The 1-hr blood xylose test in the evaluation of malabsorption in infants and children[1,2]

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ABSTRACT One hundred ninety-seven 1-hr blood xylose absorption tests with 5 g of D-xylose were performed on 171 infants and children for the evaluation of malabsorption. The mean ± 1 SD blood xylose level in 78 controls was 37.0 ± 7.7 mg/dl, and 71 patients with post infectious diarrhea was 28.4 ± 11.0 mg/dl. A significant reduction ($P < 0.001$) was found in 10 patients with Celiac disease (12.0 ± 8.6 mg/dl) and 18 patients with intractable diarrhea syndromes (18.3 ± 12.5 mg/dl). Forty-four patients had a blood xylose level less than 20 mg/dl, and the majority (35/44) were in the groups with postinfection and intractable diarrhea syndromes. Multiple tests were performed on 20 patients. Sixty-two intestinal biopsies were correlated with 1-hr blood xylose levels. The rate of false positives was 0. The rate of false negative tests varied between 4 to 32.7% depending on the assessment of intestinal damage. Our results confirm that the 1-hr blood xylose absorption test is a sensitive indicator of severe intestinal damage. Intestinal biopsy should be considered in all patients with a 1-hr blood xylose level less than 20 mg/dl. With borderline results (20 to 25 mg/dl), clinical decisions must be individualized. *Am. J. Clin. Nutr.* 33: 2328–2333, 1980.

The usefulness of various screening tests (e.g., serum carotene, xylose absorption, and fecal fat excretion) for upper intestinal mucosal function in children remains controversial (1). Biopsy of the upper intestine has been advocated as the procedure of choice by certain authorities (2), but despite it's safety in recent years this procedure remains unpleasant and traumatic for the patient, and requires expertise that is frequently unavailable. Rolles et al. (3) reported the 1-hr blood xylose screening test for the diagnosis of celiac disease in 1973. Their results were confirmed by others (4, 5), and it was further demonstrated that the 1-hr blood xylose test could be abnormal in a variety of other intestinal mucosal disorders including intractable diarrhea of infancy, cow's milk protein allergy, and postenteritis syndromes (5). Other investigators have been unable to confirm the usefulness of the one hour blood xylose test (6–8), and have cited false negative rates between 15 to 61%, and false positive rates of 22 to 66%.

In an attempt to clarify these widely differing results, we have analyzed our own data on 197 1-hr blood xylose tests performed over a 3-year period. The published data on the 1-hr blood xylose test in children is compared in terms of the varying dose of xylose administered, total numbers of tests performed, control population data, various diagnoses investigated, and the incidence of false negative and false positive tests. Our results confirm that the one hour blood xylose test is a sensitive index of severe small bowel mucosal damage.

Clinical material and methods

From 1976 to 1979, 197 1-hr blood xylose tests were performed on 171 patients seen at the Children's Memorial Hospital for evaluation of possible malabsorption. There were 87 males and 84 females. The age range was 2 months to 10 years (mean 21½ months). The weight range was 3 to 31 kg (mean 10 kg). After a 4- to 6-hr fast, a standard dose of 5 g of D-xylose in 100 ml of water was given to all patients. Venopuncture was performed 60 min later for xylose determination, measured by the method of Rowe and Rice (9). Blood xylose levels below 20 mg/dl were considered low, between 20 to 25 mg/100 ml were borderline, and greater than 25 mg/dl were normal.

Sixty-two small bowel biopsies were performed under fluoroscopic control using the Watson modification of

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the Crosby pediatric capsule. Hematoxylin eosin stained histological specimens were interpreted according to a modification of the method of Townley et al. (10). This involved objectively grading each specimen regarding four categories: *1*) villus atrophy and villus crypt ratio; *2*) epithelial cell appearance; *3*) degree of cellularity; *4*) the presence of edema. Each category was scored from 4 to 0, with 4 being normal and 0 being severely affected. Total scores were then added and divided into the following grades: I (13 to 16), II (9 to 12), III (5 to 8), IV (0 to 4).

