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Dermatitis Induced or Aggravated by Selected Foodstuffs

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The eczema of 113 patients with dermatitis other than classical urticaria or typical atopic dermatitis cleared or showed marked improvement after one to two months of dietary restriction. In their response to a questionnaire completed at least 6 months after the initiation of the diet, 61 (54%) of these patients said that diet restriction was effective in reducing the activity of or preventing recurrence of their dermatitis. Their most common symptoms were recurrent symmetrical hand eczema, anogenital eczema, pruritic papules and excoriations of the trunk as well as a "fixed" type of eczema. Forty-nine of the 113 patients were able to reproduce their symptoms at least 3 times with certain food items, most commonly eggs, milk, tomato, cheese and fish. It is likely that both the classical food allergens and foods containing or producing histamine or other vasoactive substances could be the cause of such dermatoses or act as a non-specific aggravating factor. This type of reactivity was most common among patients with a personal and/or family history of atopic diseases (asthma, hay fever and/or atopic dermatitis). Symptoms corresponding to those of contact urticaria to food items were commonly seen among the patients. *Key words: Eczema; Food intolerance; Atopy; Elimination diet; Questionnaire follow-up.*
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It has recently been suggested that food intolerance is of significance for some patients with eczema and that fasting can improve the dermatitis of some of these patients (1, 2). Twenty to forty years ago the association between food intake and various types of dermatitis was frequently discussed in the dermatological and allergological literature. The diagnoses in such cases were usually based on the results of elimination diets and cutaneous tests. Etiologically, allergy to specific food items was suspected (3, 4, 5, 6).

Food additives have been shown to play an important role among the non-immunological etiologies of chronic urticaria (7).

Certain food items have also been shown to play a role in the maintenance of the eczema of some patients with atopic dermatitis (8, 9).

The current study was carried out because we had seen several patients with eczema who repeatedly suffered exacerbations after ingestion of certain foodstuffs.

MATERIAL AND METHODS

One hundred and thirteen patients between the ages of 3 and 76 years (mean 32 years) took part in this study which was carried out from November 1, 1979, to January 31, 1984. The criteria for selection of the patients were 1) the presence of dermatitis which was not classical urticaria or typical atopic or seborrhoic dermatitis (10); 2) it was not possible to make an etiological diagnosis using common dermatological procedures including patch testing with a standard screening tray; 3) the dermatitis cleared or improved markedly after the food items listed in Table I had been left out of the daily diet for at least 1 month. If the patients themselves suspected other food items than those listed in the table, or consumed extraordinary quantities of other food items, they were asked to avoid these foods as well. This applied particularly to adults who normally consumed large amounts of milk, eggs and/or coffee. If there was a positive cutaneous test and/or RAST test to a given food item, this item was also eliminated.

Table I. *Food items patients were asked to avoid*

Other food items suspected by the patients to cause their dermatitis, or which were ingested in large amounts, were also avoided. This applied in particular to milk, eggs and/or coffee

Fish: Cod, plaice, shellfish, tuna fish, mackerel, herring
Fruits and vegetables: Citrus fruits, apples, strawberries, bananas, blueberries, cranberries, peas, beans, tomatoes, onions
Other foodstuffs: Chocolate, nuts, cheese (aged), salami, beer, wine, food items with liberal amounts of preservatives, colouring agents and other chemicals. (Candy, soft drinks, sausages, etc.)

The duration of the dermatitis varied from 3 months to 25 years with a mean of 6 years. Sixty patients had hand eczema, of whom 38 had recurrent vesicular eruptions on the fingers and/or palms—a few also had eruptions on the plantar aspects of the feet. Eleven patients had anogenial pruritic dermatitis; ten had a peculiar "fixed" dermatitis with recurrent eczematous dermatitis in the exact same location and no residual pigmentation between flares. Thirty-two patients had various other types of dermatoses—9 had facial eczema, 3 had acneiform eruptions of the face and/or trunk, 8 had pruritus and excoriations of the trunk, 2 had axillary eczema, and 10 had dermatoses of various other types and locations.

Five patients suffered arthralgias together with flares of cutaneous symptoms, 4 others had headaches, and 3 had abdominal pain.

Nine of the patients were children under 10 years of age; seven of these had hand and/or foot eczema, usually of the vesicular type. The two other children were girls with anogenital itching and eczema. Two of the children had previously had classical atopic dermatitis, but there had been no evidence of this for several years.

All the patients were questioned with regard to personal or family (parents and/or siblings) history of atopy (asthma, hay fever, persistent flexural eczema in childhood). They were also asked about symptoms corresponding to those of contact urticaria to food items (itching, stinging or burning of the skin or mucous membranes within a few minutes of cutaneous or mucosal exposure particularly to uncooked food items). This diagnosis was not supported by tests other than the prick test and the determination of specific IgE antibodies mentioned below.

