Reappraisal of the xylose test

Sir,

We read with interest the paper of Lamabadusuriya, Packer, and Harris (1975) and would like to make a few comments.

Firstly, we agree entirely with the authors that there is no fully satisfactory screening test for coeliac disease at present. However, neither is there a fully satisfactory diagnostic test, for not even the biopsy appearances are specific, especially in young infants (Rolles, Anderson, and McNeish, 1975). We also agree with them on the inadequacy of the 5- and 24-hour urine xylose test. It is perhaps unfortunate that they did not assess the simpler 2-hour urine xylose test, at least in their older patients, as this has been shown to be a more discriminating test (Sammons *et al.*, 1967; Kendall, 1970). Most other workers have used a fixed dose of xylose for the urine excretion test so comparisons are difficult, but even with a varying dose results of 5- and 24-hour xylose excretion as low as 0 and 1% are very difficult to explain.

With regard to the one-hour blood xylose test we were interested to see that Lamabadusuriya and his colleagues obtained results so nearly comparable to our own (Rolles *et al.*, 1973), in spite of their modifications. In fact they showed that nearly 85% of their patients with a flat biopsy had levels below the normal range—a fairly respectable percentage for any screening test.

Our paper discussing the use of the one-hour blood xylose test was specifically concerned with infants and young children, and none of our patients had ever been on a gluten-free diet. We did not present data from children over 30 kg in weight because our experience with such heavier 'new' coeliacs is limited, and what data we do have for the older children is inconsistent. Two of the five groups investigated by Lamabadusuriya *et al.* had a mean weight above 30 kg and some of their patients were well into the adult weight range at up to 60 kg. Also, some of the patients tested had returned to a normal diet after varying, but often long, periods on a gluten-free diet. Our experience with such children shows that there is considerable variation in the time taken for changes in xylose absorption and intestinal biopsy to occur. This may be attributed to the fact that many of the children remain on a low gluten diet out of unconscious preference because of past conditioning.

In our study we used a simple, single 5 g dose of D-xylose for every patient. In contrast, Lamabadusuriya and his colleagues used two dosage regimens. (1) Children weighing <18.75 kg received a dose dependent on weight (0.4g/kg). (2) Children weighing between 18.75 kg and 60 kg all received a dose of 7.5 g. From their data it is clear that well over half of their

patients received the fixed dose of 7.5 g of xylose, which is 50% greater than the dose we used. At least one of their patients received as little as 1.6 g xylose, which could make accurate estimation of urinary recovery very difficult. In fact, the only children in their study who were comparable to ours in terms of dose were those weighing exactly 12.5 kg.

In spite of the major differences in the dosage regimens used and the types of patients tested, several points of comparison emerge. The results shown by Lamabadusuriya *et al.* at one hour in control and remission coeliac patients were almost identical to our own results in these groups. This lack of relation to dose in such individuals may be explained by the fact that in the normal healthy mucosa xylose is absorbed by active transport and the early part of the blood curve is not closely dose-dependent. In contrast, in the untreated coeliac active transport may be impaired and passive diffusion may have a more important role. This would be more affected by total dose.

There are many factors that may affect one-hour blood xylose levels, and therefore in our paper we did not speculate on the reasons for the results we observed. We regret omitting to state that none of our patients were on drugs. We were unaware of any data in man indicating impairment of xylose absorption due to penicillin.

Of course no screening test is 100% reliable, otherwise it could become the 'definitive test', but we are sure that Lamabadusuriya and his colleagues would not disagree with our concluding comment that a *confirmed* low one-hour blood xylose result is *an* indication for small bowel biopsy. Although we agree that when there is clear clinical suspicion of coeliac disease an equivocal or, rarely, a normal one-hour blood xylose level should not deter one from proceeding to biopsy, we do not agree that biopsy should invariably be regarded as the first line of investigation. We hope to discuss the reasons for this comment in a future communication.

