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 ≥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.

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. 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. 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 ≥20 ppm over baseline. Breath hydrogen increases varied from 21 to 146 ppm (mean (SEM) 64 (4) ppm; fig 1); there was no significant relationship with age (fig 2A). Symptoms were noted in 12 children: abdominal pain in four and diarrhoea in three, five children experiencing both. Peak breath
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 ≥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 (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 (≥3 per day for ≥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. 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 sucrose related monosaccharide transport system, activated by the simultaneous presence of glucose (or galactose) and fructose. A recent study in rats provided strong support for this hypothesis. The α-glucosidase blocker, acarbose, not only inhibited the digestion of sucrose, but also the absorption of a glucose-fructose mixture. A case report of a child malabsorbing fructose as well as sucrose despite normal sucrase activity fits into this hypothesis. In another recently described case, 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. 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, particu-
larly of fructose-containing foods and to per-
form a 1 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 pre-
sented. 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.1 Acquired decreases in
protein S have been reported in pregnancy and
during oral anticontraceptive hormone treatment
and in patients with disseminated intravascular
coaulation (DIC) and liver disease.2 Although
patients with sepsis frequently suffer thromb-
embolic complications,3 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 thrombembolic
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 6×10⁹/l, platelet count
480×10⁹/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 throm-
bosis and computed tomography showed occlu-
sion 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 dis-
continued 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 concen-
tration) 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