Diagnostic tests other than patch tests were made in selected cases: battery prick tests to food items including egg, milk, wheat, rye flour, oats, soy bean, potato, codfish, pork and beef were performed for 76 patients. The determination of specific IgE antibodies was carried out for 74 patients using RAST tests to selected allergens, and the number of eosinophils in the peripheral blood was determined for 50 patients.

After they had followed the elimination diets for one to two months while countinuing whatever topical treatment they had used prior to the diet trial, the patients were re-examined to determine the short term effect of dieting. If the dermatitis was improved or had cleared at the end of this period, the patients were asked to continue to diet moderately and to make note of particular food items which repeatedly caused a flare of the dermatitis.

Within a period lasting from 6 months to 4 years after the follow-up examination, a questionnaire was sent to each patient to determine the long-term effect of the restrictive diet and to discover whether their symptoms could be reproduced repeatedly by specific food items (excluded or not excluded by the diet).

A control group of 209 consecutive, age-matched patients who were seen for diseases other than eczema (typically nevi, psoriasis, viral warts) were questioned about adverse reactions to food items and a possible history of atopy and/or symptoms of contact urticaria after exposure to food items as defined above.

RESULTS

Sixty-one of the 113 patients (54%, 95% confidence limits 44–53%) who experienced improvement after the first diet period stated in their responses to the questionnaire that the elimination diet provided long-term benefit. Seven patients had no long-term benefit, and for 45 no information was available.

Forty-nine patients were able to reproduce their symptoms on 3 different occasions by open challenge with one or more food items (details given in Table II).

Thirty-nine patients had a past or current history of atopic disease, while 18 others gave a history of familial atopy. Forty-two had no atopy, and for 14 no information was available.

Symptoms of contact urticaria were noted by 34 of the patients; 21 of them had symptoms on the hands, usually occurring during the preparation of meals; 9 had symptoms of the lips, pharynx, nose or eyes, and 4 had symptoms on the hands as well as of the above-mentioned mucous membranes. The food items causing symptoms of contact urticaria are listed in Table II(*b*).

Of the 50 patients for whom the number of eosinphils were determined, 13 had an increased number of these cells in the peripheral blood ($\geq 350/mm^3$).

For a total of 84 patients either prick tests and/or RAST tests to selected allergens were carried out. Nine patients had positive prick tests ($\geq$ the wheal produced by a prick test with histamine 1 mg/ml) considered to be relevant for the current eczema. Seven had positive RAST tests ($\geq$ class 3 on a scale from 0 to 4), and all were considered relevant for the dermatitis.

Nineteen of the patients who were able to reproduce the dermatitis at least 3 times by ingesting one food item from among the classical food allergens, egg, milk, wheat, beef, codfish, and plaice, had a prick test and a RAST test to that particular allergen. A comparison of the test results is presented in Table III. The total IgE in serum was determined for 4 of the patients listed in Table III, and the level of this immunoglobulin was increased for one patient.

The responses of the control persons are given in Table IV. Three of the 5 atopics who had adverse reactions to food items described rashes; the other 2 noted abdominal pain and diarrhea. Four of the 11 non-atopics who described abnormal reactions to food items had rashes, while the remainder experienced abdominal pain or headache.

DISCUSSION

Most of the patients in this study had had dermatitis constantly or intermittently for several years, and rather severe itching was common. The eruptions were usually symmetrical, and the most common morphologies were recurrent vesicular hand eczema, anogenital pruritus and/or eczema, generalized pruritus and excoriations of the trunk. Papular

Table II

(*a*) *Food items mentioned by the patients as causing flares of dermatitis*

Open challenge 3 times or more: Egg (11), milk (9), tomato (4), cheese (4), food items with artificial colouring agents (4), plaice (3), cod (2), wine (2), wheat (2), chocolate (1), bitter (Gammel Dansk) (1), carrot (1), beef (1), strawberries (1), soy sauce (1), herring (1), shrimp (1)

Open challenge 1 or 2 times: Soft drinks, candy, salami (26), citrus fruit (16), apples (13), chocolate, cocoa (8), wine (8), coffee (7), nuts (7), beer (7), egg (7), mackerel (6), cheese (6), tomato (5), banana (5), rye bread (4), peas (3), wheat (3), marcipan (3), strawberries (2), onion (2), leeks (2), shellfish (2), tea (1), beans (1), celery (1), radishes (1)

(*b*) *Food items causing contact urticaria symptoms (for definition, see text) which were seen in 34 patients, many of whom had symptoms from more than one item*

Tomato (12), potato (11), cheese (6), fish (6) (cod 3, mackerel 3), meat (6) (pork 2, beef 2, chicken 3), fruit (5), (apple 3, cherries 1, citrus fruit 2), shellfish (4), flour (1), milk (1), peas (1), nuts (1), parsley (1)

acneiform eruptions were less commonly seen. Ten patients had an asymmetrical eruption similar to fixed drug eruption with pruritic nummular eczematous lesions at one or a few sites and recurrences at exactly the same sites with no other cutaneous abnormalities. There was no pigmentation of the involved sites between flares, thus distinguishing this eruption from the clinically typical fixed drug eruption. A patient with a similar unilateral axillary eruption was described by Livingood & Pillsbury (4) in 1949.

