Transient lactose intolerance in infancy

ROGER W. BARTROP and DAVID HULL

From The Hospital for Sick Children, Great Ormond Street, London

Bartrop, R. W., and Hull, D. (1973). *Archives of Disease in Childhood*, 48, 963.
Transient lactose intolerance in infancy. The clinical details of 100 infants with disaccharide intolerance secondary to a variety of bowel disorders were examined. Malnourished infants under 6 months of age were particularly at risk.

The difficulty of establishing the relevance of sugar intolerance is emphasized.

The analysis suggested that infants with troublesome, persistent diarrhoea under the age of 6 months, particularly those underweight, should be treated with a lactose-free diet, but that lactose might be introduced once the child is thriving and stools have returned to normal consistency.

It has been known for many years that some infants are unable to tolerate milk for a variable period after a bowel disorder. Only recently has it been appreciated that one major factor contributing to this milk intolerance is a limitation in handling lactose, the disaccharide in milk, and that removal of this sugar greatly improves the rate of recovery. Transient lactose intolerance may follow gastroenteritis (Clarke, Quillian, and Shwachman, 1964; Burke, Kerry, and Anderson, 1965; Lloyd-Still, 1969), neonatal surgery (Howat and Aaronson, 1971), various forms of malnutrition (Kerpel-Fronius, Jani, and Fekete, 1966; Prinsloo *et al.*, 1971; James, 1970), gluten enteropathy (Arthur *et al.*, 1966; Townley, 1966; Lubos, Gerrard, and Buchan, 1967), cystic fibrosis (Gibbons, 1969), and immune deficiency disorders (Dubois *et al.*, 1970). However, it is difficult to assess the frequency and importance of this complication for the disturbance ranges from trivial episodes of brief duration to severe life-threatening conditions which may last for many months.

The diagnosis is most firmly based on clinical observation. Clinical improvement after removal of lactose from the diet suggests the diagnosis: the return of diarrhoea with reintroduction of lactose confirms it. A number of investigations have been proposed to assist in diagnosis, but their relevance is often difficult to interpret. The simplest technique, introduced by Kerry and Anderson (1964) and Anderson *et al.* (1966), is the measurement of the sugar content and acidity of the stool. However, a number of children with acute diarrhoea may have

an excess amount of sugar in their stool with accompanying acidity and yet they may still be able to tolerate lactose. Clarke *et al.* (1964) described measurement of lactic acid content of the stool. Lactic acid concentration, like stool sugar content and pH, changes very rapidly in a fresh specimen due to exogenous bacterial fermentation, and therefore immediate analysis is essential. Excess lactose in the urine is another valuable test, but it does not specifically indicate a deficiency of lactose digestion. Lactose loads have also been used as diagnostic criteria, but patients with poor lactose absorbing power as judged by a lactose load do not necessarily suffer from sugar intolerance (Prinsloo *et al.*, 1971). On the other hand, lactose loads may well present an abnormal challenge to an infant with a bowel disorder, especially to an infant who has been on a lactose-free diet for some time (Lubos *et al.*, 1967; Lloyd-Still, 1969).

Duodenal biopsy to establish the diagnosis is rarely justified, but even here the finding of low disaccharidase activity does not necessarily indicate an inability to tolerate lactose (Lubos *et al.*, 1967; McMichael, Webb, and Dawson, 1965, 1966). Normally, infants have high lactase levels, but the levels usually fall after weaning except in communities where milk remains a common dietary constituent (Bolin *et al.*, 1970; Fung and Kho, 1971; Kretchmer *et al.*, 1971). In some adults alactasia is symptomless unless they are given an excessive lactose load.

The clinical symptoms of lactose intolerance reflect not only the activity of the disaccharidase in the mucosal lining of the small bowel, but also the compensatory capacity of the large bowel to handle

an excess of osmotic load due to deficient lactose breakdown.

In view of the difficulty of establishing the diagnosis beyond doubt, it is tempting to treat all infants with persistent troublesome diarrhoea with a lactose-free diet. The question then arises of when disaccharide should be introduced. This paper reports an analysis of the clinical course of 100 infants with a variety of bowel disorders complicated with disaccharide intolerance. In retrospect it seems that the infants might have tolerated disaccharide sooner. It seems justified to reintroduce lactose once the infant has begun to gain in weight and the stools return to normal.

Material

Between January 1962 and October 1971 over 200 infants at this hospital were diagnosed as suffering from secondary lactose intolerance. The clinical details of the first 100 infants who fulfilled the following criteria were analysed.

(a) The child suffered from diarrhoea which improved when lactose was removed from the diet.

