

Lactose Intolerance in Childhood Coeliac Disease

Assessment of its Incidence and Importance

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There is dispute about the frequency and importance of disaccharide intolerance in childhood coeliac disease. Arthur and his co-workers (1966) considered that intolerance to disaccharides, especially lactose, was common, whereas Anderson and her colleagues (1966) thought that it occurred only rarely.

Arthur *et al.* recommended the routine exclusion from the diet of lactose and sucrose as well as gluten in the early months of treatment of all coeliac children, because they were unable to predict those children who would fail to improve after gluten withdrawal alone. Anderson *et al.* considered that the presence of raised quantities of sugars in the faeces was an essential factor in the diagnosis of disaccharide intolerance (Kerry and Anderson, 1964; Anderson *et al.*, 1966). Using this criterion, they found that children with coeliac disease were only rarely intolerant of lactose or sucrose. Furthermore, they questioned the diagnosis of coeliac disease in the case reported in detail by Arthur *et al.*, and suggested that the patient might have had a 'secondary disaccharidase deficiency', a separate condition that had been described previously (Burke, Kerry, and Anderson, 1965; Anderson, 1966).

Laws and Neale (1966) described the use of a lactose-barium sulphate mixture in screening for primary intestinal lactase deficiency with lactose intolerance. However, in a small series of adult patients with coeliac disease, they were unable to diagnose lactose intolerance by this technique (Laws, Spencer, and Neale, 1967).

The present study was designed to investigate the incidence and importance of lactose intolerance in children with coeliac disease using conventional parameters. At the same time we have assessed the worth of a modified lactose-barium examination in detecting secondary lactose intolerance.

Patients and Methods

Investigations were made on 24 children aged 4

months to 9 years (mean 2 years 4 months) because of persistent diarrhoea and failure to thrive. All had subtotal villous atrophy of the proximal jejunal mucosa. Supporting evidence of malabsorption in the upper small intestine was obtained by 5-day fat balances, D-xylose absorption studies, serum iron and folate levels, and Figlu excretion in varying combinations. Cystic fibrosis and chronic intestinal infections had been excluded.

Special Investigations

Radiological. The method of Laws and Neale (1966) was modified as follows. Each child had a barium meal and follow-through using liquid barium sulphate suspension (Micropaque*). The dose varied with the age of the patient: 30 ml. if under 1 year; 60 ml. if 1-3 years; 90 ml. if 4-7 years; 120 ml. if over 7 years. The barium suspension was given undiluted after an overnight fast, and supine films were taken at $\frac{1}{2}$, 1, and 2 hours.

Within a few days the investigation was repeated using the same quantity of barium suspension mixed with 1 g./kg. body weight of powdered lactose.

All films were reviewed by one of us (E.M.S.) without knowledge of the clinical or other findings. The following features were determined.

- (i) Dilatation of the small bowel: (a) subjective, (b) objective measurement (McCrae and Sweet, 1964).
- (ii) Rate of passage of the head of the barium meal.
- (iii) Blurring of small bowel loops, evidence of dilution of luminal contents.
- (iv) Coarsening of the small bowel mucosal pattern: absent, present, severe.

Lactose tolerance tests. Lactose, 2 g./kg., in a 10% aqueous solution was given orally, and capillary blood was taken half-hourly for 2½ hours. Total sugar and true glucose levels were measured in each specimen.

Assay of jejunal disaccharidases. Lactase, sucrase, and total maltase levels were determined by one of us (A.S. McN.) using the method of Dalqvist (1964). Normal values are shown in Table I.

Faecal pH. This was determined by narrow range indicator papers.

* Damancy.

