

rather extrinsic antigens that have become localized in the skin, e.g. a C-retrovirus (6, 14).

At first, the neoplastic T-cells in skin appear to belong to a slowly proliferating cell population. Later, however, rapid rates of cell renewal occur at extracutaneous sites. Autoradiographic studies seem to indicate that the peripheral lymph node is the major candidate for a primary site of cell renewal in more advanced stages of the disease (3). How early lymph nodes become involved is unknown. The LG findings cannot answer the question whether the early changes found in our studies—as well as in those of others (4, 7, 10)—represent precursor abnormalities, or the disease itself. It is worth noting, however, that in the present study, even before a sure histological diagnosis could be established, 5 of 7 patients showed abnormal LG's, and that altogether about 60% of early cases had a pathological lymphography.

Our findings may have some bearing on therapy. In general, the custom has been to treat the skin—and the skin only—until MF has progressed to an advanced stage. It is conceivable that systemic therapy should be used much earlier in order to achieve a more favourable cure rate. This is in spite of negative data from a retrospective study by Redmond & Rahbari (9) which, however, may be questioned (1), as no information was given regarding the presence or absence of lymphadenopathy and because Sézary's syndrome cannot be ruled out in their patients with erythroderma.

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## Contact Urticaria to Commercial Fish in Atopic Persons

Hans-Iver Beck<sup>1</sup> and Birge Knudsen Nissen<sup>2</sup>

<sup>1</sup>Department of Medicine, Thisted Hospital, DK-7700 Thisted, Denmark, and  
<sup>2</sup>Clinic for Diseases of the Skin, DK-7800 Skive, Denmark

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**Abstract.** The frequency of contact urticaria provoked by certain fish prepared in the Danish fish industry was examined in 14 persons with atopia. In 71.4% of the test persons we found positive confirmation in a 20-minute scratch patch test to one or more fish species. All occluded patch tests were negative, while 33.9% of the scratch patch tests were positive. It was impossible to make a correlation between positive scratch patch tests and atopic allergen/total IgE. The investigation emphasizes that atopics have a higher frequency of contact urticaria to fish than have non-atopics.

**Key words:** Fish, atopia; Contact urticaria; Occupational dermatitis; Skin testing

Table I. *Clinical data of 15 patients with atopic diseases*

	No. of cases	%
Age		
16-30	9	60
31-45	5	33
46-	1	7
Sex		
Female	6	40
Male	9	60
Atopic symptoms		
Allergic rhinitis	13	87
Asthma bronchiale	7	47
Atopic eczema	2	12
Urticaria	2	13
2-3 atopic symptoms	7	47

Previously it has been shown that atopics more frequently develop contact urticaria when they are working in the food industry or in kitchens (1-3).

To our knowledge no investigations have been published to show the frequency of contact urticaria caused by fish in atopics who are *not* employed in the fish or food industry. The purpose of this investigation was to determine this frequency.

#### MATERIAL AND METHODS

A total of 15 volunteers with an acknowledged atopia were tested. The atopia was defined as previous or present atopic dermatitis, allergic rhinitis/conjunctivitis, asthma, or urticaria (Table I). The specific allergens were demonstrable cutaneous prick test, radio-allergosorbent test (RAST), or nasal/bronchial provocation test. Total IgE was measured (norms: 3-263 units/ml). Age, sex, IgE total and allergens are shown in Table IV.

Subject no. 8 was employed in the fish industry but he had never shown any signs of skin disease. Two of the test persons had atopic eczema (nos. 7 and 10); the others had no skin diseases.

Each volunteer was tested with eight different fish:

Table II. *Results of 20-min closed patch tests and scratch patch tests on normal skin of atopic persons*

Test form	Number of persons			Pos. (%)
	Total	Neg.	Pos.	
Closed patch tests	14	14	0	0
Scratch patch tests	14	4	10	71.4

Table III. *The total number of tests in atopic persons*

Test form	Number of test			
	Total	Neg.	Pos.	Pos. (%)
Closed patch tests	112	112	0	0
Scratch patch tests	112	74	38	33.9

plaice, whiting, common dab, witch, codfish, Norwegian haddock, herring, and halibut (Table IV).

