THE XYLOSE TOLERANCE TEST AND RENAL FUNCTION IN THE TROPICS

HLA-YEE-YEE and M. MYA-TU*

Department of Physiology, Institute of Medicine 1 and *Department of
Medical Research, Rangoon, Burma.

INTRODUCTION

Employment of the 5gm and 25gm oral xylose tests assessment of intestinal absorption have revealed low excretions in a large percentage of persons in the tropics (Gardner and Perez-Santiago, 1965; Butterworth et al., 1959; Lindenbaum et al., 1966; Troncale et al., 1967; Aung-Than-Bátu et al., 1971). These values are also low when compared to Americans and Westerners resident in the tropics (Lindenbaum et al., 1966; Keusch et al., 1970) The low excretions in tropical peoples, taken at face value, would seem to point to a remarkably high incidence of malabsorption in the tropics. However, results of the xylose test do not always correlate well with other measures of intestinal absorption such as small intestinal biopsies (Russell et al., 1966) and fat absorption tests (Goldstein et al., 1970). However, adequate blood levels (Keusch et al., 1970; Aung-Than-Batu et al., 1971), seen in a large percentage of subjects having low excretions would rule out low absorption as a cause.

It would thus appear that apart from malabsorption low excretions may also be due to one or both of two possibilities: either (1) an increased uptake by the tissues and extracellular spaces or increased metabolism in the liver; or (2) a difference in the renal handling of xylose in the tropics. The maintained blood levels make the first explanation unlikely and the objective of the present work was to study the renal handling of xylose.

MATERIALS AND METHODS

Subjects and design: 28 normal adult Burmese male volunteers, 18-22 years of age, took the 5 gm oral xylose tolerance test (XTT). They were screened for renal and gastro-intestinal disorders by clinical history, clinical examination and routine urinanalysis. Taking 1 gm/5 hour urinary xylose excretion and 15 mg per cent as criteria, the subjects fell into four groups (1) those with low excretions associated with low plasma levels; (2) those with low plasma levels but having high excretion; (3) those with high plasma concentration and high urinary excretion; (4) those with low excretion despite high plasma levels (Table 1).

The first group apparently had poor absorption, as there was no rise in plasma concentration to the critical level. The second and third groups are seemingly normal, excretion being 20 per cent of oral dose and above. The fourth group was taken as the "TEST" group in further observations, as they exhibited low excretions despite high plasma levels. Glomerular filtration rates (GFR) were done on all subjects. Simultaneous xylose clearance and GFR were done to assess tubular reabsorption of xylose on 8 subjects of the "excretion deficient" group (group 4) and 9 subjects of the "normal" group who served as controls.

Xylose tolerance test: After 5 gm oral dose of xylose, a 5-hour pooled urine sample was collected using toluene as a preservative. Blood samples were taken at 0, 1/2, 1, 2

Table 1

The responses to the 5 gm oral xylose tolerance test in 28 normal subjects. The criteria are 15 mg per cent plasma concentration and 1 gm urinary excretion in 5 hours.

Plasma xylose	Urine xylose	No. of subjects	Percentage of subjects	Group
Low	low	10	35.7	Malabsorption
Low	high	7	25.0	Normal
High	high	2	7.1	Normal
High	low	9	32.1	Excretion deficient

and 5 hours, as a check of absorption. Deproteinisation of plasma was done by the method of Somogyi (1945). Urine specimens were diluted 1:100 prior to development of colour, in duplicate, by the method of Roe and Rice (1948). The ambient temperature during the tests was relatively constant (75°-76°F), with a relative humidity of 50 to 71 per cent.

Inulin clearance: No fasting was required, but food was withheld at least one hour before the commencement of the test. One litre of tap water was taken in the hour before the test and urine could be voided on inclination. Priming intravenous injections of inulin were given in amounts calculated, on the basis of their estimated volumes of distribution, to achieve plasma levels of 20 mg per cent. Infusion rates were calculated from the desired concentration and concentration of the infusing solution. Rates of delivery by the peristaltic pump (Sigma-12) were checked three times pre- and post- infusion, the maximum error allowed being 0.2 ml in 2 ml. A check was also made by marking the infusion bottles at varied intervals. Blood was drawn, after allowing one hour for infusion equilibrium to be established, at 60, 70, 80, 90 and if necessary, 100 minutes.

