THE D-XYLOSE EXCRETION TEST IN COELIAC DISEASE IN CHILDHOOD

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The value of the d-xylose test in the investigation of malabsorption in children has recently been discussed (Clark, 1962; Jones and di Sant' Agnese, 1963). Clark (1962) employed it in five untreated, and four treated, children suffering from coeliac disease, and Jones and di Sant' Agnese (1963) reported its use in two patients with coeliac disease before and after treatment. These authors regarded it as a valuable and simple test in the diagnosis of malabsorption in childhood.

We have used this test in the last two years in the diagnosis of malabsorption and coeliac disease and in the follow-up of patients in whom the diagnosis of coeliac disease had been established. The criteria used for the diagnosis of coeliac disease were those stated by Cameron, Astley, Hallowell, Rawson, Miller, French and Hubble (1962), viz. the clinical manifestations of the disorder, the presence of steatorrhoea and other evidence of malabsorption, the exclusion of other diseases causing steatorrhoea, a dilated small intestine by radiography, the demonstration of the coeliac change in the mucosa of the small intestine and remission of the disease on a gluten-free diet. In few of our 35 patients with coeliac disease reported here was one of these criteria absent, and in none of these patients was more than one of these criteria missing. The investigation and observation required are both laborious and lengthy, yet since the treatment is prolonged and imposes some difficulty on the patient and his mother it is important that the diagnosis should be accurately established. We have investigated the d-xylose test because it offered a reliable and simple test for malabsorption.

The absorption of simpler sugars is impaired in coeliac disease, and although the oral glucose tolerance test has been widely used as a test of carbohydrate malabsorption it has long been recognized to be unreliable. For some years the pentose, d-xylose, has been employed instead of

glucose, and the xylose levels in the blood or urine measured after an oral dose had been given. About 65% of the dose administered is absorbed and about 25% is excreted in the urine, the amount absorbed but not excreted being metabolized. Absorption occurs in the duodenum and proximal jejunum and is dependent on an intact intestinal mucosa, but not on any process of digestion. We have not thought it necessary to repeat here the large amount of physiological information concerning d-xylose which is adequately reviewed in all the papers quoted (Clark, 1962; Jones and di Sant' Agnese, 1963; Fourman, 1948; Benson, Culver, Ragland, Jones, Drummey and Bougas, 1957; Christiansen, Kirsner and Ablaza, 1959; Fowler and Cooke, 1960). It is of some interest to paediatricians that McCance and Madders in 1930 performed some of the earliest experimental work with d-xylose.

Methods

We have used the measurement of urinary excretion of xylose, after the method established by other authors (Fourman, 1948; Benson *et al.*, 1957; Christiansen *et al.*, 1959; Fowler and Cooke, 1960) in adults; the chief difference in our method being that we have used a fixed dose of 5 g. xylose. This was recommended to us by Dr. H. G. Sammons and has proved to be quite satisfactory. The patients were fasted for eight hours, the 5 g. xylose being given in 100 ml. water, and followed by a further 150 ml. water or in 50 ml. followed by 200 ml. water. Only occasionally has it been necessary in young children to administer the xylose by gastric tube. The bladder was emptied before the dose was given and urine collections started immediately afterwards and continued for five hours. The volume of urines excreted varied from 60 ml. to 485 ml., and the amount of xylose excreted in the smaller volumes proved that these were adequate for the test. In the younger children it was necessary to collect the urine in a plastic bag. The xylose content of the urine was then estimated by the method of Roe and Rice (1948). The results were expressed as a percentage of the administered dose.

The Subjects

The d-xylose excretion test was performed in 11 normal children who had either recovered from their illness in hospital or were not thought to have any disorder that would interfere with absorption or excretion. It was used as a diagnostic test in seven children later established to be suffering from coeliac disease. It was also used as a diagnostic test in five children suspected of suffering from malabsorption. In 28 children suffering from coeliac disease it was employed to assess the results of therapy.

Results

The results are set out in Tables 1, 2 and 3 and in the chart. In the Tables are given the child's age and sex, the average daily excretion of fat, the percentage of xylose excreted in the urine, the findings by small intestine radiography and the results of duodeno-jejunal biopsy. Table 1 lists the seven new cases in whom the diagnosis of coeliac disease was established. In Table 2 are the 28 patients with established coeliac disease who had been treated by a gluten-free diet for a varying

TABLE 1
NEW CASES

Case No.	Sex and Age (yrs.)	Average Daily Fat Excreted (g.)	Xylose Excreted (%)	X-ray Small Intestine	Biopsy
1	F 10	11.2	11	+++	—
2	M 1 $\frac{1}{2}$	4.4	10	+++	+++
3	F 1 $\frac{1}{2}$	7.4	10	+++	+++
4	F 1 $\frac{1}{2}$	4.0	6.9	+++	+++
5	F 3	11.0	24	+++	+++
34	F 1 $\frac{1}{2}$	4.1	9	+++	+++
36	F 1	4.7	4.5	—	+++

