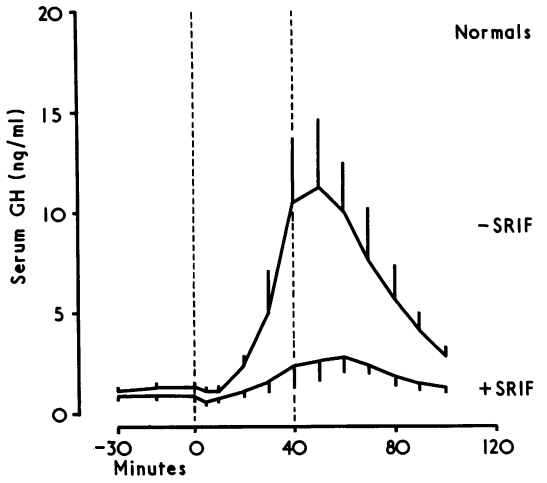

FIG. 1—Exercise-induced growth hormone (GH) curve produced by seven normal subjects with and without somatostatin.

The results for the nine male diabetics are shown in fig. 2. Somatostatin also caused suppression in this group. This effect was statistically significant 20 and 30 minutes after beginning exercise (2 $P < 0.05$ and < 0.025 respectively). The experiments without somatostatin show that fasting growth hormone values were higher and the rise during exercise occurred earlier and was more pronounced in the diabetics. This is in accordance with earlier findings (Hansen, 1972).

It should be emphasized that the metabolic state of the diabetics was similar in the experiments with and without somatostatin (average fasting blood glucose 138 mg/100 ml in control experiments and 130 mg/100 ml in the somatostatin experiments).

Before therapeutic experiments with somatostatin are feasible it is necessary to develop a mode of long-term suppression. One possibility is to produce a delayed absorption compound. Another is to try somatostatin or some modification of the molecule given by mouth. If a preparation which can suppress the growth hormone hypersecretion of diabetics in a clinically acceptable way is found it should be used in con-

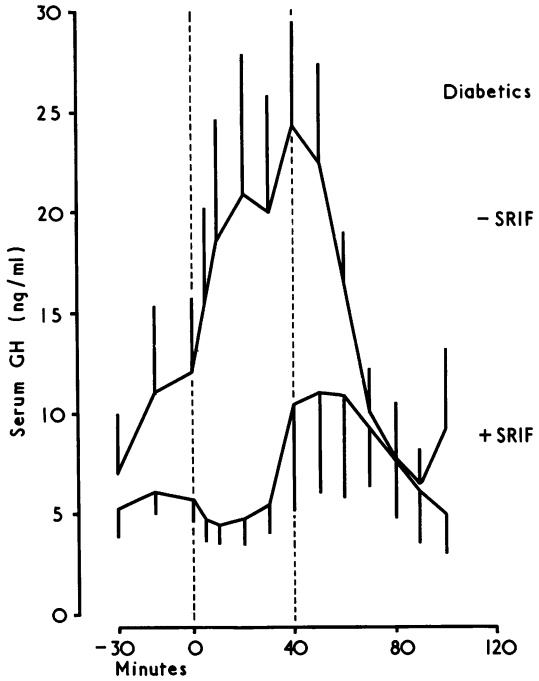

FIG. 2—Exercise-induced growth hormone curve produced by nine male diabetics with and without somatostatin.

trolled clinical trials to observe its effect on the development of diabetic angiopathy.

The somatostatin used in this study was prepared and characterized as described by Sarantakis and McKinley (1973).

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MEDICAL MEMORANDA

Acute Pancreatitis in Coxsackie B Infection

BO URSING

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The aetiology and pathogenesis of acute pancreatitis still challenge research. Gall stones and the abuse of alcohol are thought to be common casual factors (Edlund, 1970; Lundh, 1970). Infectious agents are rarely responsible (Everett, 1969; Kunz, 1971), though mumps is a well known cause, sometimes leading to diabetes mellitus (Melin and Ursing, 1958). Pappenheimer *et al.* (1951) showed that injection of material from a patient with meningoencephalitis and pleurodynia damages the pancreas in mice. In generalized Coxsackie virus infection in infants virus and lesions are found in the pancreas, liver, myocardium, and meninges (Kibrick and Benirschke, 1958; Fechner *et al.*, 1963). Reports of Coxsackie virus as a probable cause of acute pancreatitis in adults are rare (Murphy and Simmul, 1964; Nakao *et al.*, 1964).

In 1972 acute pancreatitis was diagnosed in two adults with Coxsackie B5 infection. Their cases are reported here.

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Case 1

A woman aged 27 who had been previously healthy and had no history of gall bladder or liver disease fell ill on 4 September with pyrexia, arthralgia, and pain in the right chest. On 9 September she had exanthema and severe abdominal pain and was admitted to hospital. During the following week she developed a fulminant picture of acute pancreatitis, with high-grade fever, hypotension, and tachycardia. She vomited and developed paralytic ileus of seven days'

duration. On 11 September severe chest pain developed, and next day the E.C.G. showed changes of the type seen in pericarditis with raised S-T segments. These changes persisted for five days. No symptoms or signs of increased venous pressure or enlargement of the heart appeared. Between 15 September and 2 October she was given prednisolone and her condition improved. On 5 October she left hospital symptom-free.

