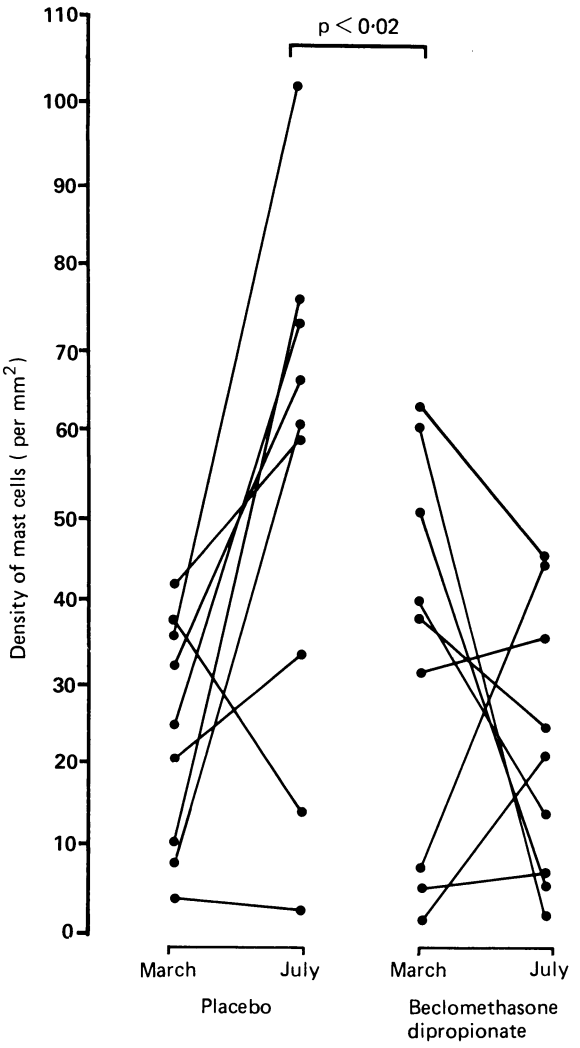
spray devices. Treatment started immediately for 10 weeks. Nasal biopsies were repeated in the second week of July 1986.

All biopsy samples were coded and examined blind. After being fixed in Carnoy's solution the sections were stained with α-naphthol AS-D chloroacetate esterase staining reaction. In addition, adjacent sections were stained with toluidine blue at pH 0·5. The mast cells were counted by light microscopy. The cross sectional area of each biopsy section was determined with a planimetric method and the cell count per mm^2 calculated (Imagan Standard, Leitz Instruments, Luton, UK). The coefficient of variation of the mast cell counts in sections was 4·2%.

The mean paired differences in the density of mast cells in the two groups (March and July) were compared by Student's *t* test. The extent of agreement between the two staining techniques was investigated by plotting the difference between the two methods against the mean of the two methods.[3] Though no agreement between the staining techniques was seen, in July both methods showed similar significant differences in the density of mast cells in the group treated with beclomethasone dipropionate compared with the group given placebo (figure; $p<0·02$, Student's *t* test).



Density of mast cells (per mm^2) in biopsy samples from single patients treated with placebo and beclomethasone dipropionate before treatment at start of pollen season and after three months.

Comment

Our results suggest that beclomethasone dipropionate inhibits the increase in density of mast cells that occurs in the nasal mucosa during the pollen season. Atopic patients have been shown to have increased numbers of mast cell progenitors in the circulation,[4] and the migration of such progenitors into the nasal mucosa may be inhibited by corticosteroids. Alternatively, these drugs may act by inhibiting the growth and differentiation of mast cell progenitors in situ. The maturation and migration of such progenitor cells are thought to be dependent on T cell lymphokines.

Interleukin 3, the lymphokine believed to have the main role in regulating mast cells, has now been identified in humans.[5] Though the mechanism of action of corticosteroids is likely to be complex, our study suggests that corticosteroids may influence maturation or migration, or both, of mast cells, possibly by inhibiting the production of interleukin 3.

Whatever its mode of action, we believe that treatment with beclomethasone dipropionate should be started before the pollen season begins to prevent increases in mast cell density and nasal priming.

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Centre for Medical Research, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE

EVA GOMEZ, MSC, research assistant, academic department of respiratory medicine
JOHN E CLAGUE, MRCP, research fellow, academic department of respiratory medicine
DAVID GATLAND, FRCS, registrar, ear, nose, and throat department
ROBERT J DAVIES, MD, FRCP, reader in respiratory medicine, academic department of respiratory medicine

Correspondence to: Dr Davies.

