

## Elimination Diet in Young Children with Atopic Dermatitis

ANN BROBERG<sup>1</sup>, INGA ENGSTRÖM<sup>2</sup>, KIRSTI KALIMO<sup>3</sup> and LISELOTT REIMERS<sup>2</sup>

<sup>1</sup>Department of Dermatology, <sup>2</sup>Department of Pediatrics, University of Gothenburg, Sweden, and <sup>3</sup>Department of Dermatology, University of Turku, Finland.

**Thirteen children with severe current atopic dermatitis unresponsive to topical treatment were started on an elimination diet. One child was excluded because she could only keep to the diet for 3 days. Twelve children aged 0.8-4.1 years maintained the diet for 2-4 weeks. In six children the dermatologist's score showed a clear improvement while on diet, in 2 children there was a minor improvement and in 4 children the dermatologist's score did not change during elimination diet. Challenges were performed with egg, milk and wheat in 6 children and with milk and wheat in 2 children. The challenges were done in an open way except for the dermatologist, who was unaware of which food the child had received. No child in the study had an immediate reaction but 3 children had late reactions, one after egg, one after milk and one child after challenge with wheat.**

(Accepted February 24, 1992.)

Acta Derm Venereol (Stockh) 1992; 72: 365-369.

A. Broberg, Department of Dermatology, Sahlgrenska Hospital, S-413 45 Göteborg, Sweden.

Uncontrolled dietary manipulations are common among children with atopic dermatitis (AD) (1). Clinically, we often meet parents who are more eager to treat their children with various elimination diets than with basic topical treatment despite a negative history of food allergy and without evidence of improvement while on diet. Allergists and dermatologists have different opinions about the prevalence and importance of food allergy in AD (2). Despite many studies, the true prevalence of food allergy among AD children remains unclear (3-12). It is emphasized by many authors that, before giving complex dietary instructions, the physician should be certain about compliance with topical corticosteroids and emollients (10,13-15).

In this article we report our experiences with a selected group of AD children who were treated with a strict elimination diet (ED) and, if improving, were subjected to open challenges in the hospital. At inclusion, all children had severe AD in spite of adequate topical treatment and elimination of the food items to which the child was suspected to be allergic.

### MATERIAL AND METHODS

#### Patients

Thirteen children, 8 girls and 5 boys, aged 10 months to 4 years, with active severe dermatitis were included. The diagnosis was based on the criteria of Hanifin & Rajka (16). All the children were patients at the outpatient clinic of the Department of Dermatology, Sahlgrenska sjukhuset, and were selected because they did not respond well enough or had severe flare-ups despite treatment with emollients, hydrocortisone, intermittent triamcinolone, oral antihistamines and, when indicated, oral antibiotics. Most parents had received instructions about the topical treatment from a trained nurse at a special visit in what we call an "eczema school", described elsewhere (17).

Only families in which parents were interested in trying a strict elimination diet, even after having been given a thorough explanation about possible problems during the trial, were included.

#### Methods

A period of 1 month's baseline scoring was carried out before the children were started on the ED (*vide infra*). During this period, parents were asked to continue the eczema treatment as optimally as possible. The parents also recorded the eczema symptoms on a diary card. Following the baseline scoring, ED was started for 1 month. The children were examined before and after the strict ED and the physicians and parents together decided whether to continue with the challenge or not. The challenges were carried out at 1- or 2-week intervals with cow's milk, egg and wheat. If the child could tolerate the new food, this was added to the ED. We did not challenge any child with food to which there was a clear history of immediate allergy. During the challenge period, the child was checked weekly by the dermatologist, before each new challenge by the pediatrician and the dermatologist, and in case of a reaction while in the hospital by the pediatrician.

#### Parents' scoring

Throughout the study, parents were asked to record daily scores for eczema (0-4), pruritus (0-4) and disturbance of night sleep (0-3). The scores were averaged and a mean daily score for the final 10 days of the elimination period was used.

#### Dermatologist's scoring

An eczema score was assigned at each visit, based on the type, intensity and distribution of the lesions. A mean score for intensity was graded separately for erythema, lichenification, vesiculation, excoriation, papules, and dryness, and the scoring was as follows: 0=no symptoms, 1=mild, 2=moderate, 3=marked, 4=severe.