Laboratory Investigations.—E.S.R. 80-33 mm in the first hour; haemoglobin 13·6-12·1 g/100 ml; R.B.C. 3·9 × 10^6/mm³; W.B.C. 19,200-6,000/mm³ (neutrophilic differential throughout); normal platelet count. Serum creatinine and B.U.N. were normal, as were the serum Na, K, Ca, and P. The amylase levels found in the serum and urine during the acute attack are shown in table I (normal ranges in this laboratory 78-280 U/100 ml in serum, 130-1,600 U/24 hr in urine). The results of liver function tests were mostly abnormal on 22 September, with serum bilirubin 0·7 mg/100 ml; alkaline phosphatase 11 U (normal range 2-8 U); SGOT 81 U (normal range 10-35U); and SGPT 192U (normal range 5-30 U). The serum cholesterol and triglycerides were normal, as was the lipoprotein electrophoretic pattern. Serum glucose was normal.

TABLE I—*Amylase Levels recorded during Acute Attack in Case* 1

	11 Sept.	12 Sept.	13 Sept.	14 Sept.
Serum (U/100 ml)	410	3,200	1,850	637
Urine (U/24 hr)	—	22,000	8,000	3,000

Bacteriological Investigations.—No antibodies to yersinia, mumps, or toxoplasma virus were found. Paul-Bunnell and tests for hepatitis-associated antigen and antistreptolysin were negative. Several cultures from faeces and duodenal material grew Coxsackie virus B5. Neutralizing antibody titre against the virus showed more than a fourfold increase (performed by Dr. T. Edén, Institute of Microbiology, University, Lund, Sweden).

X-ray studies of gall bladder, oesophagus, and stomach showed nothing abnormal.

Epidemiology.—On 19 August the patient's father had been admitted to hospital in Helsingfors with symptoms of acute pancreatitis. This developed into pancreatic abscess and he was operated on, but he died during the postoperative period. No viral studies were done. The patient and her father had met before the onset of the illness.

Case 2

A man aged 38 without previous disease had had a cholecystectomy in 1969 at which a non-functioning gall bladder containing a single stone was found. There was no known abuse of alcohol. On 26 August he fell ill with abdominal symptoms and nausea. On 6 September he was jaundiced and was admitted to hospital. Next day he had high-grade fever and severe abdominal pain. During the following seven days he developed a typical picture of acute pancreatitis, with fever, hypotension, and tachycardia. He developed ileus and had to be fed parenterally for two weeks. Analgesics were given for the pain. On 28 September he left hospital symptom-free.

Laboratory Investigations.—E.S.R. 93-48 mm in the first hour; haemoglobin 15·4 g/100 ml; R.B.C. 5·1 × 10^6/mm³; W.B.C. 9,900/mm³ (normal differential). Serum creatinine and B.U.N. were normal, as were the serum Na and K. The amylase determinations in serum and urine during the acute attack are shown in table II. The results of liver function tests during the acute attack were abnormal.

TABLE II—*Amylase Determinations During Acute Attack in Case* 2

	8 Sept.	9 Sept.	13 Sept.
Serum (U/100 ml)	118	4,075	323
Urine (U/24 hr)	368	19,520	2,960

Serum bilirubin 5·6-0·7 mg/100 ml; alkaline phosphatase 14-7 U; glutamyltranspeptidase 1,620-345 U (normal range <70 U); SGPT 470-48 U; SGOT 344-30 U. Serum glucose was normal.

Bacteriological Investigations.—No antibodies to cytomegalovirus or to listeria, toxoplasma, or mumps virus were found. Paul-Bunnell and a test for hepatitis-associated antigen were negative. Isolation of virus from faeces yielded Coxsackie B5. Neutralizing antibodies against that virus were increased fourfold.

Intravenous cholangiography showed nothing abnormal.

Comment

Reflux of bile acids into the pancreatic duct has received much attention as a factor in the pathophysiology of acute pancreatitis. Bile acids may activate phospholipase A within the pancreas and so raise the concentration of cytotoxic phospholipids such as lysolecithin (Schmidt and Creutzfeldt, 1969).

Nothing is known about the way in which viruses attack the pancreas. Do they cause oedema of the papilla of Vater and pancreatic ducts, or do they have a direct cytopathic effect? In rats viral infection leads to widespread necrosis with more or less complete loss of glandular acini but without damage to the islets of Langerhans (Pappenheimer *et al.*, 1951). Coxsackie viruses B4 and B1 experimentally produce damage to the pancreatic acinar and islet cells of mice of different ages (Burch *et al.*, 1971; Tsui *et al.*, 1972). Microscopical examination of human neonates dying of Coxsackie infection has shown a few small foci of acute inflammation with evidence of recent destruction of pancreatic acini; in several areas the ducts were distended and contained inspissated secretion and leucocytes (Kibrick and Benirschke, 1958; Fechner *et al.*, 1963).

The role of Coxsackie viruses in clinical acute pancreatitis is obscure. The frequency and severity of this type of viral infection are still unknown. Since neither of our patients had symptoms or signs of diabetes mellitus these observations do not support a possible association between epidemics of Coxsackie virus infection and the sudden onset of diabetes in children and young people (Gamble *et al.*, 1969; Gamble and Taylor, 1969, 1973; *Lancet*, 1971).

One of our cases had coexisting hepatitis and the other pericarditis; the outcome of the pancreatitis was good in both. It is interesting that the father of our first patient died from a pancreatic abscess.

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