Intestinal lactase, sucrase and alkaline phosphatase in relation to age, sex and site of intestinal biopsy in 477 Irish subjects

R KEANE, J G O'GRADY, J SHEIL, F M STEVENS, B EGAN-MITCHELL, B McNICHOLL, C F McCARTHY, P F FOTTRELL

From the Departments of Biochemistry and Mathematics, University College, Galway and University Departments of Medicine and Paediatrics, Regional Hospital Galway, Ireland

SUMMARY Small intestinal lactase, sucrase and alkaline phosphatase activities were measured in histologically normal peroral intestinal biopsies from 477 individuals. Enzyme activities varied with age, sex, site of biopsy, and were lowest in post-weaning children and highest in young adults. Lactase activity does not decrease with advancing age.

Measurement of small intestinal brush border enzymes has been used in the investigation of a wide range of diseases. Apart from primary enzyme deficiencies, abnormalities have been reported in a variety of diseases including coeliac disease, ¹⁻³ giardiasis,⁴ viral infections,¹ amoebiasis,¹ Whipple's disease,¹ ulcerative colitis,⁵ Crohn's disease,⁵ pernicious anaemia,⁶ psoriatic enteropathy⁷ and protracted diarrhoea and malnutrition in infancy.⁸ The interpretation of enzyme activities in disease is dependent upon the availability of control data where the influence of factors such as race, age, sex, and site of biopsy of the intestinal mucosa are considered.

This paper presents the results of alkaline phosphatase, sucrase and lactase measurements from 477 Irish persons with normal intestinal morphology. Particular emphasis is given to enzyme differences due to age, sex, and site of intestinal biopsy. This study is, to our knowledge, the largest sample of white persons investigated in this way and affords an interesting comparison with a previous large study of North Americans that included white, black and native American Indians.¹³

Material and methods

A total of 477 subjects (256 male, 221 female) were studied. All biopsies were carried out in the course of appropriate medical investigation. Informed consent for biopsy was obtained in all cases. The patients included in this study were all judged to have normal mucosal histology—that is, grade 0 of grades 0–3 as previously described by McNicholl and Egan.⁹ None of the patients suffered from diseases known to be associated with intestinal abnormality.

Accepted for publication 30 June 1982.

The biopsy was obtained either from the duodenal bulb at endoscopy or by using the Watson or Crosby capsules under fluoroscopic control. Two biopsies were taken at endoscopy while material obtained with the capsule was divided into two pieces. One of these was wrapped in dry wax film and frozen until enzyme assay was carried out. The second piece was examined by dissecting and light microscopy studies.

The portion of mucosa used for enzyme assay was homogenised in distilled water ($200 \mu l/mg$ of biopsy) for two minutes at 200–300 rpm in a micro Potter Elvehjem homogeniser. After homogenisation an aliquot ($50 \mu l$) was diluted 1/5 with distilled water and all assays were carried out on the diluted and on the undiluted homogenate. Protein was measured by the method of Lowry *et al*,¹⁰ sucrase and lactase by the method of Dahlqvist¹¹ and alkaline phosphatase by the method of Kelly and Hamilton.¹²

The sites of biopsy were divided into three sections as illustrated in Fig. 1 to facilitate analysis.

Results

Brush border activity of alkaline phosphatase, lactase and sucrase was measured in all of the 477 subjects studied. The results are presented in the context of the three main variables being discussed: age, sex, and site of intestinal biopsy. Data are presented in the form of scattergrams (Figs. 2–4). In each case the sample means, 5th and 95th percentiles of the observed distributions are indicated. As the distribution of results is not Gaussian and tends to be markedly positively skewed the sample means fall in the lower half of the 5th to 95th percentile ranges.

No data are presented on enzyme activities from site 1 (duodenal bulb) in the under 18 age groups as the sample numbers are too small.

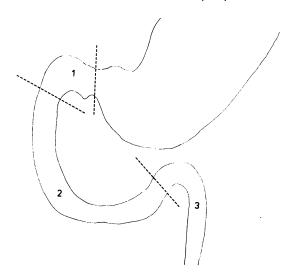


Fig. 1 Diagrammatic representation of anatomical divisions of sites 1, 2, and 3 of the upper small bowel

ALKALINE PHOSPHATASE

Alkaline phosphatase activity increases from site 1 to site 3 in all groups except females aged 12-18 yr. When ageand sex-matched comparisons are made (Fig. 2) the increase is most marked between sites 1 and 2. In comparison to lactase the alteration in alkaline phosphatase activity with age, especially in females, is not as striking.

LACTASE

Like alkaline phosphatase, lactase activity increases from site 1 to site 3 (Fig. 3). Activity varies with age, the lowest activities occurring in the 3-12 yr age group. After 12 yr, lactase activity increases towards or exceeds the activities in the 0-3 yr age group and this change is more striking in females than in males. No marked decrease occurs in lactase activity with advancing age.

SUCRASE

Enzyme activity increases from sites 1 to 3 but is less marked in the 0-3 yr age groups (Fig. 4). The pattern of change in sucrase activity with age and sex parallels that of lactase.

Discussion

Lactase activity decreases in the 3-12 yr age group when compared with the 0-3 yr group. One of the most interesting findings in this study and one that has not been previously published to our knowledge is the increase in the activity of lactase after 12 yr. The extent of this increase is more marked in females. Another aspect of both lactase and sucrase is that there is no major decrease in activity in the over 45 yr age group, about 40% of whom were over 60 yr. Lactase activities in this present European population are similar to those described in North American whites.¹³

It is tempting to speculate on the increases in both lactase and sucrase activities in females over the age of 12 yr. Although the number in this age group is relatively

45.