(b) Before introduction of the diet, one or more of the following was shown. (i) Excess lactose in stool. (ii) Excess lactose in urine. The demonstration of specific sugars in amounts greater than the normal values of 10 mg/100 ml in the stool, or 15 mg/100 ml in the urine, or both, by chromatography (Menzies and Seakins, 1969). (iii) Abnormal response to lactose load, i.e. a lactose feed which produced a clinical and biochemical disturbance. (iv) Severe disaccharidase deficiency in a specimen obtained at duodenal biopsy.

It is appreciated that some infants would be recovering spontaneously at the time a lactose-free diet was introduced and that the presence of one of the secondary criteria, though suggestive, does not confirm the diagnosis beyond doubt.

Results

Primary diagnoses are shown in Table I.

Infants were considered to have infective diarrhoea if there was a history of contact with somebody suffering from gastroenteritis, or if *Esch. coli* of the known pathogenic serotypes were cultured

TABLE I
Primary diagnoses in 100 infants with lactose intolerance

Infective diarrhoea	29
Nonspecific diarrhoea	22
Bowel surgery	7
Gluten enteropathy	20
Cystic fibrosis	2
Miscellaneous	20
Total	100

from the stool. The commonest diagnoses in those children subject to bowel surgery were Hirschsprung's disease and the bowel atresias. Lactose intolerance was a rare complication of cystic fibrosis and coeliac disease. The diagnosis in the miscellaneous group included acrodermatitis enteropathica and hiatus hernia; and it was also associated with Gram-negative septicaemia and urinary tract infections. Occasionally intolerance was found when there was no evidence either from the clinical history or pathological findings of an underlying bowel disorder.

The age at diagnosis is shown in Fig. 1. The majority of infants who showed features of lactose intolerance were below the age of 3 months. The body weights at the time of diagnosis were often below the third centile, suggesting that malnutrition

FIG. 1.—Number of children with lactose intolerance in various age groups.

is an adverse factor. The distribution for male infants is shown in Fig. 2. The data for female infants were similar.

The time at which the lactose-containing diet was reintroduced with success is shown in Table II. On average, infants were maintained on a disaccharide-free diet for over 40 weeks! However, reintroduction after 2 months was successful in 20 out of 22 children in whom it was attempted. The infants given sugar-free diets for over one year usually suffered from gluten enteropathy.

Successful reintroduction of cow's milk occurred in 83 children, the diet being continued at follow-up in 8 others. 4 children died from the primary pathology.

Five children (4 with infective and nonspecific diarrhoea, 1 with gluten enteropathy) had periods of

FIG. 2.—Body weights of boys found to have lactose intolerance.

TABLE II

Time of successful reintroduction of lactose

Duration of diet (wk)	No. of children	Reintroduction failures
0-4	10	1
5-8	12	1
9-12	9	1
13-26	19	3
27-52	11	3
53+	26	5
Not known	4	
Total	91	14

Note: 5 infants with lactose intolerance were not placed on a lactose-free diet. 4 infants died of the primary diagnosis while on a lactose-free diet.

bowel rest from several days to 2 weeks, followed by the gradual reintroduction of milk feeds containing disaccharide, despite the fact that in every case at least two criteria for disaccharide intolerance were satisfied. No deaths occurred during this regimen.

Discussion

The diagnosis of secondary lactose intolerance is difficult. The commonest primary disorder in which this diagnosis was made in our hospital was gastroenteritis. However, it is reasonable to question whether the finding of an acid stool or excess lactose in the stool or urine of a child with explosive diarrhoea constitutes grounds for diagnosis

of lactose intolerance. It is equally difficult to interpret the finding of increased stool frequency with lactose excesses in the stool or urine in an infant who has been given lactose after a period on a lactose-free diet, so confirmation of a presumed diagnosis is also difficult.

In view of this, it seems reasonable to treat all malnourished infants under the age of 6 months, suffering with persistent diarrhoea, with a lactose-free diet. However, there is little evidence to justify maintaining them on a lactose-free diet for prolonged periods. The fact that 3 out of 4 infants in the present series tolerated lactose when it was introduced 2 months after the illness suggests reintroducing lactose once the child has begun to thrive and the stools have returned to normal consistency. Only if the diarrhoea returns with the introduction of lactose should a diet be maintained for a 3-month period or more before introduction of lactose is again attempted.

In older children with diarrhoea, transient lactose intolerance is relatively rare, and making a specific diagnosis in this group by assessing the response to a lactose load before placing the child on a special diet seems reasonable. It is interesting that many children with gluten enteropathy with grossly abnormal changes in the mucosa as shown by duodenal biopsy are still able to tolerate lactose. This must reflect the ability of their large bowel to compensate for the increased lactose load.

We thank Miss P. M. Corns, Mrs. V. Scott, and Miss N. Marshall in the Medical Records Department, The Hospital for Sick Children, for their tireless assistance; Mrs. G. Rainsforth and her staff in the Computer Department for their collation of the data and many helpful suggestions.

