hormone, and luteinising hormone that we found support the concept that cyclical oedema is due to a generalised hypothalamic disturbance producing the somatic and psychological features of the condition. Alternatively, there may be an undefined peripheral factor with secondary hormonal changes that are only markers for the condition. Once an abnormality in the hypothalamic-pituitary axis has been identified the effect of diuretics, dopamine agonists, and centrally acting antidepressant drugs on this abnormality should be determined in the hope that a more effective treatment may be developed. In addition, the test using thyrotrophin releasing hormone and luteinising hormone releasing hormone may enable a more precise and objective diagnosis to be made in this common and distressing disorder.

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References

1 Streeton DHP. Idiopathic oedema: pathogenesis, clinical features and treatment. *Metabolism* 1978;**27**:353-83.
2 Anonymous. Idiopathic oedema of women [Editorial]. *Br Med J* 1976;i:979.
3 Thorn GW. Approach to the patient with "idiopathic oedema" or "periodic swelling." *JAMA* 1968;**206**:333-8.
4 Kuchel O, Cuche JL, Buu NT, *et al.* Catecholamine excretion in "idiopathic" oedema: decreased dopamine secretion, a pathogenic factor? *J Clin Endocrinol Metab* 1977;**44**:639-46.
5 Ferris TF, Chonko AM, Williams JS, Reineck HJ, Stein JH. Studies of the mechanisms of sodium retention in idiopathic oedema. *Trans Assoc Am Physicians* 1973;**86**:310-1.
6 Edwards OM, Bayliss RIS. Idiopathic oedema of women. *Q J Med* 1976;**177**:125-44.
7 McKendry JBR, McClaren MC, Bloom GM. Idiopathic intermittent oedema of women with interpersonal conflict. Amsterdam: Exerpta Medica, 1966:59-63. (*International Congress Series* No 134.)
8 Gordon ES, Graham DT. Metabolic oedema. *J Lab Clin Med* 1959;**54**:818-9.
9 Ettigi PG, Brown GM. Psychoneuroendocrinology of affective disorder: an overview. *Am J Psychol* 1977;**134**:493-501.
10 Anonymous. The new psychiatry [Editorial]. *Br Med J* 1981;**283**:513.
11 Kiyoshi M, Tanimoto K, Yamaguchi N, Iwaski Y, Chihara K, Fujita T. Increased prolactin response to TRH in mania. *N Engl J Med* 1979;**25**:1400.
12 Horrobin DF, Mtabaji JP, Karmali RA, Manku MS, Nassar BA. Prolactin and mental illness. *Postgrad Med J* 1976;**52**:79-85.
13 MacGregor GA, Markandu ND, Roulston JE, Jones JC, de Wardener HE. Is "idiopathic" oedema idiopathic? *Lancet* 1979;i:397-400.
14 de Wardener HE. Idiopathic oedema: role of diuretic abuse. *Kidney Int* 1981;**19**:881-92.
15 Streeten DHP. Idiopathic oedema. *Lancet* 1979;i:775-6.
16 Dunnigan MG, Lawrence JR. Idiopathic oedema. *Lancet* 1979;i:776-7.
17 Edwards OM, Dent RG. Idiopathic oedema. *Lancet* 1979;i:1188.
18 Lagrue G, Behar A, Baillet J. Idiopathic oedema. *Lancet* 1979;i:1188.
19 Edwards CRW, Besser GM, Thorner MO. Bromocriptine responsive form of idiopathic oedema. *Lancet* 1979;ii:94.
20 Al-Khader AA, Aber GM. The relationship between the "idiopathic oedema syndrome" and sub-clinical hypothyroidism. *Clin Endocrinol* 1979;**10**:271-9.
21 Wortsman J, Singh KB, Murray J. Evidence for the hypothalamic origin of the polycystic ovarian syndrome. *Obstet Gynecol* 1981;**58**:137-41.
22 Mills DE, Buckman MT, Peake GT. Effects of prolactin administration and suppression on blood pressure and body fluid compartments in the rat. *Endocrinology* 1981;**109**:1590-6.
23 Evered DC, Horrobin DF, Vice PA, Cole EN, Nassar BA. Idiopathic oedema and prolactin. *Proceedings of the Royal Society of Medicine* 1975;**69**:427-8.
24 Favre H, Mach RS. Etude du "facteur natriurétique" chez des malades atteints d'oedèmes idiopathiques. *Schweiz Med Wochenschr* 1980;**110**:1107-11.