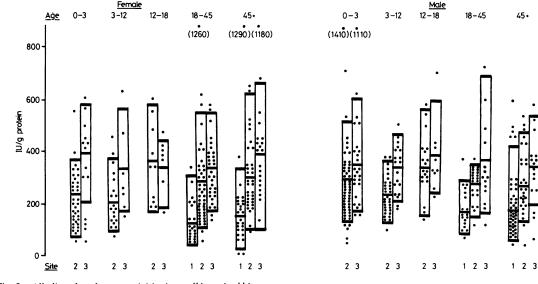


Fig. 2 Alkaline phosphatase activities in small intestinal biopsy

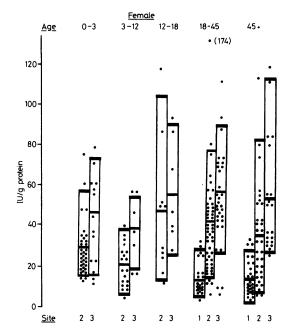


Fig. 3 Lactase activities in small intestinal biopsy

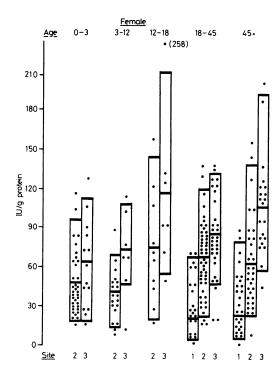
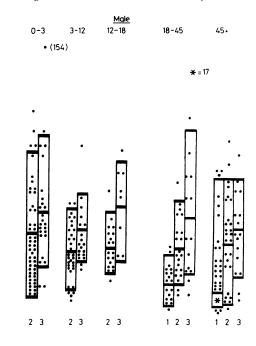
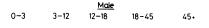
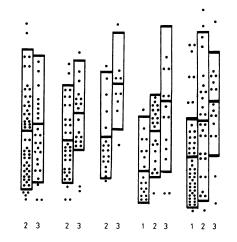


Fig. 4 Sucrase activities in small intestinal biopsy







small (17) compared with other age groups similar alterations occurred at two different intestinal sites. One possibility is that the increased activity reflects hormonal changes associated with puberty.

The progressive increase in enzyme activity down the proximal small intestine has been described previously.^{14 15} The present study is the most extensive site by site comparison of intestinal alkaline phosphatase, lactase and sucrase activity. The results indicate that data from biopsy material from either site 2 or 3 is sufficiently accurate to diagnose enzyme deficiency states. The study emphasises the importance of factors such as age and sex of patient as well as site of biopsy when comparing small intestinal alkaline phosphatase, lactase and sucrase activities.

We thank the Medical Research Council of Ireland and the Wellcome Trust for generous grants.

References

- ¹ Campbell CB, Cowen AE, McGeary HM, Gaffney TJ. Mucosal enzyme activity as a quantitative index of early functional improvement in the management of coeliac disease and other small intestinal diseases. *Aust NZ J Med* 1972;2:220–77.
- ² Peters TJ, Jones PE, Wells G. Analytical subcellular fractionation of jejunal biopsy specimens: enzyme activities, organelle pathology and response to gluten withdrawal in patients with coeliac disease. *Clin Sci Mol Med* 1978;55:285-92.
- ³ Jennings W, Rowland R, Hecker R, Givson GE, Fitch RJ, Reid DP. The

significance of lowered jejunal disaccharidase levels. Aust NZ J Med 1976;6:556-60.

- ⁴ Ament ME, Rubin CE. Relation of giardiasis to abnormal intestinal structure and function in gastrointestinal immunodeficiency syndromes. *Gastroenterology* 1972;**62**:216–26.
- ⁵ Arvanitakis C. Abnormalities of jejunal mucosal enzymes in ulcerative colitis and Crohn's disease. *Digestion* 1979;**19**:259–66.
- ⁶ Pena AS, Callender ST, Truelove SC, Whitehead R. Small intestinal mucosal abnormalities and disaccharidase activity in pernicious anaemia. Br J Haematol 1972;23:313-21.
- ⁷ Roberts DM, Preston FE. Intestinal disaccharide activity in psoriatic enteropathy. Scand J Gastroenterol 1971;6:93-6.
- ⁸ Greene HC, McCabe DR, Merenstein GB. Protracted diarrhoea and malnutrition in infancy. Changes in intestinal morphology and disaccharidase activities during treatment with total intravenous or oral elemental diets. *J Pediatr* 1975;**87**:695–704.
- ⁹ McNicholl B, Egan-Mitchell B. Jejunal biopsy in coeliac disease. Clin Pediatr (Phila) 1968;7:544-52.
- ¹⁰ Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem 1951;193:265-75.
- ¹¹ Dahlqvist A. Assay of intestinal disaccharidases. Anal Biochem 1968;22:99-107.
- ¹² Kelly MH, Hamilton JR. A micro-technique for the assay of intestinal alkaline phosphatase. *Clin Biochem* 1970;3:33–40.
- ¹³ Welsh JD, Polly FR, Bhatia M, Stevenson DE. Intestinal disaccharidase activities in relation to age, race and mucosal damage. *Gastroenterology* 1978;75:847-55.
- ¹⁴ Lojda Z, Koctanova J, Maratka Z. Histochemistry of the human duodenal mocosa with special reference to the gradient of activities of the brush border enzymes. *Scand J Gastroenterol* 1979;14:7-13.
- ¹⁵ Bergaz R, Grissen M, Infante F, de Peyer R, Valloton MC. Significance of duodenal disaccharidases. *Digestion* 1981;22:108-12.

Requests for reprints to: Professor CF McCarthy, Department of Medicine, Regional Hospital, Galway, Ireland.