REFERENCES

- Anderson, C. M., Burke, V., Messer, M., and Kerry, K. R. (1966). Sugar intolerance and coeliac disease. *Lancet*, **1**, 1322.
- Arthur, A. B., Clayton, B. E., Cottom, D. G., Seakins, J. W. T., and Platt, J. W. (1966). Importance of disaccharide intolerance in the treatment of coeliac disease. *Lancet*, **1**, 172.
- Bolin, T. D., Davis, A. E., Seah, C. S., Chua, K. L., Yong, V., Kho, K. M., Siok, C. L., and Jacob, E. (1970). Lactose intolerance in Singapore. *Gastroenterology*, **59**, 76.
- Burke, V., Kerry, K. R., and Anderson, C. M. (1965). The relationship of dietary lactose to refractory diarrhoea in infancy. *Australian Paediatric Journal*, **1**, 147.
- Clarke, J. T., Quillian, W., and Shwachman, H. (1964). Chronic diarrhoea and failure to thrive due to intestinal disaccharidase insufficiency. *Pediatrics*, **34**, 807.
- Dubois, R. S., Roy, C. C., Fulginiti, V. A., Merrill, D. A., and Murray, R. L. (1970). Disaccharidase deficiency in children with immunologic defects. *Journal of Pediatrics*, **76**, 377.
- Fung, W.-P., and Kho, K. M. (1971). Importance of milk intolerance in patients presenting with chronic (nervous) diarrhoea. *Australian and New Zealand Journal of Medicine*, **1**, 374.
- Gibbons, I. S. E. (1969). Disaccharides and cystic fibrosis of the pancreas. *Archives of Disease in Childhood*, **44**, 63.
- Howat, J. M., and Aaronson, I. (1971). Sugar intolerance in neonatal surgery. *Journal of Pediatric Surgery*, **6**, 719.

- Kerpel-Fronius, E., Jani, L., and Fekete, M. (1966). Disaccharide malabsorption in different types of malnutrition. *Annales Paediatrici*, **206**, 245.
- Kerry, K. R., and Anderson, C. M. (1964). A ward test for sugar in faeces. *Lancet*, **1**, 981.
- Kretchmer, N., Ransome-Kuti, O., Hurwitz, R., Dungy, C., and Alakija, W. (1971). Intestinal absorption of lactose in Nigerian ethnic groups. *Lancet*, **2**, 392.
- James, W. P. T. (1970). Sugar absorption and intestinal mobility in children when malnourished and after treatment. *Clinical Science*, **39**, 305.
- Lloyd-Still, J. (1969). Gastroenteritis with secondary disaccharide intolerance. *Acta Paediatrica Scandinavica*, **58**, 147.
- Lubos, M. C., Gerrard, J. W., and Buchan, D. J. (1967). Disaccharidase activities in milk-sensitive and celiac patients. *Journal of Pediatrics*, **70**, 325.
- McMichael, H. B., Webb, J., and Dawson, A. M. (1965). Lactose deficiency in adults. A cause of 'functional' diarrhoea. *Lancet*, **1**, 717.
- McMichael, H. B., Webb, J., and Dawson, A. M. (1966). Jejunal disaccharidases and some observations on the cause of lactase deficiency. *British Medical Journal*, **2**, 1037.
- Menzies, I. S., and Seakins, J. W. T. (1969). Sugars and related compounds. In *Chromatographic and Electrophoretic Techniques*, 3rd ed., Vol. 1, p. 310. Ed. by J. Smith. Heinemann, London.
- Prinsloo, J. G., Wittman, W., Kruger, H., and Freier, E. (1971). Lactose absorption and mucosal disaccharidases in convalescent pellagra and kwashiorkor children. *Archives of Disease in Childhood*, **46**, 474.
- Townley, R. R. W. (1966). Disaccharidase deficiency in infancy and childhood. *Pediatrics*, **38**, 127.

Correspondence to Professor D. Hull, Department of Child Health, City Hospital, Hucknall Road, Nottingham NG5 1PB.

The following articles will appear in future issues of this journal:

- Diagnosis and clinical significance of parainfluenza virus infections in children. *M. A. P. S. Downham, J. McQuillin, and P. S. Gardner.*
- Open lung biopsy in children with diffuse lung disease. *C. J. Hewitt, D. Hull, and J. W. Keeling.*
- Minimizing systemic infection during complete parenteral alimentation of small infants. *R. Nelson.*
- Technetium-99m pertechnetate imaging in diagnosis of Meckel's diverticulum. *J. C. Leonidas and D. R. Germann.*
- Congenital heart disease in Nigeria: clinical and necropsy study of 260 cases. *A. U. Antia.*
- A possible cause of glandular hypospadias in man. *D. R. Abramovich.*
- Bilateral renal vena thrombosis: recovery after peritoneal dialysis. *R. Counahan.*