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Serum pancreatic lipase activity in cystic fibrosis

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Abstract

Patients with cystic fibrosis have been found to have abnormal serum concentrations of immunoreactive trypsin and abnormal activities of pancreatic isoamylase. A study was undertaken to discover whether activity of pancreatic lipase is also altered in cystic fibrosis. Serum from 23 patients with cystic fibrosis was assayed for immunoreactive trypsin and pancreatic lipase. Median serum pancreatic lipase activity was significantly lower in patients with cystic fibrosis than in controls, as was immunoreactive trypsin concentration ($p < 0.0001$). Some patients had supranormal lipase concentrations but these were not always associated with absence of malabsorption.

Serum pancreatic lipase activity is considerably changed in cystic fibrosis.

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Introduction

Patients with cystic fibrosis have been found to have abnormal serum concentrations of immunoreactive trypsin[1 2] and abnormal activities of pancreatic isoamylase.[3] There have, however, been no observations on pancreatic lipase activity in sera of these patients. We therefore undertook a study to examine whether the activity of this enzyme is altered in cystic fibrosis.

Patients and methods

Blood samples were collected from 23 patients with known cystic fibrosis (age range 12 to 38 years) with sweat sodium and chloride concentrations greater than 70 mmol(mEq)/l. The serum was separated and stored at −20°C.

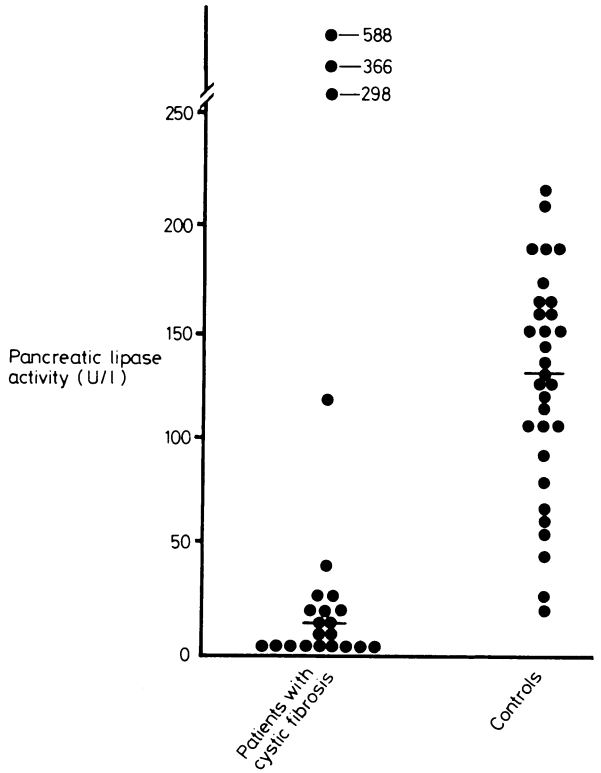
Serum was thawed on the day of the assay, and the assays for immunoreactive trypsin and pancreatic lipase were undertaken on

the same day to avoid repeated freezing and thawing of sera. Immunoreactive trypsin was measured by a specific radioimmunoassay (Hoechst kit) as described before.[2] Pancreatic lipase activity was measured by a turbidimetric method which uses a triolein suspension as substrate and a purified colipase to render the assay specific for the pancreatic enzyme.[4] The reagents for this assay were obtained from Boehringer, and the assay was performed on the Abbott bichromatic analyser ABA 100 at 30°C.[4]

Results

The distribution of serum immunoreactive trypsin concentrations and pancreatic lipase activities was non-parametric and is hence expressed as medians with ranges. The statistical comparisons were carried out by Mann-Whitney U test and χ^2 test.