The distribution of the lesions was scored from 0 to 4 as follows: 0=no eczema, 1=one local site affected (symmetrical lesions always counted as one locus), 2=two local sites affected, 3=three local sites affected, 4=four or more local sites affected. The six different intensity scores were multiplied by the distribution score and the sum of these became the total eczema score. The maximum score was 96. Photographs were taken at each visit.

#### Elimination diet

The ED contained only the following items: caseinhydrolysate (Nutramigen®), lamb's meat, rice, corn, corn oil, potato, cucumber, melon, bilberries, salt, sugar, and gluten and milk-free bread. Instructions about ED were given by a dietician to the parents and when indicated also to day-mothers or personnel at the day-care centres. The information was given orally as well as in writing on a handout with menu suggestions for different age-groups. The dietician participated at all return visits and usually had telephone contact with the families between visits. Parents were instructed to give the children calcium supplementation and vitamins if the children did not take the caseinhydrolysate.

#### Challenge

The challenges were carried out in an open way. Only the dermatologist was unaware of which food the child had received. The first 2 days of challenge were performed in the hospital. In most cases the child was kept as an inpatient, and if immediate reactions appeared these were treated by the pediatrician. The children stayed in the

Table I.

Case #	Age (years)	Ige (Ku/l)	SPT $\geq 2+$	RAST $\geq 2$	Positive history	Parents' score <sup>a</sup>	Physician's score <sup>a</sup>	Challenged with
1	3.2	210	Soybean	Soybean, wheat		6.3/8.9	36/20	Egg, wheat, milk <sup>b</sup>
2	2.3	60				4.4/2.9	15/13	
3	3.1	90	Egg, fish	Egg, fish	Egg, fish	4.9/5.3	26/5	Wheat, milk
4	3.8	990	Egg	Egg	Egg	7.6/5.6	36/34	Wheat, milk
5	4.1	210				3.9/1.8	12/2	Egg, wheat, milk
6	2.3	30				7.4/4.3	49/5	Egg, wheat, milk
7	2.6	100	Fish		Fish	10.2/9.0	44/8	Egg <sup>b</sup> , wheat, milk
8	2.2	130				7.3/9.9	24/20	-
9	2.9	35	Fish		Fish	7.5/8.4	52/34	-
10	0.8	50	Egg	Egg		6.6/6.0	9/8	-
11	3.1	70		Wheat		8.7/5.4	54/2	Egg, wheat <sup>b</sup> , milk
12	1-3	4.2	Egg		Fish	6.0/4.3	34/2	Egg, wheat, milk

000 = > 2 SD (24), <sup>a</sup>before diet/after diet, <sup>b</sup>positive to challenge.

hospital until 4 h after challenge the second day, and if no reaction occurred the new food was included in the diet. On the first day of challenge, each new food was given at 30-min intervals as follows: whole egg was given as a gluten- and milk-free cake containing 0.15 g egg per g cake, as follows: 1 g, 5 g and 10 g of the cake and on the second day one boiled egg. Wheat was given as a milk-free bread, and this was given as follows: 1 g, 5 g and 10 g of the bread and on the second day a free amount. Nonfat cow's-milk was given as follows: 5 ml, 10 ml and 100 ml. On the second day, the child received a free amount of milk.

#### Laboratory

Specific circulating IgE antibodies to cow's milk, egg, fish, soybean, and wheat were determined before ED by means of the radio-allergo-sorbent test (RAST, Pharmacia) Total IgE was also determined.

Skin prick tests (SPT) were performed with green pea, egg, cow's milk, fish, soybean, and wheat (ALK, Allergologisk Laboratorium, Hellerup, Denmark) separately. Histamine (10 mg/ml) was used as positive control. Wheals greater than or equal to half of the histamine reaction were considered positive, provided that the vehicle control was negative and that the diameter of the histamine wheal was at least 3 mm.

## RESULTS

Twelve of the 13 children completed the study. One child could only keep to the diet for 3 days and was therefore excluded. The data of the 12 children who completed the study are presented in table I. In one patient (no. 5), the parents found it difficult to adhere to the restricted diet for more than 2 weeks, but since the child had improved so much, they were motivated to agree to the challenges.