The patients were categorized as follows: group A—control. This group comprised 72 children. Thirty-nine had chronic nonspecific diarrhea (11) characterized by recurrent episodes of diarrhea unresponsive to various dietary or medicinal manipulations, normal growth and physical examination, and normal laboratory findings. Thirty-five patients had miscellaneous diagnoses and were found not to have significant small bowel disease. Group B—postinfectious. Seventy-one patients had either an enteropathogenic organism isolated, evidence of malabsorption, and/or documented onset in association with dehydration. Group C—celiac disease. Ten patients had total villus atrophy while on gluten containing diets, and improved on a gluten free diet. Group D—intractable diarrhea of infancy. Eleven patients had the syndrome characterized by an ill defined etiology, chronic nutritional failure, and septic complications (12). None of these patients had consumed gluten containing foods. All required intravenous alimentation and elemental diet. Seven patients had primary immunodeficiency syndromes. Two had severe combined immunodeficiency, one had chronic mucocutaneous candidiasis with steatorrhea, one had Nezelof's syndrome (deficient cell-mediated (T cell) immunity with variable antibody (B cell) deficiency), and three had variable combined immune deficiency syndromes.

Results

One hundred ninety-seven 1-hr xylose absorption tests were performed on 171 patients (**Table 1**). The mean blood xylose value in the controls (group A) was 37.0 ± 7.7 mg/dl. No patient had a 1-hr blood xylose value less than 22.0 mg/dl. The mean values in patients with celiac disease (group C) and intractable diarrhea (group D) were 12.0 ± 8.6 mg/dl and 18.3 ± 12.5 mg/dl, and were significantly ($P < 0.001$) less than the controls. One of the 10 patients with celiac disease had a 1-hr blood xylose of 26 mg/dl. The levels in group B (postinfectious) showed a mean of 28.4 ± 11.0 mg/dl with a wide range (6.0 to 56.9 mg/dl).

Forty-four patients had a 1-hr blood xylose level less than 20 mg/dl. All 10 celiac patients (group C) were confirmed by intestinal biopsy. Two of the 18 patients with intractable diarrhea did not undergo biopsy as their diagnosis was known. Only 12 of the 21 (57%) patients with postinfectious diarrhea and a 1-hr xylose level less than 20 mg/dl had an intestinal biopsy. In four of these patients the primary diagnosis was known, and in two other patients a repeat xylose level was in the normal range. In the three remaining patients intestinal biopsy was recommended, but was not performed. Ideally, all of these nine patients should have had an intestinal biopsy as we are unable to exclude celiac disease in these patients.

In **Figure 1** the relationship of a total of 62 intestinal biopsies performed on 55 patients is correlated with the 1-hr blood xylose levels. By this means the sensitivity of the test can be compared. When the xylose levels in patients with grade I biopsies are compared with the xylose levels from grade II, III, and IV combined, the false positive rate (low xylose level with normal biopsy) is 0, and the false negative rate (high xylose level with grade II, III, and IV biopsies) is 32.7% (7/52 patients). When the xylose levels from grade I biopsies are compared with only those from the most severely damaged mucosa the false negative rate (high xylose levels with grade III and IV biopsies) drops to 4% (1/24 patients).

