are liberated, at twice the enzyme concentration of other products.[5]

The present double-blind cross-over trial in 20 patients has confirmed the effectiveness of Nutrizym in reducing faecal fat excretion even when grossly raised, in patients with pancreatic insufficiency. All patients felt a marked improvement in their symptoms while on Nutrizym, and there were no side-effects in this trial. Weight gain was not significant in the short term, but there was an arrest in the weight loss in 14 patients. Over a longer period, after cessation of the trial, there was a slow gain in weight in 19 of the patients, and the weight remained constant in the remaining patient.

In a study to compare the effectiveness of Nutrizym with that of Pancrex V Forte,[1] Nutrizym was shown to be clearly superior. *In vitro* tests have demonstrated that Nutrizym is the most effective of 20 compounds tested.[5]

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