TABLE 2
TREATED CASES

Case No.	Sex and Age (yrs.)	Average Daily Fat Excreted (g.)	Xylose Excreted (%)	X-ray Small Intestine	Biopsy	Duration of Treatment
6	F 3	4.3	25.0	++	++	9 mths. gluten-free (not strict)
7	F 10 $\frac{1}{2}$	1.9	33.0	+	++	8 yrs. gluten-free
8	F 10	—	34.8	N	N	1 yr. gluten-containing
9	M 10 $\frac{3}{4}$	—	25.0	+	+++	2 yrs. gluten-free
10	M 12 $\frac{1}{2}$	2.1	42.0	N	N	3 yrs. gluten-containing
11	M 8	3.3	41.0	N	N	7 yrs. gluten-free
12	M 16	5.5	40.0	N	+	7 yrs. gluten-free
13	F 9 $\frac{1}{2}$	1.9	30.0	N	++	1 yr. gluten-containing
14	F 14	2.0	18.0	++	++	10 yrs. gluten-free (not strict)
15	F 12 $\frac{1}{2}$	4.2	44.5	++	++	4 yrs. gluten-free
16	M 15	5.2	28	+	++	2 yrs. gluten-containing
17	M 13	3.3	44	++	N	8 yrs. gluten-free
18	F 12	0.8	33	++	+++	2 yrs. gluten-containing
19	M 7	3.4	27.1	—	N	6 yrs. gluten-free
20	F 4	0.9	34	+	+	3 yrs. gluten-free
21	F 14 $\frac{9}{10}$	1.4	34.5	+	+	3 yrs. gluten-free
22	F 11 $\frac{1}{2}$	0.9	25.0	N	+	4 $\frac{1}{2}$ yrs. gluten-free
24	F 6 $\frac{6}{12}$	2.0	22.0	N	+	2 yrs. gluten-free
26	M 7 $\frac{1}{2}$	—	36.0	N	+	1 yr. gluten-free
27	F 10	1.9	31.0	+	+	2 yrs. gluten-free
29	F 6 $\frac{1}{2}$	1.9	26.9	++	+++	2 yrs. gluten-free (not strict)
30	M 15	0.8	31.0	++	+++	4 yrs. gluten-free (not strict)
31	F 4	1.9	30	++	++	5 yrs. gluten-free (not strict)
32	F 5	3.4	35.5	++	++	2 yrs. gluten-free (not strict)
33	M 11	4.8	12	+++	+++	2 yrs. gluten-containing
38	F 12	2.7	8	+++	+++	1 yr. gluten-free (not strict)
39	F 3	5.8	39	+	+	2 yrs. gluten-free (not strict)
41	M 12	—	26	+	++	3 yrs. gluten-free (not strict)
		9.1	22.2	+	N	2 yrs. gluten-free
		2.9	13.6	+	+	1 yr. gluten-free (not strict)
			15.0	+	+	3 yrs. gluten-free

+ Mild ++ Moderate +++ Severe N Normal

TABLE 3
NEW CASES SUSPECTED OF MALABSORPTION

Case No.	Sex and Age (yrs.)	Average Daily Fat Excreted (g.)	Xylose Excreted (%)	X-ray Small Intestine	Biopsy	Final Diagnosis
23	F 1 $\frac{0}{12}$	0.74	8.6	+	—	Cow's milk allergy
25	M 4 $\frac{5}{12}$	4.4	10.6	+	+	Giardiasis and ? coeliac disease
35	M 1 $\frac{10}{12}$	2.8	9.5	++	Non-specific jejunitis	Anaemia and non-specific jejunitis
37	M 3 $\frac{5}{12}$	1.8	26.5	N	Non-specific jejunitis	Giardiasis and non-specific jejunitis
40	M 7	2.6	12.6	—	—	Anaemia and giardiasis

length of time and with a varying degree of strictness in their adherence to the diet. In Table 3 are five new patients who were suspected of malabsorption but in whom the final diagnosis was not coeliac disease.

In the Figure these cases are analysed further in regard to the xylose excretion tests. In the first column are charted the results in normal hospital patients. These patients were not ill at the time of the test, nor were they suffering from renal disease or from malabsorption. In the second column are the seven patients suffering from untreated coeliac disease. In the third column are the 10 patients treated by a gluten-free diet in whom

either the histological appearance of the mucosa, or small intestine radiography, or both, were normal. In the fourth column are the 18 patients treated by a gluten-free diet in whom the mucosa and the radiographical appearances were abnormal. In the three patients in whom the test was repeated the results are joined by a line with an arrow pointing in the direction of the second test.