The median serum pancreatic lipase activity in patients with cystic fibrosis (13 U/l; range 0-588) was significantly lower ($p < 0{\cdot}0001$) than that in controls (median 125; range 25-210 U/l; see figure). The



Range (—median) of serum pancreatic lipase activity in 23 patients with cystic fibrosis and in 31 controls.

median immunoreactive trypsin concentration was 0 μg/l (range 0-1010), which was also significantly lower ($p < 0{\cdot}0001$) than that in controls. Serum pancreatic lipase activity and immunoreactive trypsin concentrations were significantly correlated ($r = 0{\cdot}96$, $p < 0{\cdot}0001$). The prevalance of subnormal pancreatic lipase activity (19 patients had activity of less than 50 U/l) and subnormal immunoreactive trypsin concentration (19 patients had concentration less than 140 μg/l) was considerably greater in patients with cystic fibrosis than in controls ($p < 0{\cdot}001$). Three patients who had greatly raised lipase activity also had raised concentration of immunoreactive trypsin. Only one patient had both immunoreactive trypsin concentration and pancreatic lipase activity within the normal range. Two of the three patients with raised lipase activity and raised immunoreactive trypsin concentration did not have steatorrhoea (foecal fat content of less than 5 g in 24 h); the third had steatorrhoea and had to be given pancreatic enzyme supplements.

Discussion

Our results show that serum pancreatic lipase activity is considerably changed in cystic fibrosis. The activities were abnormal in 22 out of 23 patients studied, and a similar prevalence was found for immunoreactive trypsin, as previously reported in patients over the age of 12 years.[2] As in the previous study, we found that some patients had supranormal lipase concentrations; in each case immunoreactive trypsin concentration was also high.

The only patient with a normal lipase activity and two with supranormal lipase activity had no evidence of malabsorption. One patient with malabsorption, however, had raised lipase and immunoreactive trypsin in serum. Hence, although subnormal values of lipase and immunoreactive trypsin are satisfactory indicators of pancreatic hypofunction, supranormal concentrations are not necessarily associated with the absence of malabsorption.

The observation that pancreatic enzyme activity may be greatly raised in the absence of acute pancreatitis in some patients with cystic fibrosis (three out of 23 in this study) remains intriguing. We have observed similar enzyme concentrations in β-thalassaemia with iron overload.[5] After our initial studies on immunoreactive trypsin in cystic fibrosis we thought that the raised concentrations of immunoreactive trypsin could be caused by a leak of the proenzyme from the damaged pancreatic acinar tissue into the circulation; this hypothesis was based on the fact that the radioimmunoassay of trypsin measures both trypsin and trypsinogen. We had not then expected that the raised immunoreactivity would be associated with an actual rise in enzyme activity. Our present results show that a leakage of enzymatic lipase from the pancreatic acini actually occurs.

As the amount of enzyme delivered by the pancreas into the duodenum in cystic fibrosis is negligible, it is not likely that any of the serum enzyme is derived through reabsorption from the gut. This challenges the concept that an appreciable proportion of pancreatic enzyme in circulation is derived through absorption from the gut.

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References

1 Crossley JR, Elliott RB, Smith PA. Dried blood spot screening for cystic fibrosis in the newborn. *Lancet* 1979;i:472-4.
2 Dandona P, Hodson M, Bell J, Ramdial L, Beldon I, Batten JC. Serum immunoreactive trypsin concentrations in cystic fibrosis. *Thorax* 1981;**36**:60-2.
3 Foo Y, Rosalki SB, Hodson ME, Batten JC, Dandona P. Serum pancreatic isoamylase concentrations in cystic fibrosis. In: Sturgess JM, ed. *Perspectives in cystic fibrosis. Proceedings of the International Cystic Fibrosis Congress, Toronto.* Toronto: Canadian Cystic Fibrosis Foundation, 1980:15a.
4 Junglee D, de Albarran R, Katrak A, Freedman DB, Beckett AG, Dandona P. Serum pancreatic lipase activity in diabetes mellitus. *J Clin Pathol* 1983;**36**:200-2.
5 Hussain MAM, Dandona P, Fedail M, Flynn D, Hoffbrand AV. Serum immunoreactive trypsin in thalassaemia major. *J Clin Pathol* 1981; **34**:970-1.

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