In 6 of the 12 children, the dermatologist's scores showed a clear improvement (cases no. 3, 5, 6, 7, 11 and 12), in a further 2 (cases no. 1 and 9) there was a less marked improvement and in 4 children (cases no. 2, 4, 8 and 10) the dermatologist's score did not change during ED. The parents' scores did not always tally with the dermatologist's score. In 3 cases considered improved by the dermatologist the parents' score did not show any improvement (no 1, 3 and 9). In patient no. 3 the reason was obvious, whooping-cough which made her wake up several times every night.

Challenges were performed in 8 of the 12 children. One child (no. 9) who improved according to the dermatologist's score was not challenged because the mother was not motiva-

ted to continue with the diet. One child (no. 4) was challenged in spite of no improvement in the dermatologist's score. This child had a very unstable eczema before and during the study but the mother's assessment was that the flare-ups were fewer during the ED. In 2 other children (no. 1, 7) eczema deteriorated during the study in connection with infection. No child reacted with immediate symptoms when challenged. Three children reacted with one item each. The positive cases reacted as follows:

#### Case no. 1

Eczema worsened slowly during the first week when milk was introduced. The other challenges were uneventful. After the challenges, he was eating a diet devoid of cow's milk and had only minimal eczema.

#### Case no. 7

An itchy erythematous eruption developed mainly on the trunk 8 h after challenge with egg. The other challenges were uneventful. After the challenges, he was given a diet devoid of egg and the eczema disappeared, although he continued to be bothered by itching.

#### Case no. 11

Abdominal pain, vomiting and flushing in the face developed 24 h after challenge with wheat. Because of difficulty in interpreting this reaction, wheat was withdrawn and a new challenge with wheat was done after 1½ months. After this second challenge, she reacted only with skin symptoms after 2 days, when a severe itchy papular eczema developed on her entire body (Figs. 5, 6). The other challenges were uneventful. After the challenges, she was given a diet devoid of wheat and the eczema improved. An accidental challenge later at home with a wheat-cracker started an extensive papular eruption once more. This girl also had a positive RAST for wheat.

Patients no. 5 and 12 improved during the ED period: the situation remained unchanged during the challenges, and these 2 children were returned to their normal diets, which for patient no. 12 was fish-restricted. In patients no. 3, 4, and 6, the eczema worsened several times during the challenge period but with no clear relation to the challenged food. Of these

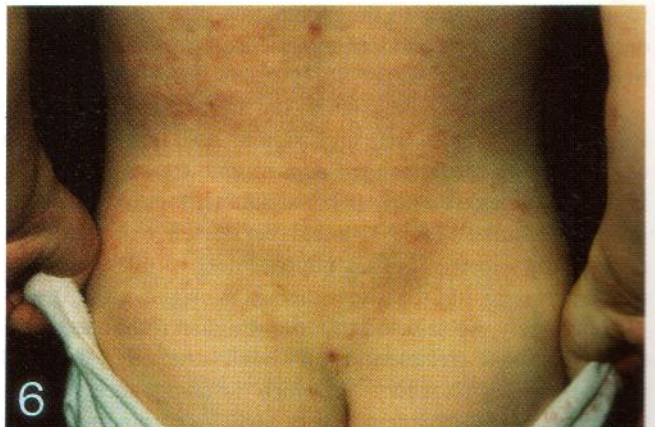
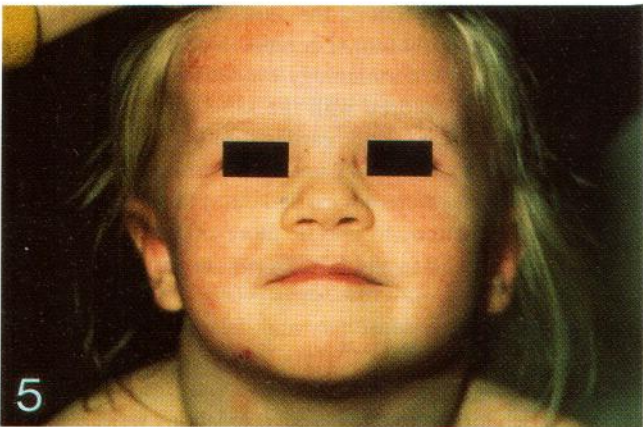
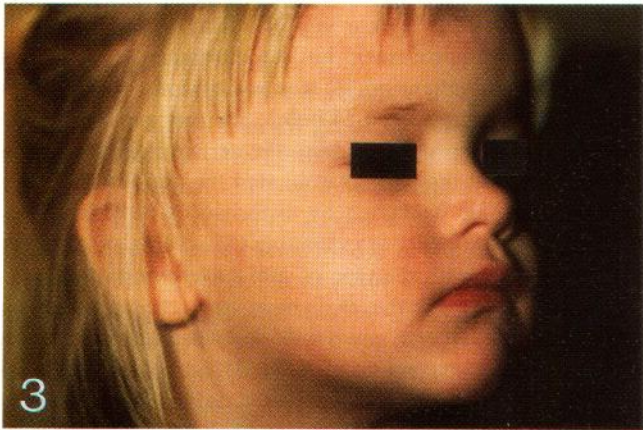
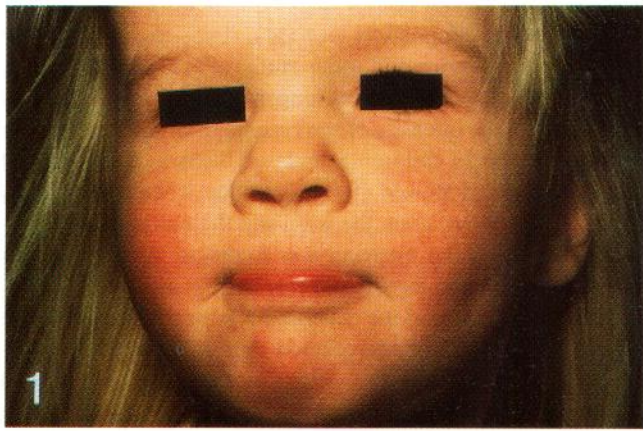