Inulin was measured by the method of Roe et al., (1949).

Plasma values differing by more than 6 per cent were taken as reflective of an unstable equilibrium, and so were not used in the calculation of inulin clearance.

Clearances were calculated by the formula $C_{In} = \frac{IV}{P}$, where C_{In} is the clearance of inulin in ml/min; I the concentration in mg per cent of infusing solution; V the volume in ml of solution infused per minute; P the concentration of inulin in mg per cent in plasma.

The mean GFR's are expressed corrected to 1.73 m^2 body surface area, using a nomogram prepared from the formula of Dubois and Dubois (1916).

Tubular reabsorption of xylose: Food was withheld one hour before the test, after a light breakfast. Blood and urine "blanks" were taken while the subjects took 1 litre of tap water over approximately 30 minutes. Priming dose of 30 ml of 10 per cent inulin and 20 ml of 20 per cent xylose were given over a period of 2-3 minutes, followed by a sustaining infusion of 70 ml of 10 per cent inulin and 10 ml of 10 per cent xylose in 420 ml of normal saline, given at a rate of 80 drops per minute. Urine samples were taken at 30, 50 and 70 minutes after completion of the priming dose and blood samples were taken at the midpoints.

Inulin in blood and urine were estimated by the method of Roe et al., (1949). Xylose concentrations were determined by the method of Roe and Rice (1948).

Clearances were calculated by the standard formula: $C = \dfrac{UV}{P}$, where C is the clearance in ml/min, U and P are the concentrations in mg per cent in urine and plasma, V is the volume of urine in ml excreted per minute.

Per cent reabsorption of xylose was calculated by the following formula used by Brodehl and Gellissen (1968) for assessment of per cent tubular reabsorption:-

$$\text{Per cent tubular reabsorption} = 100 \left(1 - \frac{C \text{ xylose}}{C \text{ inulin}}\right)$$

RESULTS

It may be seen from Table 1 that impaired xylose absorption was found in 35 per cent of the Burmese subjects tested, and there was decreased urinary excretion with normal blood levels in 32 per cent.

Table 2 shows the mean, S.D. and range of GFR for 21 subjects representing 3 types of responses to the XTT (the Malabsorption, Normal and Excretion deficient groups). The values were corrected for 1.73 m², Body Surface Area using the DuBois formula. Diffe-

rences between mean GFR's of those excreting normally and the low excretors was not significant (P > 0.05). Those in the "Malabsorption" group had a lower mean GFR, but not significantly less (P > 0.05) than those excreting normally.

Comparison of tubular reabsorption of xylose in the two groups of subjects (1) those excreting 1 gm and above and (2) those excreting below 1 gm in 5 hour urine is shown in Table 3. Fig. 1 shows the correlation between xylose excretion and tubular reabsorption. The mean tubular reabsorption of xylose for the "normal" excretors was 13.07 ± 12.6 per cent (range 0-35.6 per cent), where as that of the "excretion deficient" groups was 35.2 ± 25.6 per cent (range 0-59.3 per cent).

There was a negative correlation between xylose excretion and tubular reabsorption in 13 out of 17 subjects.

DISCUSSION

The mean GFR of the 23 subjects fell within the normal range quoted by Smith (1951) and Goldring and Chasis (1944). These results would confirm the findings of Kenney (1954), Keusch et al., (1970) and Aung-Than-Batu et al., (unpublished) that GFR in the tropics is not low. There was no significant difference between mean GFR's of the three

Table 2

Mean glomerular filtration rates in 21 subjects with different responses to the xylose test.

Group	No. of subjects	Glomerular filtration rate ml/min/1.73 m²	
		Mean ± S.D.	Range
Normal	8	136.3 ± 31.1	94.5-192.8
Excretion deficient	6	134.0 ± 30.2	96.2-166.3
Malabsorption	7	126.5 ± 26.9	93.3-178.9

Table 3

Mean tubular reabsorption in subjects with different responses to the xylose test.