Kinesiology and food allergy

The report on food intolerance and food aversion noted that a wide variety of symptoms have been incorrectly attributed to the effects of food and recommended that diagnostic tests for food allergy should be strictly evaluated.[1] In the proceedings of a recent symposium kinesiology was reviewed under the heading "Untested or invalid methods for diagnosis,"[2] though in the subsequent discussion it was claimed that the effect on which the test depends "exists and is repeatable."[3]

Patients, methods, and results

The kinesiology test is performed as follows. Allergens to be tested are prepared in stoppered neutral glass bottles. The patient holds the bottle in one hand, and a positive test is indicated by a decrease in muscle power in the contralateral arm. No physiological basis for this effect is known. To see if the effect "exists and is repeatable" a set of 12 prick test solutions (Bencard, Brentford, Middlesex) of milk, cheese, candida, maize, yeast, ethanol, beef, lamb, pork, cod, orange, and grasses was prepared and correctly labelled, and another set of 12 identical bottles was prepared and labelled A-L. These contained (in random order and in duplicate) prick test solutions of milk, cheese, candida, maize, and yeast, the remaining two bottles containing saline solution. The tester was asked, when the response was positive to one or more of the labelled bottles, to test all the "blind" bottles on the same patient and to score the results on a form provided.

The table shows the results obtained with 20 consecutive patients who entered the trial. On open testing six patients gave a positive reaction to milk (cases 1, 2, 10, 11, 13, and 14). These six patients then had 12 blind challenges with milk, of which only one (case 2, second blind challenge) gave a positive result. Among the 14 remaining patients who gave negative results to milk on open testing there were four positive reactions on blind testing. If the reactions to milk, cheese, candida, maize, and yeast were summed eight of 50 blind tests (16%) gave positive results among those patients who gave positive results on open testing with these antigens, and 24 of 150 (16%) gave positive results among patients who gave negative results on open testing. Saline solution caused positive reactions in seven of 40 blind tests (18%).

Because the blind testing was done on duplicate samples we were able to see if the concordant results within the pair (that is, both positive or both negative) exceeded the frequency that would be predicted by chance. This analysis showed that the number of concordant results within duplicates was similar to that that would be expected by chance, given an overall positive response rate of 39 of 120.

Comment

Our experience indicates that the kinesiology response is not reproducible under conditions of blind testing and therefore cannot be a reliable indicator of food allergy. This does not deny that patients who have undergone the test

Responses of 20 patients to 12 labelled antigens and to five antigens and saline in duplicate tested blind.

	Case																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Twelve labelled antigens																				
Milk	\	\								\	\		\	\						
Cheese		\		\				\		\										
Candida		\	\		\		\	\				\			\	\			\	
Maize			\								\					\		\		\
Yeast															\					
Ethanol		\						\												
Beef				\				\								\		\		
Lamb						\														
Pork					\															
Cod																				
Orange		\																		
Grasses		\	\				\		\								\			
Five blind antigens and saline																				
Cheese		+		(−)				+		(−)	(+)			(+)		(+)			(+)	
Candida		+	(−)		(−)		(−)	+			(+)	(−)			+	(−)			(−)	
Milk	(−)	(−)	(+)				(+)			(−)	(−)		(−)	(−)						
Yeast						(+)		(+)							(−)	(+)		(+)		
Yeast			(+)										(+)		(−)					
Maize		(+)	(−)								(−)					(−)	(+)	(−)		(−)
Milk	(−)	+		(+)						(−)	(−)		(−)	(−)	(+)					
Candida		(−)	(−)		(−)		(−)	(−)	(+)			(−)			(−)	(−)			(−)	
Cheese		(−)	(+)	(−)	(+)			(−)		+										(+)
Saline					(+)							(+)				(+)				
Maize	(+)	(+)	(−)	(+)							(−)					(−)		+		(−)
Saline		(+)					(+)	(+)		(+)										

\ = Positive response to labelled antigen. + = Correct blind positive response. (+) = False blind positive response. (−) = False blind negative response.

and subsequently modified their diet may well feel better. It is, however, quite a serious step to advise someone to avoid important staple foods, especially if many foods are involved, or if the patient is a young child.[4] The experimental procedure described above is simple and inexpensive and requires only the cooperation of an impartial observer who will prepare the "blind" antigens. Practitioners who use tests without formal validation may wish to apply similar investigations to their own diagnostic procedures.

