

# Food Antibodies in Serum— A Screening Test for Coeliac Disease

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**Carswell, F., and Ferguson, A. (1972).** *Archives of Disease in Childhood*, **47**, 594. **Food antibodies in serum—a screening test for coeliac disease.** Food antibody tests were performed on the sera of 52 children undergoing investigation for suspected coeliac disease. 30 of these were subsequently shown to have coeliac disease. The food antibody tests were at least as effective a screening test for coeliac disease as the whole blood folate determination, serum immunoglobulins, or the barium meal and follow-through.

The diagnosis of coeliac disease is ultimately established by the demonstration of a flattened mucosa in the upper small bowel and by subsequent clinical improvement on a gluten-free diet (Rubin, Eidelman, and Weinstein, 1970; Booth, 1970). Many screening tests have been advocated for coeliac disease, and it seems reasonable that any new procedure should be shown to be more effective than the existing methods. In this paper we compare the usefulness of the whole blood folate estimation (McNeish and Willoughby, 1969); the barium meal and follow-through (MacRae and Sweet, 1964); serum immunoglobulin determinations (Asquith, Thompson, and Cooke, 1969); and tests for blood antibodies to various impure food antigens (Heiner, Lahey, and Wilson, 1964; Ferguson and Carswell, 1972).

### Methods

All the patients were studied after admission to this hospital. Comparisons were made between two groups of patients.

**Group 1.** Those with coeliac disease as shown by a flat or nearly flat upper intestinal biopsy and a clinical response to a gluten-free diet. There were 30 such patients. The mean age of the group was 46 months and the youngest patient was 6 months. The male : female ratio was 1 : 1.14.

**Group 2.** Those in whom the diagnosis of coeliac disease was initially suspected but subsequently rejected after intestinal biopsy with or without a trial of gluten-free diet. The final diagnosis on these patients is

indicated in Table I. There was a total of 22 patients in this group; the male : female ratio was 1 : 0.57 and the mean age 42 months.

TABLE I  
*Eventual Diagnosis of Patients Who Did Not Have  
Coeliac Disease (Group 2)*

Diagnosis	No. of Patients
No abnormality detected .. .. .	4
Constitutional dwarfism .. .. .	4
Incorrect feeding .. .. .	2
Postinfective diarrhoea .. .. .	2
Maternal deprivation .. .. .	2
Giardiasis .. .. .	2
Cystic fibrosis .. .. .	1
Hypophosphataemia rickets .. .. .	1
Iron deficiency anemia .. .. .	1
Congenital lipase deficiency .. .. .	1
Cyclic neutropenia and agammaglobulinaemia	1
Cerebral tumour .. .. .	1
Total .. .. .	22

There was one additional patient in whom the diagnosis of coeliac disease could not be confidently excluded. This patient is excluded from this paper.

The whole blood folate test was performed on capillary blood samples when the diagnosis of coeliac disease was suspected. A level of less than 60 ng/ml was regarded as suggestive of coeliac disease. A barium meal and follow-through was performed as part of the diagnostic work-up in most cases. The criteria of MacRae and Sweet (1964) were used in diagnosing coeliac disease. Blood samples for precipitating antibody tests were obtained from patients when venepuncture was performed for routine diagnostic procedures. Precipitating antibodies against gluten,

wheat, oats, rice, milk, calf's serum, sheep's serum, egg white, and egg yolk were sought. These tests were simple to perform and can all be carried out on 0.2 ml serum (Ferguson and Carswell, 1972).

The serum immunoglobulin concentrations were determined by radial immunodiffusion (Mancini, Carbonara, and Heremans, 1965).

**Results**

The relative concentrations of immunoglobulins in the serum of patients with (Group 1) and without (Group 2) coeliac disease are shown in Table II.

TABLE II

Number of Patients With (Group 1) and Without (Group 2) Coeliac Disease Who Had High, Normal, or Low Immunoglobulin Levels by Immunodiffusion

Level	IgA		IgG		IgM	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
High	9	3	2	2	6	6
Normal	18	14	26	15	21	10
Low	1	1	0	1	1	2
Total	28	18	28	18	28	18

The mean levels of immunoglobulins in the two different groups of patients did not show any significant differences. It appears unlikely that any immunoglobulin concentration determination would be a good screening test for coeliac disease, but a high IgA concentration seems likely to be the most useful of the three. The number of patients who had precipitating antibodies to the various test substances is shown in Table III.

