

Octreotide is a synthetic octapeptide analogue of somatostatin and shares its biological activity as a result of four common amino acids. The mode of action seems to be at two levels, by a direct receptor specific inhibition of adenylylase activity and by inhibition of calcium flux across cell membranes. The exact physiological role of somatostatin and octreotide on the gastrointestinal tract has not been precisely defined, however, somatostatin and octreotide can be regarded as 'pan inhibitors' of gastrointestinal, pancreatic exocrine, and endocrine functions, and gastrointestinal motility.<sup>4</sup> Action on the human pancreas appears to be by a reduction of enzyme secretion, with no reduction in bicarbonate secretion.<sup>5</sup>

Octreotide's advantage over somatostatin is a much longer half life (1 to 2 hours compared with only 2 minutes). It can therefore be given by subcutaneous injection rather than continuous infusion. Somatostatin has been used with some benefit in the management of pancreatitis in adults,<sup>6</sup> although further trials are needed to establish its exact role in treatment.

In our patient octreotide treatment resulted in a marked reduction in the production of

ascitic fluid and improvement in the condition of the child. No side effects were seen. We suggest that octreotide may have a place in children with acute pancreatitis and its complications. The long term prognosis in this patient is uncertain but treatment with free radical scavengers has a possible role in preventing recurrence.<sup>7</sup>

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## Fructose breath hydrogen tests

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### Abstract

Fructose absorption was studied by the breath hydrogen test in 114 healthy children aged 0.1–6 years, given either 2 g/kg or 1 g/kg of fructose. All 57 children given 2 g/kg had peak breath hydrogen excretions  $\geq 20$  ppm. At 1 g/kg only 25/57 (44%) showed incomplete absorption and the percentage incompletely absorbing fructose and the peak breath hydrogen value were significantly higher in children aged 1–3 years. Interestingly, this age distribution correlates with that of toddler diarrhoea.

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It has been shown by means of the breath hydrogen test that intestinal absorptive capacity for fructose is limited, partly depending on the presence of glucose.<sup>1</sup> Malabsorption of fructose would have clinical consequences, especially for toddlers, as they may consume relatively large amounts of apple juice. Discussion continues as to whether incomplete absorption of fructose in young children is normal, as opposed to a specific absorption defect.<sup>2,3</sup> We therefore reinvestigated fructose absorption, using the breath hydrogen test, in children under 6 years of age.

### Subjects and methods

The study group comprised 114 healthy children

(59 boys). Mean age was 3.5 years (range 0.1–6.0). They were recruited from day care centres and kindergartens. The parents completed a questionnaire concerning actual diets and bowel habits.

Fifty seven children each were given 2 g/kg or 1 g/kg of fructose as a 20% solution after at least a six hour fast. The two groups were comparable in terms of age and sex. Breath samples were taken before fructose ingestion and at 30 minute intervals until 2.5 hours after ingestion and analysed using the Lactoscreen (Hoek Loos) breath tester. An increase in breath hydrogen of at least 20 ppm over baseline was considered indicative of incomplete absorption of fructose. During the test and for two hours thereafter the children were observed for the presence of abdominal discomfort or diarrhoea.

The results are expressed as mean (SEM). Statistical analysis was performed using the  $\chi^2$  test and Student's *t* test for unpaired data (two sided).

### Results

All 57 children given fructose at 2 g/kg had breath hydrogen increases  $\geq 20$  ppm over baseline. Breath hydrogen increases varied from 21 to 146 ppm (mean (SEM) 64 (4) ppm; fig 1); there was no significant relation with age (fig 2A). Symptoms were noted in 12 children: abdominal pain in four and diarrhoea in three, five children experiencing both. Peak breath

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hydrogen in the symptomatic children (74 (10 ppm) was not significantly different from that in those without symptoms (61 (4) ppm).

Of the children given 1 g/kg of fructose, 25/57 (44%) had peak breath hydrogen increases  $\geq 20$  ppm. This is significantly different from the 2 g/kg group ( $p < 0.001$ ). Peak breath hydrogen ranged from 0–139 ppm (mean (SEM) 26 (4) ppm; fig 1). More children 1–3 years of age

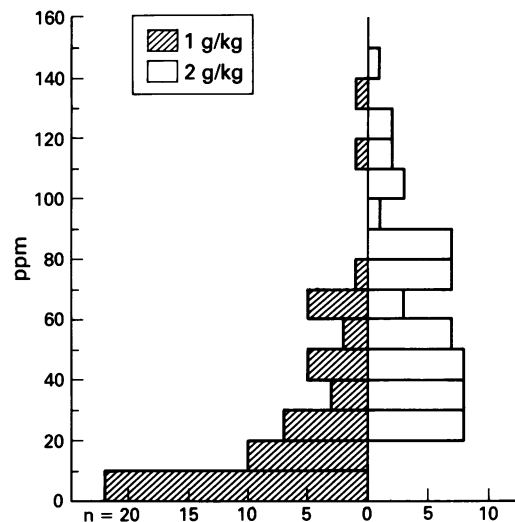


Figure 1 Distribution of peak breath hydrogen excretion after ingestion of fructose 1 g/kg (left) and 2 g/kg (right) with 57 children 0–6 years of age in each group.