Twenty patients had more than one blood xylose test performed. The xylose results can be used to denote improvement or relapse. Three patients with the intractable diarrhea

TABLE 1
Analysis of different groups investigated

Group	No. of xylose tests	No. of patients	No. of patients biopsied	Mean ± 1 SD and range 1 hr blood xylose	No. of xylose tests <20 mg/100 ml	No. patients with xylose <20 mg/100 ml	No. patients biopsied with xylose <20 mg/100 ml
A	78	72	14	37.0 ± 7.7 (22.0–64.0)	0	0	0
B	79	71	17	28.4 ± 11.0 (6.0–56.9)	23	21	12 (57.1%)
C	10	10	10	12.0 ± 8.6 (1.0–26.0)	9	9	9 (100%)
D	30	18	14	18.3 ± 12.5 (3.9–67.0)	20	14	12 (85.9%)
Totals	197	171	55		52	44	33

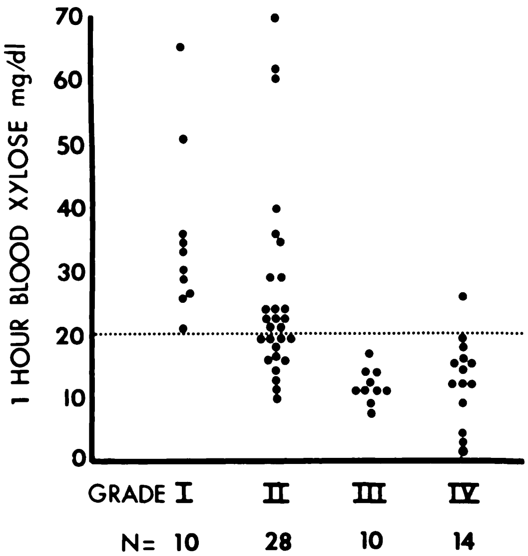

FIG. 1. Comparison of the 1-hr blood xylose levels in mg/dl with the grades of intestinal damage (grade I was normal and grade IV showed total villus atrophy).

of infancy syndrome pursued a chronic course with only partial recovery (xylose levels less than 25 mg/dl) over 18 months of follow-up. The results of the xylose tests in these patients correlated well with the changes seen on consecutive intestinal biopsies which continued to show varying degrees of villus atrophy (grades III and IV).

In **Table 2** we have compared our data on the 1-hr blood xylose absorption test with several of the series reported in the pediatric literature (3–8, 21). Differences can be seen in the number of patients investigated, dosage of xylose administered, lack of controls in some series, and markedly varying results for both false negative (2 to 61.5%) and false positive tests (0 to 66.6%).

Discussion

Our data confirm that the 1-hr blood xylose absorption test is a good screening test for the diagnosis of celiac disease provided the patient is still consuming gluten. One patient had a 1-hr blood xylose value of 26 mg/dl, but she had been on a gluten-free diet for 1 week before the test, and Rolles et al. (3) showed that the test may become normal within 4 days of starting a gluten-free diet. This may be one of the explanations for the failure of others (6) to find a good discrimination in their patients with celiac disease. Thus, we would agree with the recommendation (4, 6, 13) that a clinical suspicion of celiac disease remains the most important single factor in determining whether to perform a jejunal biopsy.

The 1-hr blood xylose test is a sensitive indicator of small intestinal damage. In our experience, postinfectious or intractable diarrhea syndromes of infancy account numerically for a greater proportion of abnormal tests (35 patients) compared to celiac disease (9 patients). In the two studies from the United States where data are given (reference 5 and our own), few patients with celiac disease are seen compared to those reported from Canada (5) or Europe (3, 4, 6). Intestinal damage due to rotavirus and adenovirus gastroenteritis has been implied from the finding of abnormal xylose absorption in infants (14), and has been confirmed on histology by others (15). In adults, the 1-hr xylose test has been reported to be abnormal in patients with contaminated small intestinal contents (16), and several of our patients had abnormal fecal flora in their upper intestine (17). Although this may be attributed to direct catabolism of xylose by intraluminal bacteria (16), it is more probably related to the degree of bile salt deconjugation and the effect of these unconjugated bile salts on the active intestinal transport of sugars (18). Other conditions where the 1-hr blood xylose test has been shown to be abnormal include intestinal damage caused by cow's milk allergy (19), and secondary to methotrexate administration in the treatment of acute leukemia when compared to controls (20).

