

organisms treated with co-trimoxazole suggests differences in the clinical activities of these drugs. Amoxicillin alone is limited in its activity against urinary pathogens owing to the frequent presence of β -lactamases. Martinelli *et al* reported that 36% of urine isolates were resistant to ampicillin or amoxicillin,³ and we found a similar incidence. This resistance can be successfully countered by adding clavulanate to amoxicillin as Augmentin.⁴

The clinical appropriateness of Augmentin is now reinforced by our findings, which show that Augmentin is more rapidly effective than co-trimoxazole in the treatment of urinary tract infection.

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¹ Matts SGF. The hypnotic and sedative effects of 3-methyl-3,4-dihydroxy-4-phenyl-butin-1, a two phase investigation employing double blind techniques and sequential analysis. *Psychopharmacologia (Berlin)* 1966;9:73.

² Armitage P. *Sequential medical trials*. 2nd ed. Oxford: Blackwell Scientific, 1975.

³ Martinelli R, Da Silva Lopez AA, De Oliveira MMMG, Rocha H. Amoxicillin-clavulanic acid in the treatment of urinary tract infections due to Gram-negative bacteria resistant to penicillin. *Antimicrob Agents Chemother* 1981;20:800-2.

⁴ O'Grady FW. Twenty one years of beating beta-lactamases. *Br Med J* 1982;284:369-70.

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Grobby Road Hospital, Leicester LE3 9QE

G J FANCOURT, MB, MRCP, medical registrar
S G FLAVELL MATTS, MB, FRCP, consultant physician

Public Health Laboratory, Leicester Royal Infirmary, Leicester LE1 5WW

C J MITCHELL, BSC, MRCPATH, director

Correspondence to: Dr S G Flavell Matts.

Evaluation of a gluten free product containing wheat gliadin in patients with coeliac disease

In coeliac disease a characteristic lesion of the mucosa of the upper small intestine results in malabsorption. Wheat, rye, barley, and possibly oats have been shown to be toxic to patients with coeliac disease. Gliadin, the ethanol soluble fraction of wheat flour, can be divided into α , β , γ , and ω subfractions, each of which exacerbates coeliac disease.¹⁻³ Normal bread contains about 1.25 g gliadin per standard 30 g slice. A radioimmunoassay for wheat gliadin showed that bread made from a nominally gluten free flour based on wheat starch contained up to 6.4 mg gliadin per 30 g slice,⁴ and the product was withdrawn. Juvella and Rite Diet gluten free bread mixes contain only 0.4 mg and 0.2 mg gliadin per 30 g slice respectively. Although such quantities of gliadin are less than those previously reported to be enterotoxic,³ we wanted to test the products in patients with coeliac disease.

Patients, methods, and results

We studied seven well adult patients with histologically proved coeliac disease who had been receiving a gluten free diet for at least a year. They gave written informed consent and followed a gluten free diet without any

commercial gluten free products for one week, when a jejunal biopsy specimen was taken with a Watson jejunal biopsy capsule. They continued the same diet but each day ate six slices of bread that they had baked from Juvella gluten free bread mix. A second jejunal biopsy specimen was taken after the second week.

The biopsy specimens were fixed in formal saline and their dissecting microscopical appearances were assessed blind. Sections were stained with haematoxylin and eosin and assessed blind for the ratio of villus height to crypt depth, the height of epithelial surface cells, and the intraepithelial lymphocyte count. The mean (SD) of 10 observations for each variable was recorded.

The table shows the dissecting microscopical appearances and morphometric measurements of the seven patients before and after challenge. There was no deterioration in the dissecting microscopical appearances of the biopsy specimens except in one patient (case 5) who had broad villi and ridges instead of leaves and villi. The results before and after challenge were: ratio of villus height to crypt depth 2.4 (0.7) v 2.0 (0.5); height of epithelial surface cells 36 (5) μ m v 33 (4) μ m; and intraepithelial lymphocytes 37 (3) v 36 (6) per 100 enterocytes. The fall in the ratio of villus height to crypt depth was significant at the 5% level, but the other morphometric variables were not significantly different using a paired Student's *t* test.

Comment

Gluten free products based on wheat starch have been shown to contain trace amounts of gliadin,^{4,5} which could be toxic. We have shown previously that 10 mg gliadin by intraduodenal infusion over eight hours did not change the jejunal mucosa in one patient with coeliac disease, although 100 mg gliadin produced minor changes.³ Bread made from normal wheat flour contains about 1.25 g gliadin/30 g slice, while that made from Juvella and Rite Diet gluten free bread mixes contains 0.2-0.4 mg/slice (unpublished observation).

This study suggests that this nominally gluten free product based on wheat starch is not toxic to patients with coeliac disease when eaten for one week. Further studies are required, however, to exclude possible toxicity of the small amounts of gliadin in these products when eaten daily for long periods. In the meantime they can be recommended to patients with coeliac disease.

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Gastroenterology Units, United Medical School of Guy's and St Thomas's Hospitals, London SE1

P J CICLITIRA, MD, MRCP, Wellcome senior research fellow in clinical science

H J ELLIS, BSC, SRD, research assistant and dietitian

Department of Histopathology, Guy's Hospital, London

N L K FAGG, MB, MRCPATH, lecturer in histopathology

Correspondence to: Dr P J Ciclitira, The Rayne Institute, St Thomas's Hospital, London SE1 7EH.

Dissecting microscopical appearance of mucosa, ratio of villus height to crypt depth, height of epithelial surface cells (μ m), and intraepithelial lymphocyte count/100 enterocytes in jejunal mucosal biopsy specimens from seven patients with coeliac disease before and after challenge with gluten free bread (figures are means (SD) of 10 observations)

Case No	Microscopical appearance of mucosa		Ratio of villus height to crypt depth		Height of epithelial surface cells (μ m)		Intraepithelial lymphocyte count/100 enterocytes	
	Before	After	Before	After	Before	After	Before	After
1	Leaves and ridges	Leaves and fingers	2.9 (0.7)	1.9 (0.4)	35 (6)	34 (6)	35 (5)	41 (5)
2	Broad villi and ridges	Broad villi and ridges	1.7 (0.6)	1.8 (0.7)	30 (1.5)	30 (5)	36 (4)	35 (6)
3	Leaves and ridges	Leaves and fingers	3.4 (0.8)	2.9 (0.6)	38 (6)	37 (3)	31 (4)	32 (7)
4	Broad villi	Broad villi	1.4 (0.8)	1.4 (0.6)	38 (10)	26 (2)	45 (7)	31 (5)
5	Leaves and fingers	Broad villi and ridges	2.4 (1.0)	1.8 (0.9)	38 (7)	39 (5)	33 (6)	35 (11)
6	Ridges	Broad villi	2.2 (0.6)	2.1 (0.8)	43 (5)	31 (10)	43 (6)	48 (8)
7	Broad villi and ridges	Broad villi and ridges	2.7 (1.1)	2.1 (0.8)	29 (2)	34 (5)	38 (8)	31 (9)
Mean			2.4 (0.7)	2.0 (0.5)	36 (5)	33 (4)	37 (3)	36 (6)