The lowest level for the percentage excretion in our normal hospital controls was 25%. In six of the seven new patients with coeliac disease, the amount of xylose excreted was less than 15% of the administered dose. In Case 5, a girl aged 3 years,

FIGURE—Results of xylose excretion tests.

the xylose excretion was 24% despite considerable steatorrhoea (average daily fat excretion 11 g.) and the presence of severe changes, both radiographical and histological in the small intestine (Figure, column 2). The treated patients are separated (columns 3 and 4) according to whether the biopsy or the radiographical appearances, or both, were *normal* (column 3, 10 patients) or whether both the biopsy and the radiographical appearances were *abnormal* (column 4, 18 patients). In the 28 patients under treatment by a gluten-free diet the excretion of xylose was 25% or over in 22. In two of the remaining six patients under treatment the excretion of xylose was 15% or below (Cases 31 and 39). Case 31 was a girl of 5 years in whom the xylose excretion was 8% and in whom the dietetic control was known to be inadequate, who had steatorrhoea (average daily excretion of fat 4.8 g. daily) and in whom both the radiographical and histological changes in the small intestine were graded as 'severe'. Case 39 was a girl aged 3 years in whom the xylose excretion was 14% and by whom the diet was not strictly kept. She had steatorrhoea with an average excretion of fat of 9.1 g. daily and the radiographical and histological changes were graded as 'mild'.

In four other patients under treatment the xylose excretion was between 15% and 25% (Cases 14, 24, 38 and 41). Case 14 had a xylose excretion of 18% and no steatorrhoea (average daily excretion of fat 2 g. daily). She was a girl aged 14 years who had been on a gluten-containing diet for three years following a period of eight years on a gluten-free diet. The histological and radiological changes were regarded as moderate. Her nutrition was excellent and absorption was considered to be normal despite the persistence of structural changes in the small intestine. Case 24 who had a xylose excretion of 22.0 was a girl aged 6½ years who had been on a gluten-free diet for only one year but who had no steatorrhoea (average daily fat excretion 2 g.). The radiographical appearances of the small intestine were normal and the histological changes were graded as 'mild'. With a further two years on a gluten-free diet the xylose excretion improved to 36%. Case 38 was a girl aged 12 years who had been on a gluten-free diet for two years. The xylose excretion was 22.2% and she was considered to be in full clinical remission. Her nutrition was excellent, the histological appearance of the small intestine was normal despite minimal radiographical evidence of dilatation. The fat excretion was not estimated but she gave a normal result to the folic acid absorption tests. Case 41 was a boy aged 12 years who had no steatorrhoea (daily fat excretion

2.9 g.). He had been on a strict gluten-free diet for three years and the changes both radiographically and histologically were regarded as minimal. The xylose excretion was 15%, but he was judged not to be suffering from malabsorption.

In summary then, of the five patients whose xylose excretion values lay between 15% and under 25%, two were thought to have malabsorption (Cases 5 and 24) and three were regarded as having normal absorption (Cases 14, 38 and 41). Of the 35 patients investigated then only five gave results which lay in this equivocal range.

Discussion

From the results recorded by other workers and from these reported here, it appears to be necessary to regard the range of between 15% and below 25% as one in which absorption may be normal or abnormal.

The lowest levels of excretion established for normal adults by other authors were 16% (Benson *et al.*, 1957), 22% (Christiansen *et al.*, 1959) and 19% (Fowler and Cooke, 1960). The lowest level of excretion in 36 normal children (we have excluded four children quoted who gave levels below 15% but who were recovering from illness) investigated by Clark (1962) was 15%, and Jones and di Sant' Agnese (1963) recorded the lowest level in 12 normal children as 24%. In our normal children the lowest level of excretion was 25%. The 15 patients recorded in column 4 with excretion rates above 25% in whom both the small intestine radiograph and the histological appearances of the mucosa were abnormal, demonstrates again that in treated patients (some of whom may be taking a varying amount of gluten in their diet) absorption of nutrients may be entirely adequate despite the persistence of structural disease (Cameron *et al.*, 1962).

Xylose urinary excretion is an excellent test for malabsorption in coeliac disease. It is useful not only in the initial diagnosis but also in the follow-up of treated patients. Like any other test of absorption it cannot be relied on to give an unequivocal answer in all patients, but in the present investigation this only occurred five times in 35 patients and in 38 tests. We regard it as both the simplest and the most reliable of all tests of absorption which we have used in coeliac disease in childhood.

It cannot, of course, be relied on by itself to make the diagnosis of coeliac disease. In Table 3 are recorded four patients in whom the excretion of xylose was abnormally low but in whom the final diagnosis was not coeliac disease. The diagnosis in these four patients does not include all known causes of malabsorption in childhood.

Summary

The use of the xylose excretion test in coeliac disease in childhood is reported, employing an oral test dose of 5 g.

Normal excretion of 25 % or above of the administered dose; values below 15 % indicate malabsorption; between 15 % and below 25 % the excretion values may, or may not, indicate malabsorption. This we regard as the equivocal range; in only five of our 35 patients did the results lie in this range.

The xylose excretion test is an excellent test of malabsorption in childhood; though coeliac disease is the commonest cause of malabsorption in childhood (fibrocystic disease of the pancreas excluded) a low urinary excretion of xylose does not establish this diagnosis.

The results reported have confirmed the known fact that it is common in treated coeliac disease for the patients to show normal absorption and excellent nutrition, despite the persistence of abnormal appearances in radiographs of the small intestine and of the coeliac change demonstrated histologically in the mucosa of the small intestine.

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