Fig. 1-2. Patient no. 11 in Nov-88, before diet. Dermatologist's score 54.

Fig. 3-4. Patient no. 11 in Dec-88 after 1 month's diet. Dermatologist's score 2.

Fig. 5-6. Patient no. 11 in Feb-89 after challenge with wheat. Dermatologist's score 38.

5 improved but challenge-negative children, one deteriorated after reverting to a normal diet (no. 4).

## DISCUSSION

Dietary manipulation of children with AD is common. Weber et al. (1) found that 71% of children seen in a dermatology outpatient clinic had had significant alterations made to their diet before the first hospital visit. Many of these children had only mild eczema and only a few parents felt that diets had been helpful.

In spite of many studies on selected groups of children with AD, the prevalence of food allergy among all children with AD is not known, nor is the importance of food hypersensitivity in the pathogenesis of AD clear (11, 18). According to a report from a symposium published in 1986, pediatric allergists and dermatologists clearly expressed different opinions about the role of diet in the treatment of AD (2).

A high prevalence of IgE-mediated food hypersensitivity among children and young adults with AD has been shown in a number of challenge studies. In these studies, 33–96% of patients aged 4 months to young adults reacted to food challenge (8, 10, 12). Unfortunately the children in these studies were selected and thus do not reveal the true incidence of food allergy in AD.

However, it is not known how often IgE-mediated hypersensitivity is involved in the pathogenesis of AD. Sampson et al. found that children prescribed an antigen-restricted diet for 2–3 years did significantly better than a group of children who were not found allergic to any foods or who did not comply with the ED (8). Pike et al. found that 36% of 66 children responded favourably to the elimination diet (11). However, only 12 of these 66 children experienced prolonged benefits from the diet.

Based on the available studies, the Task Force on Pediatric Dermatology came to the conclusion in 1986 that elimination diet cannot be recommended as a routine treatment in AD. Instead, the basic therapy (i.e. emollients, topical corticosteroids and antihistamines) should be started before dietary manoeuvres because it offers improvement with less inconvenience to family life than does dietary management (13).

In our study, we selected children who had responded inadequately to basic treatment, even when instructed by a special nurse, i.e. "eczema school", in which the compliance with the topical treatment is generally very high. According to earlier studies, hypersensitivity to food is more common among the youngest children (14, 15) and we therefore selected only children who were 4 years of age or younger.