TABLE I
Range (and Means) of Jejunal Disaccharidases*

Patients	Lactase	Sucrase	Maltase
24 patients in study ..	0-1.76 (0.75)	0.12-4.02 (1.82)	3.33-17.04 (6.99)
45 untreated coeliac children studied previously ..	0-1.85 (0.62)	0.11-4.07 (1.74)	1.48-17.04 (6.68)
20 normal children ..	2.30-8.10 (4.75)	3.70-11.60 (6.48)	12.67-35.56 (19.93)

* Units = number of micromoles of substrate split per minute per g. wet weight mucosa at 37° C.

Faecal sugars. The bedside method of Kerry and Anderson (1964) was used. This depends on the reduction of Clintest tablets under standard conditions.

Results

Radiological

(a) *Barium meal.* 21 of the 24 patients showed dilatation of the small intestine subjectively and by direct measurement. In the remaining 3 subjects dilatation was marginal. 7 had slight blurring of intestinal contents in addition. 19 showed coarsening of mucosal folds. The transit time to the colon was 2 hours or more in 15 children, and was between 1 and 2 hours in the others.

(b) *Lactose-barium meal.* 5 patterns were seen (Table II). The commonest was a slowing of the rate of passage through the small intestine, often associated with delayed gastric emptying. Some

TABLE II
Radiological Features of Lactose-barium Meal Compared to Standard Barium Meal

Lactose-barium Compared to Standard Barium	No. of Cases
No change	3
Small bowel transit time increased ± delayed gastric emptying	6
Small bowel transit time increased + blurring and dilution of bowel contents	10
Small bowel transit time reduced; blurring, dilution, and dilatation absent	1
Small bowel transit time reduced; blurring, dilution, and dilatation present—may be marked	4

blurring of intestinal loops was also common in this group. In 4 patients the triad was found of increased speed of passage, blurring, and dilution, and an increase in dilatation of the bowel. These findings correlated with clinical lactose intolerance, and the relevant patients are described below and in Tables III and IV.

Lactose tolerance tests. The maximum rise in blood glucose was 0-9 mg./100 ml. in 15 cases, 10-19 mg./100 ml. in 7, 20-29 mg./100 ml. in 1, and over 30 mg./100 ml. in only 1 child (actual rise 33 mg.).

Jejunal disaccharidases. These are summarized in Table I. The results in all cases fell within the range previously seen in untreated coeliac disease (McNeish, 1968).

Further progress. The 20 children with

TABLE
Summary of 4 Patients

Case No., Sex, and Age (yr.)	Height (H) and Weight (W) Centile	Symptoms and Duration	Jejunal Biopsy	Fat Balance (FB) or Faecal Fat (FF)
1 F 5/12	H3 W<3	Cereals introduced at 8 wk.; diarrhoea began 2 wk. later and persisted	SVA*	FB 78%
2 M 2 11/12	10<H<25	Diarrhoea from 3 mth.; recurring abdominal distension	SVA	FB 87%
3 F 1 8/12	H<3 W<3	Pale stools and poor weight gain for 9 mth.	SVA	—
4 F 1 3/12	H3 3<W<10	Pale frequent foul stools for 3 mth.	SVA	FF 4.5 g. daily

* SVA, Subtotal villous atrophy.

lactose-barium appearances of groups 1-4 in Table II were given a standard gluten-free diet with polyvitamin supplements. 19 showed a rapid response, with loss of diarrhoea and a gain in weight within 1 to 3 weeks. One child failed to gain weight within 3 weeks, so that lactose was withdrawn from the diet in addition. No improvement resulted in the next month and therefore the sugar was reintroduced. Over the next 3 months he responded slowly to continued gluten withdrawal, and now, 6 months later, he is progressing well.

The 4 children considered to have radiological evidence of lactose intolerance are considered separately (Tables III and IV).

Case 1 had a stool pH of 5.5: no reducing substances were detected in the faeces with Clinitest tablets (Kerry and Anderson, 1964). She was given a lactose-free gluten-containing diet. Within 3 days the diarrhoea had subsided and she gained 1.8 kg. in the first 6 weeks of treatment.