This table confirms that multiple precipitating antibodies of foods are commonly present in the serum of patients with coeliac disease (Heiner *et al.*,

TABLE III

Patients With Food Antibodies in Their Serum

Food Product	Group 1 (Coeliac)	Group 2 (Not Coeliac)
Gluten	12	0
Wheat	13	0
Oats	7	0
Rice	3	0
Milk	12	2
Calf serum	17	1
Sheep serum	15	0
Egg white	1	0
Egg yolk	4	0
Total number of patients tested	30	22

1964). Only two patients in Group 2 (not coeliac) had antibodies. The eventual diagnoses in these patients were postinfective diarrhoea (milk antibodies present) and no abnormality detected (antibodies to milk and calf serum). When the antibodies to milk and antigenically-related calf serum are excluded, 23 of the 30 patients with coeliac disease (Group 1) had precipitating antibodies as compared with none of the 22 patients in Group 2 who did not have coeliac disease.

Table IV compares the effectiveness of the screening tests, using the presence of food antibodies, to any one of the 7 food substances (excluding antibodies to milk and the antigenically-related calf serum); raised serum IgA levels; whole blood folate; barium meal and follow-through.

TABLE IV

Comparison of Screening Tests

Screening Test	Patients with Positive Test		P
	Coeliac Disease (Group 1) (%)	Not Coeliac (Group 2) (%)	
Food antibodies in serum	77	0	<0.0005
Raised serum IgA level	32	21	0.50-0.40
Whole blood folate	67	42	0.30-0.20
Ba meal and follow-through	77	25	0.001-0.002

\*Significance of the difference between the two groups of patients is calculated by the  $\chi^2$  test with Yates correction applied. P value indicates the possibility that this difference is due to chance variation.

The food antibodies tests most efficiently separated the patients with coeliac disease from the patients without coeliac disease. The barium meal and follow-through was the only other test which showed a statistically significant difference between patients with and without coeliac disease.

Sixteen patients with coeliac disease had all 4 screening tests performed. One of these patients would not have been detected if the serum IgA, whole blood folate, and barium meal tests had been used alone. This patient had food antibodies to sheep serum and calf serum.

**Discussion**

Food antibodies probably occur in the serum of patients with coeliac disease because the food proteins penetrate the damaged intestinal mucosa (Alarcón-Segovia *et al.*, 1964; Booth, 1970). Our own results (Ferguson and Carswell, 1972) confirm that antibodies to many food substances occur in the blood and upper intestinal secretions in coeliac

disease. This does not conform to the clinical pattern of specific gluten intolerance and supports the hypothesis that the presence of food antibodies in the serum indicates a damaged intestinal mucosal barrier rather than a specific aetiological process.

It is apparent that a screening test which utilizes the presence of food antibodies in the serum is at least as likely to detect undiagnosed coeliac disease as estimation of the serum immunoglobulins, whole blood folate, or the barium meal and follow-through. The whole blood folate appears less effective than in its initial demonstration (McNeish and Willoughby, 1969). This may be related to the greater mean age of the patients in the present series. Obviously the composition of such a series depends on the population referred to the clinician, and the clinician's judgement as to who is likely to have coeliac disease. The patients were selected in the present series by clinicians (usually not the authors) as patients in whom coeliac disease seemed possible. Other series may show different incidences of positive results with the present screening tests. However the blood antibody tests are simple, cheap, and easy to perform. They require only 0.2 ml serum, and, once the method is established, 40 tests can be done in 4 hours. There appears to be a place for food antibody testing as a screening test for coeliac disease. From the results shown here tests for antibodies to gluten, wheat, oats, rice, sheep serum, egg white, and egg yolk would be of value in patients with suspected coeliac disease. It is apparent that none of the 4 tests examined here will invariably suggest coeliac disease when it is present. The food antibody tests, like all the screening tests so far described, cannot be used alone as false negative

and false positive results may occur. However they may provide useful support for a decision to admit a patient with possible coeliac disease for full investigation.

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