The fresh, non-frozen fish were cleaned of slime and the skin was removed. The fish meat was then frozen at  $-18^{\circ}\text{C}$  and was thawed out the day before testing (1).

The persons were tested with small amounts of fish which were applied in an aluminium chamber (Finn Chamber<sup>®</sup>). Each person was tested with eight 20-min closed patch tests and eight scratch patch tests on normal skin on the volar side of the forearm. The scratches were approximately 10 mm long. Histamine (1%) was used as a positive control and physiological saline as a negative control. Reactions in the form of edema and erythema with a size at least equal to the histamine control were regarded as positive, but minor reactions as negative.

#### RESULTS

One of the 15 persons was excluded from further examination because both forearms had been treated with desoxymethasone (Ibaril<sup>®</sup>) one hour before the examination (subject no. 10).

The results of the 20-min closed patch tests were negative in all 14 persons (100%). 33.9% of the scratch patch tests were positive (Table III). Ten persons (71.4%) had positive 20-min scratch patch tests (Table II). All the controls with histamine were positive and all the controls with physiological saline were negative.

Table IV shows the reactions positive or negative to the scratch patch tests in each test person. Positive reactions numbered from one to seven (five on average).

Table V lists the distribution of all the positive scratch patch tests in proportion to the various fish species. 70% reacted with a positive scratch patch test to common dab and halibut, but only 20% to herring. The mean result was 47.5%.

#### DISCUSSION

It has previously been reported that atopic persons more frequently develop contact urticaria to vari-

Table IV. Total number of 20-min scratch patch tests with frozen fish

Subject no. 8 had been employed in the fish industry. No. 10 was excluded because of local treatment with steroid. M=male, F=female, NT=not tested. Norms: IgE total: 3-263 units/ml. Allergen: 1. *Dermatophagoides pteronyssinus*, 2. Grass pollen, 3. Birch pollen, 4. Dog, cat, etc., 5. *Apsis mellifera*, 6. *Artemesia vulgaris*, 7. *Taraxacum vulgare*, 8. *Altanaria iridis*

Person no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Total IgE	216	88	172	341	182	121	399	812	215	1000	NT	475	510	544	1 039
Age, sex	35, M	17, F	17, M	19, M	49, F	18, F	22, F	17, M	35, F	25, M	37, F	19, M	36, M	32, M	28, M
Allergen	1	2	1+2	2+3	2+4	2	1	1+2	5	multiple	6+7	2+4	2	2+4	2+8
Plaice	+					+		+					+		
Whiting	+					+							+		+
Common dab						+		+	+				+	+	
Witch	+	+				+		+	+				+	+	
Codfish	+					+		+					+		
Norwegian haddock				+				+					+	+	
Herring								+						+	
Halibut	+			+		+		+				+	+		+
Histamine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Physiological saline															

ous foods (1-3). In earlier publications the possible etiology and pathogenesis of contact urticaria to fish has been discussed (1, 3-6).

This investigation, carried out using frozen fish in atopic persons, confirms the general opinion, as all 20-minute closed patch tests proved negative, whereas 71.4% of the atopics had positive 20-minute scratch patch tests to two or more fish.

Only one of the tested persons had been employed in the fish industry, preparing shrimps. He had never shown any signs of skin disease, but in the investigation he showed contact urticaria to seven of the fish. This observation, together with the increased frequency of positive scratch patch tests (33.9%) in atopic persons compared with non-atopics in an earlier, similar investigation (1), could be explained by specific immunological factors against the fish allergen in atopic persons. However, most of the atopics should, from a theoretical point of view, not be allergic to fish. The high frequency of positive scratch patch tests therefore stresses another possibility, that contact urticaria might be caused by non-immunological factors in the fish meat.

To determine these factors a further examination with compound 48/80 and passive transfer factor must be carried out (7).