Case 2 fulfilled all modern criteria for coeliac disease except that he gained only 0.2 kg. in weight during the first month of gluten withdrawal, and his stools remained loose (pH 6-6.5, Clinitest negative). After withdrawal of lactose, there was improvement in the consistency of his stools, and he gained 1 kg. in the next month.

Cases 3 and 4 were clinically cases of coeliac disease whose weight responded well to a gluten-free diet, but the stools remained loose and frequent for 4 months and 6 months, respectively. Lactose withdrawal was not attempted.

Discussion

The present evidence suggests that lactose

TABLE IV
Progress after Treatment of 4 Patients with Lactose Intolerance

Case No.	Progress
1	Lactose-free, gluten-containing diet: diarrhoea stopped in 3 dy.; weight on 25th centile in 6 wk.; partial regeneration of jejunal mucosa in 5 mth.
2	Gluten-free diet for 6 wk.; no weight gain, persistent diarrhoea; lactose- and gluten-free diet; loss of diarrhoea in 1 wk.; weight on 25th centile in 6 wk.
3	Gluten-free diet: weight >3rd <10th centile in 1 mth.; loose stools continued for 4 mth.
4	Gluten-free diet: weight >50th centile in 6 mth.; loose stools for 6 mth. and folic acid deficiency recurred

intolerance is not common in coeliac disease. Of the 24 children studied, 20 (83%) had no sugar intolerance and 2 (8.5%) had only mild symptoms attributable to sugar. Lactose intolerance of a major degree was found in only 2 children (8.5%). Of these, one probably does not have gluten-induced coeliac disease (see below).

The maximum rise in blood glucose after an oral lactose tolerance test failed to separate the affected children from the group. 22 of the 24 children had a maximum rise of less than 20 mg/100 ml.: this is a non-specific finding characteristic of several malabsorptive states, but also found in normal subjects (Newcomer and McGill, 1966).

The faecal pH was measured in 16 children, and was less than 6.5 in both children with major lactose intolerance, but was between 6.5 and 8 in affected children without symptoms attributable to sugar

Table III
with Lactose Intolerance

5-hour D-Xylose Excretion	Barium Meal	Lactose-barium Meal	Lactose Tolerance Test: Maximum Rise of Blood Glucose (mg. 100 ml.)	Faecal pH	Jejunal Lactase (units)
-	Moderate dilatation; coarse mucosal pattern; transit to colon 4 hr.	Marked dilatation; marked dilution; transit to colon >1 <2 hr.	0	5-6	0.54
-	Moderate dilatation; coarse mucosal pattern; transit to colon 2 hr.	Moderate dilatation; marked dilution; transit to colon 1 hr.	9	6	0.20
10%	Moderate dilatation; coarse mucosal pattern; 2 hr. to colon	Marked dilatation; marked dilution; 1 hr. to colon	8	6	1.62
-	Moderate dilatation; coarse mucosal pattern; 4 hr. to colon	Marked dilatation; marked dilution; >1 <2 hr. to colon	10	-	0.93

Arch Dis Child first published online 10.1136/adc.2019.119.1191

This confirms the value of this simple test in screening for fermentative diarrhoea. However, reducing substances were not detected in the faeces of any patients, using Clinitest tablets (Kerry and Anderson, 1964); sugar chromatography of the faeces was not performed.

The levels of jejunal disaccharidases were a reflection of the degree of villous atrophy (A. S. McNeish, unpublished observations), and confirm that general reduction in activity of these enzymes is a feature of coeliac disease (Plotkin and Isselbacher, 1964; Shmerling *et al.*, 1964). No separation of the patients with lactose intolerance was apparent. This emphasizes the limited value of disaccharidase assay in a few milligrams of tissue for predicting the ability of the whole small intestine to handle sugar.