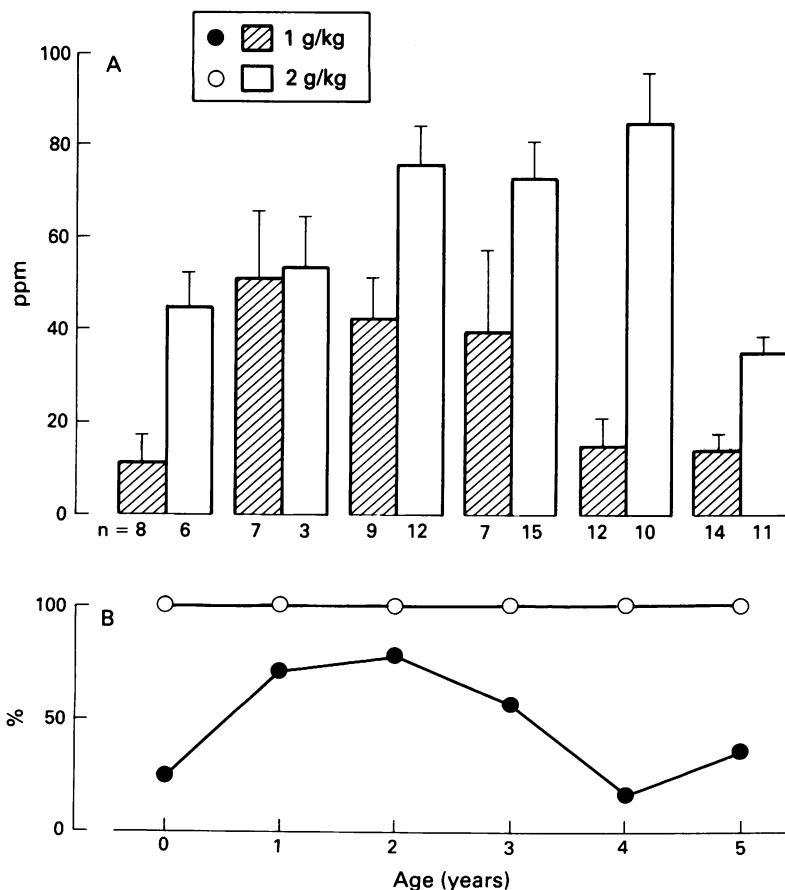


Figure 2 (A) Mean (SEM) of peak breath hydrogen excretion in children given 1 g/kg or 2 g/kg fructose in six age groups. Number of children in each group indicated under respective columns. (B) Percentage of children given 1 g/kg or 2 g/kg fructose in each age group with peak breath hydrogen excretion  $\geq 20$  ppm.

(16/23) absorbed 1 g/kg fructose incompletely than did younger (2/8) and older (7/26) children; because of small numbers this was only significant for the older group ( $p < 0.01$ ) (fig 2B). Similarly, mean peak breath hydrogen was higher for children 1–3 years of age than for younger ( $p < 0.02$ ) and older ( $p < 0.001$ ) children (fig 2A). Three children, with peak hydrogen excretions of 11, 55, and 139 ppm, had abdominal pain during the test.

Thirty two children were reported regularly to have frequent stools ( $\geq 3$  per day for  $\geq 2$  days per month) and/or recurrent abdominal pain (at least once a week). The results of the tests in these children were not different from those in the remaining 82 children.

## Discussion

Our study corroborates previous results indicating that incomplete absorption of fructose is the normal situation, even in younger children.<sup>1</sup> Based on the observation that the addition of glucose improves fructose absorption considerably, Kneepkens *et al* were the first to hypothesise that the fructose carrier was part of a sucrase related monosaccharide transport system, activated by the simultaneous presence of glucose (or galactose) and fructose.<sup>1</sup> A recent study in rats provided strong support for this hypothesis.<sup>4</sup> The  $\alpha$ -glucosidase blocker, acarbose, not only inhibited the digestion of sucrose, but also the absorption of a glucose-fructose mixture.<sup>4</sup> A case report of a child malabsorbing fructose as well as sucrose despite normal sucrase activity,<sup>5</sup> fits into this hypothesis. In another recently described case,<sup>2</sup> however, insufficient proof is presented for the absence of the fructose carrier as it may well be an example at the extreme of the range of normal fructose absorption.