The 1-hr xylose absorption test can be used in the follow-up of patients with intestinal damage. We have performed more than one test on 20 patients. Our results showed an excellent correlation with biopsy findings in this group of patients, and the xylose absorption test can be used to assess clinical recovery in the intractable diarrhea syndrome of infancy, thus reducing the number of intestinal biopsies that have to be performed. Rolles et al. (21) have used this test in confirming the persistence of gluten intolerance in children diagnosed as having celiac disease in infancy. Fifteen of 16 of their patients showed intestinal xylose malabsorption by the 1-hr blood

TABLE 2
Comparison of the 1-hr blood xylose absorption test results from eight reported series in the pediatric population

Reference	No. tests	Xylose dose	Controls		No. intestinal biopsies	No. celiac disease	No. tests for follow-up	False negative tests	False positive tests
			no.	mean mg/dl					
Rolles et al. 1973 (3)	254	5 g	75	37.0	117	53	4	1/53 (2%)	0
Lamabadusuriya et al. 1975 (6)	68	0.4 g/kg	19	37.0	68	43	11	3/19 (15.8%)[a] 8/12 (61.5%)[b]	4/6 (66.6%)
Rolles et al. 1975 (21)	16	5 g	(Rolles et al. 1973 (3))		16	15	16		
Schaad et al. 1978 (4)	148	5 g	102	32.8	148	46		1/46 (2%)	6/102 (12%)
Christie 1978 (7)	33	5 g			33	6		5/20 (25%)	6/13 (46%)
Buts et al. 1978 (5)	435	14.5 g/m^2	126	49.4	73	47		2/47 (4%)	0
Liebman 1979 (8)	46	0.5 g/kg			46	?		3/9 (33%)	8/37 (22%)
Kraut and Lloyd-Still	197	5 g	78	35	62	10	20	1/24 (4%)[a] 17/52 (32.7%)[c]	0

[a] Grade III and IV atrophy. [b] Grade II. [c] Grade II, III, IV.

xylose level within 1 to 28 days of starting ingestion of gluten.

The most common cause of chronic diarrhea referred for consultation in our hospital is the chronic nonspecific diarrhea syndrome of infancy (11, 22). We now routinely use the 1-hr xylose absorption test in our evaluation of these patients. The 1-hr blood xylose level should be normal in chronic nonspecific diarrhea of infancy, and implies normal upper intestinal mucosal function. This information is reassuring for the family and physician, and may result in a reduction in the number of intestinal biopsies and other procedures that have to be performed on these patients (22).

The variety of factors influencing the concentration of xylose in blood and urine after an oral load of xylose were summarized by Lamabadusuriya et al. (6), and include the proportion of load actually ingested, the load dose and osmolarity of the solution, the rate of gastric emptying, intestinal transit, intraluminal bacteria and drugs, and the rate of disappearance of the ingested xylose from the intravascular compartment into peripheral tissues. Recently the 1-hr blood xylose absorption test (with 5 g of D-xylose) has been used in a group of 70 adults with proven malabsorption and 146 controls (16). The xylose absorption was significantly impaired in the groups of patients with jejunal mucosal disease and contaminated small intestinal contents, compared to normal controls and those with other intestinal diseases. The incidence of false negatives and false positives was found to be 4.8 and 2.2%, respectively. The authors concluded that the 5-g xylose absorption test was most discriminating at all ages if the blood value at 1 hr is measured and corrected to a constant surface area.

Comparison of some of the reported series of one hour blood xylose absorption tests reveals some contrasting findings (Table 2). Two of the series with poor discrimination (6, 8) gave lower doses of the sugar (0.4 and 0.5 g/kg). Two series reported no data on control patients (7, 8), and both these groups reported false negative rates between 25 to 33%, and false positive rates between 22 to 46%. Our results are similar to three large series performed with the same dose of xylose (5 g) and including data on controls (3–5).

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