One-hour serum xylose as an absorption test in the tropics

PG HILL, IN ROSS,* R JACOB, S JYOTHEESWARAN, AND VI MATHAN

From the Wellcome Research Unit and The Gastroenterology Clinic, Christian Medical College Hospital, Vellore—632 004, India

SUMMARY The 1-hour serum xylose (surface area corrected) as an indication of xylose absorption after 5 g oral D-xylose has been compared with the 5-hour urine excretion test in a tropical population. The study confirmed that the peak serum xylose concentration occurs at 1 hour and that correction to a constant body surface area improves the discrimination between subjects with normal and impaired xylose absorption. The significantly lower reference range for the 1-hour surface area corrected serum xylose (0.55-1.11 mmol/l) compared to the UK figure reflects the reduced absorptive capacity of the jejunum, a result of tropical enteropathy. In view of the difficulties in obtaining accurate urine collections in tropical countries, especially in field studies, it is recommended that the 1-hour serum xylose (surface area corrected) should be adopted as the standard test of xylose absorption.

Measurement of D (+) xylose excretion in a timed urine collection after oral administration is the method most widely used to estimate absorption of D-xylose, an index of small bowel function. Delayed gastric emptying, renal disease, and inadequate urine collection are factors that reduce urinary excretion of D-xylose, giving a false impression of impaired small intestinal function.^{1,2} The discrimination of small bowel abnormality has been shown to be better if the concentration of serum xylose is measured 1 hour after ingestion of the oral dose, and is further improved if the measured concentration is corrected for body surface area.³ In view of earlier findings⁴ that the pattern of urinary xylose excretion in southern India is different from that in temperate zones, it is necessary to validate the observations of Haeney *et al.*³ for tropical climates. The observed differences between tropical and temperate regions may be related to the prevalence of non-specific tropical enteropathy—the occurrence of structural and possibly functional abnormalities of the small intestinal mucosa in apparently healthy individuals in the tropics.⁵⁻⁸

We report the results of a study carried out in southern India of the serum xylose concentration after administration of 5 g D-xylose orally, validating the applicability of this test in a tropical population.

*Present address: Hope Hospital, Salford, UK.

Accepted for publication 13 August 1980

Subjects studied and methods

A total of 111 subjects admitted consecutively in a metabolic ward were studied; these included apparently normal volunteers and patients with a variety of diseases associated with malabsorption. Informed consent was obtained from all subjects. Absorption of fat,⁹ D-xylose urinary excretion,⁴ and vitamin B12 absorption¹⁰ were tested in all patients. In addition, 1-hour serum samples were obtained after oral xylose from nine healthy laboratory staff from the upper socioeconomic group, who were well nourished and had no gastrointestinal illness. The height and weight of each subject were recorded. D-xylose (5 g) in 300 ml water was given at 0730 to subjects after an overnight fast. Solid food was withheld for a further 2 hours, although at least 500 ml of water was given to ensure adequate urine volumes. Urine collection in three timed fractions (0-2, 2.1-5, 5.1-8 hours) and estimation of D-xylose in urine were done as described earlier.^{4,11,12}

In all subjects, blood samples were collected before (basal) and 1 hour after oral xylose administration. Five millilitres of venous blood was collected on each occasion without anticoagulants, and the serum was separated and stored at -20°C till analysed. Analysis of aliquots of the same frozen sample over a 10-week period did not show significant differences. In each batch an aliquot from a pooled serum sample was used for quality control.

Serum xylose was measured by ferricyanide reduction in an automated continuous-flow system after destruction of glucose in the sample by glucose oxidase as described by Haeney *et al.*³ Measured serum xylose was expressed as the 1-hour value minus the basal value to correct for non-glucose, non-xylose reducing substances. The measured serum xylose was corrected to a constant surface area of 1.73 m² as described by Haeney *et al.*³

Full absorption curves were done in 25 subjects, 13 of whom had normal and 12 reduced 5-hour urinary xylose excretion. Venous blood samples were collected before and $\frac{1}{2}$, 1, 1 $\frac{1}{2}$, 2, 3, and 4 hours after the administration of xylose.