Most foods contain either sucrose or equal amounts of fructose and glucose. This explains why the consumption of fructose-containing foods seldom gives rise to gastrointestinal symptoms. Foods rich in fructose are honey and, especially, apples, pears and their juices. Indeed, 'apple juice malabsorption' has been shown to play a part in many cases of toddler diarrhoea.<sup>6</sup> Interestingly, we found fructose absorption to be impaired to a greater extent in children 1–3 years of age, reflecting the typical age distribution of toddler diarrhoea. This study suggests a possible reason for the age dependency of this condition. Other factors known to be involved in this syndrome might similarly be limited to this age group.

In the present study we compared two different doses of fructose. The frequency of abnormal tests with 2 g/kg of fructose is higher than previously published; this might well be due to the fact that only children up to 6 years of age have been included. Clearly, the 2 g/kg dose is not suitable to determine any suspected relationship between fructose consumption and gastrointestinal complaints in young children. The 1 g/kg dose also failed to discriminate between children with a history of gastrointestinal symptoms and those without. In clinical practice, therefore, with children suspected of

fructose related gastrointestinal symptoms we prefer to take a careful dietary history, particularly of fructose-containing foods and to perform a two week trial of appropriate dietary measures, rather than performing fructose breath hydrogen tests.

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## Transient protein S deficiency with deep venous thrombosis during *Salmonella typhimurium* infection

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### Abstract

**A patient with deep venous thrombosis and low protein S activity during the course of *Salmonella typhimurium* infection is presented. Although protein S deficiency has been reported in patients with disseminated intravascular coagulation, it was not present in this patient and his protein S activity was normal after the findings of infection and deep venous thrombosis disappeared.**

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Congenital protein S deficiency is inherited as an autosomal dominant trait and it may cause recurrent thrombotic disease with or without a precipitating condition.<sup>1</sup> Acquired decreases in protein S have been reported in pregnancy and during oral contraceptive hormone treatment and in patients with disseminated intravascular coagulation (DIC) and liver disease.<sup>2</sup> Although patients with sepsis frequently suffer thromboembolic complications,<sup>3</sup> protein S deficiency or inactivity in these patients is often not recognised if they do not have DIC.

Here, we describe a patient who presented with deep venous thrombosis together with low protein S activity during the course of *Salmonella typhimurium* infection. He did not have any clinical and laboratory findings of DIC and his protein S activity returned to normal after the findings of infection and deep venous thrombosis disappeared.

### Case report

A 13 year old boy was admitted with complaints of fever, swelling of the ankles and knees, a rash on the trunk and extremities, pain in the lumbar region, and progressive oedema. There was no history of bleeding or thromboembolic abnormalities in the patient nor in either maternal or paternal family members. Physical examination revealed fever (39.7°C), an

erythematous macular rash on the lower extremities, hepatomegaly, and pitting oedema in both pretibial regions and the dorsa of the feet.

Initial laboratory findings were: haemoglobin concentration 100 g/l, packed cell volume 0.32, white cell count  $6 \times 10^9/l$ , platelet count  $480 \times 10^9/l$ , prothrombin time 12 seconds, partial thromboplastin time 42 seconds, fibrinogen concentration 2.9 g/l, fibrinogen degradation products 10-40 µg/ml, and the Ham test was normal. Stool and blood cultures revealed *S typhimurium*. Venography of the lower extremities showed deep venous thrombosis and computed tomography showed occlusion of inferior vena cava and both iliac and femoral veins. Abdominal ultrasonography showed hepatosplenomegaly and occlusion of the inferior vena cava.

The patient was given anticoagulants with 50 U/kg/hour heparin until changed to 225 mg/day dipyridamole, and 1 g/day salicylate on day 7. For salmonella infection ciprofloxacin was started and by day 3 his temperature was normal and on day 10 oedema of the lower extremities disappeared.

On day 20, antibacterial treatment was discontinued and the patient was discharged on antiplatelet drugs. Sixty days later abdominal ultrasonography and computed tomography showed no thrombosis and the antiplatelet treatment was stopped.

### Methods

Routine coagulation tests (prothrombin time, partial thromboplastin time, fibrinogen concentration) were performed in fresh plasma and fibrinogen degradation products were measured in serum using standard methods. Venous blood was drawn by direct venepuncture into Vacutainer glass tubes containing 1 part 0.13 mol trisodium citrate for 9 parts of blood, and centrifuged at 3000 rpm for 10 minutes. Plasma was then separated and stored in 0.5 ml aliquots

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