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We showed the letter by Dr. Rolles and his colleagues to Dr. Lamabadusuriya and his colleagues, who replied as follows:

The purpose of our article was to draw attention to the limitations of the xylose tolerance test as a screening procedure for coeliac disease in childhood, and we note that Dr. Rolles and colleagues agree with us that there are no fully satisfactory screening tests available at present. In the majority of children the diagnosis of coeliac disease is made before 5 years, an age when accurate timed collections of urine are notoriously difficult to obtain, even in a well-staffed ward. On the basis of our results for the 5- and 24-hour urinary xylose outputs we are of the opinion that the urinary xylose test should be abandoned in the paediatric population. We did not assess the value of the 2-hour urine xylose test, since we strongly suspected that this would also be indiscriminate. The loading dose of xylose in our study was determined according to body weight (0.4 g/kg up to a maximum of 7.5 g/kg) and was administered as an isomolar solution (3%), for the reasons discussed in our paper. Variation in total dose of administered xylose is an unlikely explanation for our finding that 2 children with newly diagnosed coeliac disease had normal 1-hour blood xylose levels, since they received 4 and 4.8 g of xylose as a loading dose.

The comments by Rolles and colleagues on the relation between xylose transport mechanisms, total dose of xylose, and 1-hour blood xylose levels may be a misinterpretation of the kinetics of xylose transport. Initial luminal disappearance rates of xylose from the proximal small intestine (and therefore 1-hour blood levels) are likely to be related more closely to the luminal concentrations of xylose rather than to the total dose administered, whether transport across the mucosa is by a process of passive diffusion or by an active carrier-mediated one. In our study all administered solutions contained the same concentration of xylose (3%) and, assuming an approximately similar degree of dilution of the oral load, xylose concentrations in the proximal small intestine would be anticipated to be similar; thus it is unlikely that the total dose of xylose would appreciably influence the 1-hour blood level.

Penicillin has been shown to inhibit D-xylose transport in rat intestine (Giorgi, 1970) and presumably would do so in the human, since the transporting mechanism is the same in both species.

It is now well established, of course, that the histological appearances of the jejunal mucosa in coeliac disease are not specific; specificity lies only in the temporal relation between dietary gluten withdrawal or reintroduction, and the associated mucosal changes. An unequivocal diagnosis of coeliac disease can only be made when such a specific relation has been shown by means

of sequential biopsies and a carefully controlled dietary intake of gluten.

We consider that Rolles and colleagues (1973) somewhat overstated their case for the 1-hour blood xylose test, e.g. '... a normal one-hour blood xylose test almost certainly excludes coeliac disease'. We should like to make the simple plea that a normal 1-hour blood xylose does not exclude coeliac disease.

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Diabetes mellitus after mumps vaccination

Sir,

There are many published reports indicating a temporal relationship between antecedent mumps infection and the development of diabetes mellitus (Harris, 1899; Patrick, 1924; Kremer, 1947; Hinden, 1962; McCrae, 1963; Messaritakis, *et al.*, 1971). Overt diabetes appeared in all reported cases within weeks after a natural infection with mumps virus. No case of diabetes mellitus has been reported after infection with an attenuated mumps virus as in the present case.

A 6½-year-old boy was admitted in May 1973 with a history of polydipsia, polyuria, and bed-wetting of 5 day's duration. One month before onset of symptoms the patient had received mumps vaccine (Mumpsvax). Physical examination on admission was unremarkable. Urine examination showed glycosuria (1 g/dl) and 1+ reaction for ketones. Blood sugar was 345 mg/dl. Serum and urine amylase were normal. He was soon stabilized on 5 units of lente insulin. He has been followed regularly and his diabetes persists 30 months later.

Family history was negative for diabetes, and in both parents an oral glucose tolerance test was normal.

The role of mumps infections in the development of diabetes mellitus was suggested a long time ago (Harris, 1899), and it has been the subject of considerable controversy. Because of well-known association of mumps with pancreatitis, it has been suggested that diabetes mellitus, following mumps infection, is the result of damage to the islet cells though in the majority of reported cases, as in ours, clinical or laboratory evidence of pancreatitis was lacking. Another possibility is that in our patient a latent state of diabetes was activated by the attenuated mumps virus contained in the vaccine.

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