It has earlier been shown that there is an immunological relationship between allergen extracts

from birch pollen and potato and apple (2, 8). Our investigation offers no possibility of making such comparison as there is no correlation between the positivity of positive scratch patch test to fish and specific pollen allergy in the tested persons (Table IV). Furthermore there were no correlations to total IgE and the frequency of positive scratch patch tests.

Our investigation confirms that contact urticaria due to fish which are normally prepared in the Danish fish industry is more frequent in atopic persons.

Table V. Results of 20-min positive scratch patch tests on normal skin of atopic persons with different fish species

Allergen	No. persons tested	No. tests	Number of tests	
			Pos.	Pos. (%)
Plaice	10	10	4	40
Whiting	10	10	4	40
Common dab	10	10	7	70
Witch	10	10	6	60
Codfish	10	10	4	40
Norwegian haddock	10	10	4	40
Herring	10	10	2	20
Halibut	10	10	7	70

To our knowledge, there are several unsolved skin problems among employees in the fish industry. We are therefore making a further examination.

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## The Effect of H<sub>1</sub> and H<sub>2</sub> Receptor Antagonists on the Dermographic Response

John Cook and Sam Shuster

*University Department of Dermatology,  
Royal Victoria Infirmary,  
Newcastle-upon-Tyne, NE1 4LP, England*

Received September 4, 1982

**Abstract.** The effect on dermographic wealing of an H<sub>1</sub> and H<sub>2</sub> receptor antagonist was studied separately and in combination. A double-blind protocol was used and dermographism was measured as the diameter of weal response to a measured force. Both H<sub>1</sub> and H<sub>2</sub> antagonists

had a small but non-significant effect, but the combination of H<sub>1</sub> plus H<sub>2</sub> antagonist had an approximately additive effect which was significant. Although this indicates a role for H<sub>2</sub> receptors in dermographism it does not establish the degree of involvement, nor whether H<sub>2</sub> antagonists necessarily have any advantage over a potent H<sub>1</sub> blocker alone in the treatment of dermographism.

**Key words:** H<sub>1</sub>, H<sub>2</sub>, receptor antagonist; Dermographic response

Histamine is thought to be a mediator of dermographism (5) and H<sub>1</sub> antagonists are generally used for its treatment. H<sub>2</sub> receptors are also involved in weal and flare reactions (2, 4, 8) but it is still not clear what part they play in dermographism. We therefore studied the effect of H<sub>1</sub> and H<sub>2</sub> receptor antagonists singly and in combination on the production of dermographic weals.

### PATIENTS AND METHODS

**Patients and procedures.** 14 female and 6 male otherwise healthy patients with dermographism, aged 19–45 years, were studied. They were assessed at their first visit and all medication was stopped. They were seen 7 days later and their dermographic response was measured, after which they were given various treatment: either 4 mg chlorpheniramine plus an inert tablet, 400 mg cimetidine plus an inert tablet, or a combination of 4 mg chlorpheniramine plus 400 mg cimetidine. All the tablets looked alike and their order had been randomized according to a latin square design and they were given double-blind. The patients took the tablets with water 2 hours before each visit and the time between visits was at least 2 days. At each visit the dermographic response was measured and a new medication given until each patient had taken all three treatments. The code was broken when the study had been completed.

**Measurement of dermographism.** Dermographic weals were produced with a spring-loaded stylus which travelled down a slit in a flat guide plate as described by Kerby et al. (6). The instrument was calibrated and the responses to forces of 24.5 and 36.1, 48.6, 60.9 and 74.6 g/mm<sup>2</sup> were measured in each subject. The weals were raised on the left side of the back below the spine of the scapula with a gap of approximately 3 cm between each weal, by passing the stylus backwards and forwards three times along the same track. The diameter of each weal was measured at 3 points 2 cm apart 10 minutes after initiation and the mean weal diameter was calculated.

### RESULTS

The dose-response curves of stylus pressure and weal diameter were linear, both before and after each treatment, and the results are expressed as means of standard errors (in Fig. 1) and as the cor-