Another criterion used was whether parents could comply with the diet. In this age-group, around 60% of Swedish children have day-care or a day-mother outside the home, and it is thus not always easy to adhere to a strict diet over several months (19). In our study, 6 of the 12 children were taken care of by another person during the daytime. It appears from other studies also that noncompliance with diets is common. In the studies by Atherton (3) and Nield (9), 25% of the patients could not complete the trial. Pike et al. selected only families which they thought capable of managing complex dietary in-

structions and all but one of their 66 patients completed one period of strict elimination diet (11). Two- to six-week diet periods have been used in other studies (7, 9, 11). We chose 4-week periods but shorter or longer periods may be needed depending on the intensity of the eczema from the start. In our study, 11 of the 13 children completed the 4-week strict ED period and one followed it for 2 weeks. There were many practical difficulties along the way, and the unlimited possibility of contacting the dietician was found to be essential for compliance with the diet.

Based on the state of the child at the return visit, and on the parents' assessment of the eczema during the preceding period, the parents and the dermatologist together decided whether or not the child had improved sufficiently to continue with the challenges; continuing meant several more weeks on the ED. Small variations in the dermatologist's scores did not always correspond to a clear improvement. The photographs showed a clear improvement but the difference, e.g. between 24 and 20 as in patient no. 8, was not obvious compared to patient no. 11, who scored 54 before the diet and 2 after the diet (Figs. 1–4). In some children, the dermatologist found an improvement but the parents evaluated the period differently and this could be explained by disturbances of night sleep. This shows the difficulty of evaluating the severity of AD over a period of time with the type of subjective criteria we have.

The food items for the challenges were chosen based on earlier findings that egg, cow's milk and wheat are most often avoided in the management of AD (13). Sampson & McCat-skill found in patients with suspected IgE-mediated allergy that egg, peanut, milk, wheat, soy and fish accounted for 90% of the positive food challenges (8). Cow's milk, egg and wheat were also found to be among the most common foods identified as causing exacerbation of eczema in children with severe AD selected from a dermatology outpatient clinic (11). We challenged all the children with the same basic foods – egg, cow's milk and wheat – since earlier studies have shown little or no correlation with RAST and SPT results (8, 11). However, the challenges were not carried out if there was a history of immediate reactions to one or more of these foods, confirmed by positive SPTs and RASTs (i.e. in patients no. 3 and 4).

IgE-mediated hypersensitivity and delayed hypersensitivity may play a role in AD (20). The majority of studies have concentrated on IgE-mediated allergy. Van Bever et al. challenged AD children, and all positive reactions were reported within 1 h (12). According to Burk et al. (10) and Sampson et al. (8), all reactions appeared within 2 h; in addition, some of the children in Sampson's study developed a "late phase reaction" after 6–8 h, but only following initial symptoms.

No child in our study had an immediate reaction but 3 children had late reactions. One child (no. 7) reacted after egg challenge and the other 2 children after milk (no. 1) and wheat (no. 11) after 8 h to 3 days. Immediate severe reactions, however, may be expected even in a selected small group like the present one (21). We thus want to stress the importance of performing food challenges under strict observation in a hospital setting.

We are aware of the difficulty of interpreting these open

challenges, because many other factors besides foods (e.g. intercurrent infections or sleep disturbances) may influence the course of AD. Double-blind food challenges might reduce some of these factors. On the other hand, our design better reflects everyday exposure and can enable us to see reactions that may develop after a prolonged time of antigen ingestion, or reactions in which skin contact may be important (22, 23). It is possible that type I reactions can also elicit type IV-like reactions in the skin, and longer periods of exposure and observation are therefore also needed. Possibly, some of the reactions are just cell-mediated.

It is also difficult to find objective criteria with which to evaluate eczema changes. We used the camera to document the eczema lesions. In case 11, these photographs could clearly capture the change in the extent and activity of the lesions during the study and they thus appeared helpful both in documenting the course of the disease and in providing a correlate with the scoring system used.

In conclusion, we found it worthwhile to work in this way with ED in a highly selected group of patients with severe eczema, not only to identify foods responsible for the worsening of the eczema, but also to allow children who do not respond to ED to return to a normal diet, which for some children meant a diet restricted for one or two foods. This also enabled the parents of non-responding children to focus their time and energy on topical treatment. Working with elimination diets is a team effort, involving, patient, parents, pediatrician, dermatologist and dietician, in which all participants are important and essential.