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Department of Human Nutrition, Medical College of St Bartholomew's Hospital, London EC1M 6BQ
J S GARROW, FRCP, professor of human nutrition

Loss of the Philadelphia chromosome in chronic myeloid leukaemia associated with coeliac disease and splenic atrophy

Splenic atrophy is common in coeliac disease.[1] Although elective splenectomy in chronic myeloid leukaemia does not appreciably affect survival, pre-existing hyposplenism due to coeliac disease may have influenced the course of leukaemia in the case reported below.

Case report

In 1972 a 41 year old woman presented with abdominal pain and symptoms of anaemia. Investigations showed deficiencies of iron and folate and hypocalcaemia. Jejunal biopsy showed subtotal villous atrophy; coeliac disease was diagnosed, and she was successfully treated with a gluten free diet. Ten years later a routine blood count showed a haemoglobin concentration of 128 g/l, platelet count 314 × 10^9/l, and white cell count 104 × 10^9/l (differential count 69% neutrophils, 5% metamyelocytes, 16% myelocytes, 2% promyelocytes, 4% lymphocytes, and 2% monocytes). Red cell changes included anisocytosis and the presence of target cells and Howell-Jolly bodies. She did not have any symptoms or hepatosplenomegaly. Alkaline phosphatase activity in neutrophils was scored at 4 (control score 126), and the appearance of bone marrow aspirate was consistent with that seen in chronic myeloid leukaemia. The Philadelphia chromosome was identified in all mitotic cells examined.

She was treated with busulphan 4 mg daily, initially, which was reduced to 4 mg weekly over three months as her white cell count and differential returned to normal. One year after busulphan was started the bone marrow karyotype was normal (table) and treatment was stopped. The bone marrow was not hypoplastic at any stage. Hyposplenism was shown by technetium scanning of the liver and spleen; the spleen showed virtually no uptake. Screening for antibodies to parietal cells and antinuclear, mitochondria, and reticulin antibodies yielded negative results. Lymphocyte subsets showed suppression of cells bearing CD4 and CD8 molecules. She remained well with a normal white cell count and no further treatment for a further three years of follow up. Karyotyping during this time showed the Philadelphia chromosome in up to 8% of cells, and DNA analysis showed no rearrangement of the break cluster region.

Results of haematological and serial karyotype studies of bone marrow of patient with chronic myeloid leukaemia, coeliac disease, and splenic atrophy

Date	Haemoglobin (g/l)	White cell count (× 10^9/l)	Platelets (× 10^9/l)	No (%) of cells positive for Philadelphia chromosome
16 August 1983	131	106·0	309	25/25 (100)
12 March 1984	128	6·6	429	11/30 (37)
5 July 1984	122	5·9	299	0/36
18 January 1985	125	6·5	317	1/70 (1)
21 May 1985	125	6·2	385	2/30 (7)
2 July 1985	131	7·2	394	1/43 (2)
7 November 1985	132	6·6	390	2/30 (7)
19 August 1986	133	7·2	335	0/35
13 February 1987	132	4·9	337	2/50* (4)
26 June 1987	129	5·9	282	0/36*

*Samples tested for rearrangement of break cluster region.

Comment

A decrease in the proportion of cells positive for the Philadelphia chromosome is uncommon in the absence of myelosuppression.[2,3] Golde *et al* suggested that a further mutation may result in a clone of cells positive for the Philadelphia chromosome that has no growth advantage over normal cells.[3] Another theory is that a clone of cells negative for the Philadelphia chromosome but otherwise abnormal may persist.[4] The pathogenesis of leukaemia is a multistep process; we suggest that in our patient pre-existing hyposplenism reduced the growth of the clone positive for the Philadelphia chromosome or increased the clone's sensitivity to treatment with busulphan.

Splenic atrophy occurs in a third of patients with coeliac disease, and impaired splenic function occurs in half.[1] T cell lymphopenia is found after splenectomy as well as in hyposplenism associated with coeliac disease. The cause of hyposplenism in coeliac disease is obscure, although it is strongly associated with the presence of autoantibodies. One theory is that splenic atrophy occurs after prolonged uptake of immune complexes.[5]