Urine and blood xylose values were compared in all 111 subjects, who were divided into three groups: group 1, 29 subjects without malabsorption of either fat or vitamin B12; group 2, 68 subjects with fat malabsorption but normal vitamin B12 absorption; and group 3, 14 subjects with malabsorption of both fat and vitamin B12. Renal function, as measured by blood urea and serum creatinine, was normal in all subjects.

Results

The peak serum xylose concentration in 11 of the 13 subjects with normal 5-hour urine excretion was 1 hour after oral administration (Table 1). The remaining two subjects had peak values at 1 $\frac{1}{2}$ hours; in both these, the 1-hour value was within the range of those with a peak at 1 hour. Of the 12 subjects with low urine xylose excretion, seven (58%) had peak values at 1 hour. A wider spread in the time of appearance of the peak was found in this group (Table 1). In both groups of subjects the highest mean serum concentration was at 1 hour, although

Table 1 Time of peak serum xylose value in normal and abnormal subjects

Subject	n	Time of peak value (hours)				
		$\frac{1}{2}$	1	1 $\frac{1}{2}$	2	3
Normal	13	0	11	2	0	0
Abnormal	12	1	7	1	1	2

Table 2 Discrimination between normal and abnormal subjects at different times after 5 g xylose

Subject	n	Serum xylose (mmol/l) corrected for surface area					
		½h	1h	1½h	2h	3h	4h
Normal							
Mean	13	0.47	0.70	0.62	0.53	0.45	0.33
SD		0.16	0.09	0.14	0.06	0.09	0.13
Abnormal							
Mean	12	0.24	0.41	0.39	0.38	0.34	0.27
SD		0.14	0.19	0.16	0.15	0.19	0.12
t		3.70	4.71	3.75	3.14	1.89	1.14

in the group with abnormal urine xylose excretion the peak was less well defined (Table 2).

Comparison of mean serum values at different times showed that the greatest discrimination between normal and abnormal xylose absorption also occurs at 1 hour ($t = 4.71$). The lower limit of normal for the surface area corrected serum xylose was calculated from the values of 21 subjects in group 1 without fat or vitamin B12 malabsorption and with normal 5-hour urine xylose excretion ($> 20\%$) and of nine members of the laboratory staff. The reference range calculated from these 30 subjects was 0.55-1.11 mmol/l (mean 0.83, SD 0.14 mmol/l).

A good correlation ($r = 0.67$, $P < 0.001$) was shown between the 5-hour urine excretion of xylose

and the 1-hour surface area corrected serum xylose in the 111 subjects studied (Figure). In 87 subjects (78%) there was concordance between the urine and serum values. In 19, the urine xylose was low with a normal serum value, and these subjects would have been considered to have xylose malabsorption on the basis of the urine result alone. In the remaining five subjects, the urine xylose excretion was normal but the 1-hour surface area corrected serum value was below the lower limit of the reference range.

Correction of the measured serum xylose concentration to a constant body surface area (1.73 m^2) narrowed the distribution of results in all three groups of subjects and improved the discrimination of the two groups with impaired xylose absorption from group 1 (Table 3). The mean 1-hour serum xylose value is decreased compared to group 1 in those patients with steatorrhoea (group 2). It is decreased to a greater extent in group 3, where there was malabsorption of both fat and vitamin B12.