The use of a disaccharide-barium sulphate meal has been recommended by Laws and Neale (1966) as a method for detecting primary disaccharidase deficiency with disaccharide intolerance. The combination of dilution of intestinal contents, dilatation of the bowel, and intestinal hurry suggests the diagnosis. These workers were uncertain of the ability of the method to detect secondary disaccharidase deficiency with fermentative diarrhoea: in their study of 3 adults with idiopathic steatorrhoea, no clear-cut radiological pattern emerged (Laws *et al.*, 1967).

The present investigation has indicated that a modification of the radiological method can show secondary disaccharide intolerance in childhood coeliac disease. The diagnostic appearances may be sufficiently obvious after a lactose-barium meal to make it unnecessary to compare these with a conventional barium meal. The triad of blurring of intestinal contents, rapid passage of the sugar-barium mixture, and dilatation of the small bowel must all be seen. It has not been found possible to estimate accurately the severity of disaccharide intolerance by this method alone.

The commonest lactose-barium finding in uncomplicated coeliac disease was a delay in passage of the meal, usually associated with delayed gastric emptying. The reason for this is not clear; Matsui (1959) made the interesting observation that the rate at which ingested lactose emptied from the stomach of infants was dependent on the rate at which the disaccharide was hydrolysed in the small intestine.

The value of the conventional barium follow-through examination in detecting childhood coeliac disease has been confirmed (McCrae and Sweet, 1964). If this examination is normal, or shows only slight dilatation of the small intestine, and if the lactose-barium appearances suggest sugar intolerance, then a 'secondary disaccharidase

deficiency' should be considered, of the type found in Australia by Anderson and colleagues (Burke *et al.*, 1965). They described a group of infants who developed a coeliac syndrome following presumed infective enteritis. Duodenal biopsy showed subtotal villous atrophy, and the mucosal disaccharidases were much reduced. Each child responded well to lactose withdrawal, gluten appeared to play no part in the pathogenesis, and there was a tendency towards spontaneous recovery.

Case 1 (Table III) fits this pattern exactly. Steatorrhoea in no way invalidates the diagnosis, because though this symptom was not included in the original description of the syndrome (Burke *et al.*, 1965), it has since been confirmed (Anderson, 1966).

Cases 2, 3, and 4 (Table III) have classical gluten-sensitive enteropathies, with lactose intolerance of varying degrees in addition. Case 2, the only patient to have severe lactose intolerance, was reinvestigated after 9 months on a diet free of gluten and lactose. Considerable regeneration of the jejunal mucosa was found, with the disaccharidase levels in the low normal range. Lactose was reintroduced into the diet without incident.

Summary

Twenty-four children with coeliac disease were investigated for evidence of lactose intolerance, using (a) a modification of the lactose-barium meal technique of Laws and Neale (1966), (b) an oral lactose tolerance test, (c) assay of jejunal disaccharidases, and (d) faecal pH and sugar content.

The following correlated well with clinical evidence of lactose intolerance: (i) lactose-barium radiological appearances of intestinal hurry, dilution of luminal contents, and dilatation of the small bowel, and (ii) a faecal pH of 6 or less. The other investigations failed to separate the patients with lactose intolerance from the group.

Of the 24 children, 20 (83%) had no evidence of lactose intolerance and thrived normally on a gluten-free diet. Two children had only minor symptoms attributable to lactose, and only 2 (8.5%) required a lactose-free diet before showing satisfactory weight gain. Of these, one was an infant of 5 months who thrived well on a lactose-free diet containing gluten. She was probably a case of 'secondary disaccharidase deficiency with symptoms', of presumed infective origin.

It is concluded that lactose intolerance is not common in childhood coeliac disease, and that it may be detected radiologically. If the diagnosis is suspected in a young infant, lactose intolerance without gluten sensitivity should be considered.

It is a pleasure to thank Dr. R. A. Shanks for encouragement and criticism, Professor J. H. Hutchison for permission to study patients in his care, Dr. S. P. Rawson for radiological facilities and advice, and Professor H. G. Morgan and Dr. R. Logan for facilities in the laboratory.

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