#### ACKNOWLEDGEMENTS

We wish to thank Mainor Åmark, registered nurse at the allergy unit of the Department of Pediatrics, for her assistance with the patients and their parents. This work was supported by grants from the First of May Flower Annual Campaign for Children's Health and the Edvard Welander Foundation.

#### REFERENCES

1. Webber SA, Graham-Brown RAC, Hutchinson P, et al. Dietary manipulation in childhood atopic dermatitis. *Br J Dermatol* 1989; 121: 91-98.
2. Atherton D, Hanifin J, Moroz B, et al. Significance of food hypersensitivity in children with atopic dermatitis. *Pediatr Dermatol* 1986; 3: 161-174.
3. Atherton D, Soothill JF, Sewell M, et al. A double-blind controlled crossover trial of an antigen avoidance diet in atopic eczema. *Lancet* 1978; *i*: 401-403.
4. Juto P, Engberg S, Winberg J. Treatment of infantile atopic dermatitis with a strict elimination diet. *Clin Allergy* 1978; 8: 493-500.
5. Hill DJ, Lynch B. Elemental diet in the management of severe eczema in childhood. *Clin Allergy* 1982; 12: 313-315.
6. Businco L, Businco E, Cantani A, et al. Results of a milk and/or egg free diet in children with atopic dermatitis. *Allergol Immunopathol* 1982; 10: 283-288.
7. Van Asperen P, Lewis M, Rogers M, et al. Experience with an elimination diet in children with atopic dermatitis. *Clin Allergy* 1983; 13: 479-485.
8. Sampson HA, McCaskill C. Food hypersensitivity in atopic dermatitis: Evaluation of 113 patients. *J Pediatr* 1985; 107: 669-675.
9. Neild V, Marsden R, Bailes J, et al. Egg and milk exclusion diets in atopic eczema. *Br J Dermatol* 1986; 114: 117-123.
10. Burks W, Mallory S, Williams L, et al. Atopic dermatitis: Clinical relevance of food hypersensitivity reactions. *J Pediatr* 1988; 113: 447-451.
11. Pike MG, Carter CM, Boulton P, et al. Few food diets in the treatment of atopic eczema. *Arch Dis Child* 1989; 64: 1691-1698.
12. Van Bever HP, Docx M, Stevens J. Food and food additives in severe atopic dermatitis. *Allergy* 1989; 44: 588-594.
13. Caputo R, Frieden I, Krafchik B, et al. Diet and atopic dermatitis. *J Am Acad Dermatol* 1986; 15: 543-545.
14. Pike M, Atherton DJ. Atopic eczema. In: Brostoff J, Challacombe SJ, eds. *Food Allergy and Intolerance*. London: Bailliere & Tindall, 1987: 583-601.
15. Bernhisel Broadbent J, Sampson HA. Food hypersensitivity and atopic dermatitis. *Ped Clin North Am* 1988; 35: 1115-1130.
16. Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol (Stockh)* 1980; suppl 92: 44-47.
17. Broberg A, Kalimo K, Lindblad B, et al. Parental education in the treatment of childhood atopic eczema. *Acta Derm Venereol (Stockh)* 1990; 70: 495-499.
18. Krafchik B. Eczematous dermatitis. In Schachner L, Hansen R, eds. *Pediatric Dermatology*. New York: Churchill Livingstone Inc, 1988: 695-724.
19. Official statistics of Sweden. *Barnomsorgsundersökningen (Förskolebarn 3 månader-6 år)*, 1990, S11 SM 9001.
20. Thestrup-Pedersen K. Immunology of atopic dermatitis. *Acta Derm Venereol (Stockh)* 1989; 69 (Suppl) 151: 77-83.
21. David TJ. Anaphylactic shock during elimination diets for severe atopic eczema. *Arch Dis Child* 1984; 59: 983-986.
22. von Krogh G, Maibach H. The contact urticaria syndrome-an updated review. *J Am Acad Dermatol* 1981; 5: 328-342.
23. Oranje A, Aarsen R, Mulder P, et al. Immediate contact reactions to cow's milk and egg in atopic children. *Acta Derm Venereol (Stockh)* 1991; 71: 263-266.
24. Kjellman M, N-I. Johansson SGO, Roth A. Serum levels in healthy children quantified by a sandwich technique (PRIST). *Clin Allergy* 1976; 6: 51-59.