Discussion

This study confirms that in the population of southern India the peak serum concentration after a 5 g oral dose of D-xylose occurs at 1 hour (Tables 1 and 2) and that correction of the measured serum value to a constant body surface area narrows the range of values and improves the discrimination between those with normal and with abnormal small

Table 3 Discrimination between normal and abnormal subjects

Group	n	1-h serum xylose		Urine xylose excretion	
		M	SA	2 h	5 h
1	29	0.94 (0.20)	0.79 (0.16)	11.7 (7.1)	23.9 (7.7)
2	68	0.75 (0.36)	0.57 (0.29)	8.2 (5.5)	17.2 (9.1)
t		2.64	3.80	2.59	3.41
3	14	0.48 (0.27)	0.38 (0.23)	5.3 (4.2)	11.1 (7.4)
t		6.13	6.62	3.05	6.06

For explanation of groups, see text. Figures indicate mean (SD). M = measured serum xylose; SA = surface area corrected serum xylose. Serum xylose is expressed as mmol/l, urine xylose as % of 5 g dose.

Table 4 Comparison of data from south India and from England

	n	5-h urine xylose (%)		1-h serum xylose (mmol/l)			
				Measured		Surface area corrected	
		Mean	SD	Mean	SD	Mean	SD
South India	49	28.2	9.1	—	—	—	—
Baker <i>et al.</i> ⁴							
This study	21	27.6	4.9	0.97	0.18	0.81	0.12
England							
Sammons <i>et al.</i> ¹³	29	35.7	7.1	—	—	—	—
Haeney <i>et al.</i> ³	130	35.0	9.2	1.03	0.21	0.94	0.18
t				1.22		3.18	

intestinal function (Table 3). While these observations are in agreement with those of Haeney *et al.*³ the range and mean value of the 1-hour surface area corrected serum xylose is significantly lower than that of a normal population in the UK (Table 4).

The mean measured 1-hour serum xylose concentration of our population was not significantly lower than that observed in the UK (Table 4), but, in general, body height and weight are less in southern India than in the UK, so that after correction to a constant surface area the mean serum concentration of control subjects was significantly lower ($P < 0.005$), indicating that the amount of xylose absorbed by our controls was less than that absorbed by subjects in the UK study. This is confirmed by the lower 5-hour urine xylose excretion in our subjects (Table 4). Non-specific tropical enteropathy is known to be widely prevalent in the asymptomatic population of southern India⁶ as in many other tropical developing countries. Non-specific tropical enteropathy is characterised by the occurrence of small bowel mucosal morphological abnormalities,⁵ which are detectable even at the ultrastructural level,¹⁴ low urinary xylose excretion,⁴ and reduced absorptive capacity of the jejunum in perfusion studies.^{8, 15} The significance of this 'lesion' is not known, but the available evidence suggests that non-specific tropical enteropathy may be the response of the small bowel mucosa to the environment, especially bacterial, viral, and parasitic agents, as well as dietary constituents that are as yet unidentified.⁶ Since all healthy southern Indian volunteers who have been biopsied so far show mucosal morphological evidence of non-specific tropical enteropathy, we conclude that the reduced absorption of D-xylose demonstrated here is a functional counterpart of the morphological lesion.

In 87 (78%) of the 111 subjects in whom urine and serum xylose levels were compared, the two tests were in concordance. In 19 subjects the 5-hour urine xylose was low but the 1-hour surface area corrected serum xylose was above 0.55 mmol/l. Careful analysis of these patients' records showed that, in 11 of them, incomplete bladder emptying at 5 hours, low urine volumes, or decreased clearance with old age were responsible for the discordant results. In a further two patients, the 5-hour urine xylose excretion was 11.4% and 13.5% with 1-hour surface area corrected serum concentrations of 0.89 and 0.71 mmol/l, respectively. For both patients, blood urea and serum creatinine values were at the upper limit of normal, and it is likely that their urine results reflect the sensitivity of the test to minimal impairment of renal clearance, as observed in the elderly.²³ One patient with 5-hour urine xylose of 19.8% and a serum level of 0.62 mmol/l

had ascites. In the remaining five of the 19 patients, no explanation for the apparently low urine results could be found, but incomplete urine collection, in spite of the supervision of the metabolic ward staff, is the most likely reason for these discordant results.