Xylose test		No.	Tubular reabsorption of xylose (per cent)	
Plasma	Urine		Mean ± S.D.	Range
high	high			
low	high	9	13.07 ± 12.6	0-35.6
high	low	8	35.2 ± 25.6	0-59.3

groups. GFR and factors influencing GFR would appear not to be operative in causing low excretions of xylose.

As regards tubular factors, it may be seen that more efficient reabsorption is taking place in subjects with low excretion (Table 3, Fig. 1). Correlation between urinary excretion and tubular reabsorption is good in 13 out of 17 subjects, correlation being negative. Aung-Than-Batu et al., (unpublished) found, on repeat xylose tests, that though the majo-

rity of subjects had reproducible results, 25 per cent of subjects showed altered responses. "Inconsistency" in responses to the xylose test (25 gm) was also reported by Keusch et al., (1970). These four subjects could possibly be reflecting this variation in response to the XTT.

If glucose and xylose do indeed share a common transport mechanism as reported by Shannon and Smith (1935), Shannon and Fisher (1938) and Kleinzeller et al., (1967), less xylose would be excreted if less sugar is present in the glomerular filtrate, leaving the reabsorptive mechanism less saturated, and so able to reabsorb more xylose. If such is the case, then more xylose should be excreted in diabetics. Win-May (1972) reported fasting levels of 72.2 ± 14.95 mg per cent in 16 normal Burmese adult males (range 51.5 to 100 mg per cent). It should be considered, however, that Win-May used the method of Asatoor and King (1954) and not the Folin-Wu method (1920). The first method tends to give lower values by 20 to 30 per cent (Varley, 1963). Adadevoh et al., (1968) showed that blood sugar levels are lowered by a diet rich in pulses. Aung-Than-Batu et al., (to be published) found low excretions of xylose in 63 per cent of a sample size of 181 in two villages in Upper Burma. The people in this region depend mainly on pulses for protein. It cannot be ruled out if the resulting low glu-
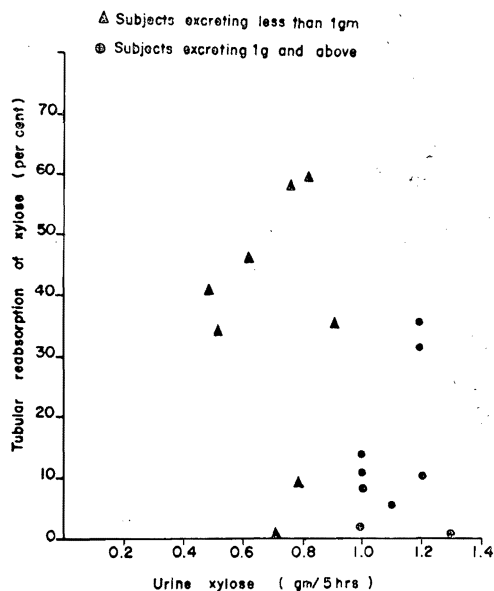

Fig. 1—Correlation between xylose excretion and tubular reabsorption in 17 subjects.

cose levels is leaving the common carrier system for glucose and xylose relatively unsaturated, which would cause increased reabsorption of xylose in those subjects.

The results therefore point toward increased tubular reabsorption as a cause of low excretions of xylose rather than low glomerular filtration rates. The mechanism of this increased reabsorption however, still needs to be clarified.

SUMMARY

Xylose tolerance test done on 28 Burmese males, 18 to 22 years of age, showed that 67.8 per cent (19 subjects) excreted less than 20 per cent of a 5 gm oral dose. Simultaneous clearances of inulin and xylose were done on 8 of the "low excretors" and all 9 of those excreting 20 per cent of dose and above the "normal" excretors. Glomerular filtration rate was assessed on 23 subjects, representatives of both groups, the mean being 128.3 ± 8.15 ml/min/1.73 m^2. Mean tubular reabsorption assessed from the xylose/inulin clearance ratio was 13.07 ± 12.6 per cent (range 0-35.6) for the "normal" excretors and 35.2 ± 25.6 per cent (range 0-59) for the "low" excretors. This suggests that different responses to the xylose tolerance test could be due to renal factors rather than reflective of intestinal factors alone.

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