Patients with atopic dermatitis in accordance with the criteria of Hanifin & Rajka (10) were excluded from this investigation. It is possible, however, that some of the patients, in particular those with a personal and/or a family history of atopic diseases, could have had an atypical atopic dermatitis.

The diagnosis of a food-induced cutaneous eruption is difficult to make. Ideally, repeated double-blind challenge with suspected food items should be carried out, but such a procedure is unsuitable for out-patients, particularly in a private practice. We chose, therefore, to compile the results of a diet trial combined with the results of repeated open challenge and the responses to a questionnaire mailed to the patients after they had had long-term experience with the effects of an elimination diet. Many of the patients whose long-standing dermatitis improved after elimination of certain food items for one month maintained in their responses to the questionnaire that they had long-term benefit of the diet, and that they had repeatedly experienced flares following intake of certain foods or drinks. This combination of circumstances makes a placebo effect unlikely.

The reactivity was clearly related to atopy. Fifty-seven of 113 patients with cutaneous symptoms compared with 52 of the 209 control persons had a personal history of atopic diseases and/or atopic diseases among siblings or patients ($\chi^2=22$, $p<0.01$). Another characteristic seen among the patients in this study was contact urticaria symptoms (34 of 113 compared with 6 of 209 controls ($\chi^2=100$, $p<0.01$).

Table III. *Results of allergy tests in 19 patients whose dermatitis was reproduced at least 3 times by open challenge with classical food allergens*

	Positive challenge	Positive Prick test	Specific IgE (RAST ≥ class 3)
Egg	6	1	0
Milk	6	0	2
Wheat	2	0	1
Beef	1	0	1
Cod fish	2	0	0
Plaice	2	0	0

Table IV. *Number of control persons who gave a history of adverse reaction to food items and/or a history of contact urticaria symptoms*

For definition of atopy and contact urticaria symptoms see text

	Persons with a personal and/or family history of atopic diseases $n=52$	Persons with no personal or family history of atopic diseases $n=157$	Total $n=209$
Adverse reaction to food items	5	11	16
Contact urticaria symptoms	3	3	6

The diet instructions used in the study were based on practical experience with the most common food allergens in combination with information from the literature concerning those food items which may contain or produce vasoactive amines (11, 12, 13, 14, 15, 16).

The diet instructions were purposely not very restrictive since compliance with such diets decreases rapidly as the diets become more difficult to keep and less consistent with a normal life-style. We found it important that the patients followed the diet for at least one to two months.

The patients who were able to reproduce their symptoms at least 3 times commonly mentioned the classical food allergens as the cause of their dermatitis. Those who could reproduce their symptoms once or twice by challenge commonly noted products with vasoactive amines as the cause (Table II *a*). An additive effect may be expected for foods containing vasoactive amines, i.e. if several items are ingested within a short period, more severe symptoms ensue. There may also be variations from time to time in the individual food items. The amount of histamine in mackerel, for example, may vary considerably. The endogenous production of compounds like benzoic acid in the gastrointestinal tract may also be of significance in this type of reaction (17), and substances like lectins could be involved.

The traditional laboratory tests for diseases associated with atopy, such as eosinophilic counts and cutaneous tests, proved to be disappointing diagnostic measures; this is in agreement with the findings of Bernstein (18). The most reliable test was the repeated reproduction of the symptoms by challenge experiments preceded by an elimination diet. Compared with this method, prick tests were not very helpful, and the RAST test was only slightly better (Table III).

In view of the paucity of positive laboratory tests, the mechanisms involved in the reactivity described here are uncertain. An immediate-type immunologic reactivity with false-negative test results is a possible mechanism, but other—possibly non-immunological mechanisms—could also be involved. It is also uncertain whether the food hypersensitivity described here is an aggravating factor or the actual cause of the dermatitis.

The food items listed by the patients as causes of contact urticaria symptoms were quite different from those causing repeated flares of the clinical symptoms. This difference may be explained by the fact that contact urticaria symptoms were typically caused by uncooked food items which came into direct contact with the target organ, while the foods ingested were typically heat treated, and the reaction to these took place after intestinal absorption. It could also be that different mechanisms are responsible for the dermatitis and the contact urticaria symptoms. Cutaneous testing and RAST tests performed to distinguish immunological contact urticaria from the non-immunological type have not proven very useful (19, 20).

It seems apparent that certain chronic dermatoses may be induced or aggravated by the intake of certain food items and that these disorders may clear or show marked improvement as a result of dietary treatment if the diet is maintained for a prolonged period of time. The clinical symptoms are primarily symmetrical hand eczema, anogenital eczema, pruritic papular eruptions and excoriated dermatoses of the trunk. An asymmetrical "fixed" eczema may also be seen. The only diagnostic tests which proved reliable were the elimination diet in combination with repeated challenge with suspected food items.

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