In five patients, the 5-hour urine xylose excretion was normal but the 1-hour surface area corrected serum xylose was less than 0.55 mmol/l. Three of them had borderline serum values (0.53 mmol/l), leaving two patients who appeared to have a genuine discrepancy between the serum and urine values.

The correlation coefficient of 0.67 indicates a highly significant correlation between the two methods of assessing xylose absorption ($P < 0.001$), which would have been better if the discordant results due to low urine values had been excluded. In view of the difficulties of obtaining accurate 5-hour urine collections, especially in the tropics and in field studies, it is recommended that the 1-hour serum xylose (surface area corrected) after 5 g oral D-xylose should be adopted as a routine test in the investigation of intestinal function. Further methodological studies are being undertaken to overcome, if possible, the need for a basal sample and the requirement of an automated system to achieve the required precision.

INR was in receipt of a special grant from the Wellcome Trust. The work of the Wellcome Research Unit is supported by the Wellcome Trust, London.

References

- Sladen GE, Kumar PJ. Is the xylose test still a worthwhile investigation? *Br Med J* 1973;3:223-5.
- Kendall MJ. The influence of age on the xylose absorption test. *Gut* 1970;11:498-501.
- Haeney MR, Culank LS, Montgomery RD, Sammons HG. Evaluation of xylose absorption as measured in blood and urine: a one-hour blood xylose screening test in malabsorption. *Gastroenterology* 1978;75:393-400.
- Baker SJ, Jacob R, Mathan VI. An evaluation of the 5 g D-xylose absorption test, with fractional urine collections in subjects living in southern India. *Indian J Med Res* 1971;59:1869-77.
- Baker SJ, Ignatius M, Mathan VI, Vaish SK, Chacko CC. Intestinal biopsy in tropical sprue. In: Wolstenholme GEW, Cameron MP, eds. *Intestinal biopsy*. London: Churchill, 1962;84.
- Baker SJ, Mathan VI. Tropical enteropathy and tropical sprue. *Am J Clin Nutr* 1972;25:1047-55.
- Baker SJ. Geographical variations in the morphology of the small intestinal mucosa in apparently healthy individuals. *Pathol Microbiol* 1973;39:222-37.
- Hellier MD, Radhakrishnan AN, Ganapathy V, Gammon A, Baker SJ. Intestinal absorption in normal Indian and English people. *Br Med J* 1976;1:186-8.
- Van De Kamer JH, Huinink Ten BH, Weyers HA. Rapid method for the determination of fat in faeces. *J Biol Chem* 1949;177:347-55.

- ¹⁰ Mathan VI, Swarnabai S, Baker SJ. Intestinal absorption of radioactive vitamin B12: a comparison of plasma, faecal and urinary tests. *Indian J Med Res* 1973;**61**: 714-23.
- ¹¹ Roe JH, Rice EW. A photometric method for the determination of free pentoses in animal tissues. *J Biol Chem* 1948;**173**:507-12.
- ¹² Goodhart JM, Kingston GR. Modification of the method for the estimation of xylose in urine. *J Clin Pathol* 1968;**22**:621-2.
- ¹³ Sammons HG, Morgan DB, Frazer AC, Montgomery RD, Philip WM, Phillips MJ. Modification of the xylose absorption test as an index of intestinal function. *Gut* 1967;**8**:348-53.
- ¹⁴ Mathan M, Mathan VI, Baker SJ. An electron-microscopic study of jejunal mucosal morphology in control subjects and in patients with tropical sprue in southern India. *Gastroenterology* 1975;**68**:17-32.
- ¹⁵ Hellier MD, Radhakrishnan AN, Ganapathy V, Mathan VI, Baker SJ. Intestinal perfusion studies in tropical sprue. *Gut* 1976;**17**:511-6.

Requests for reprints to: Dr VI Mathan, Wellcome Research Unit, Christian Medical College Hospital, Vellore 632 004, India.