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## FOOD ALLERGY IN CHILDREN WITH ASTHMA AND ECZEMA

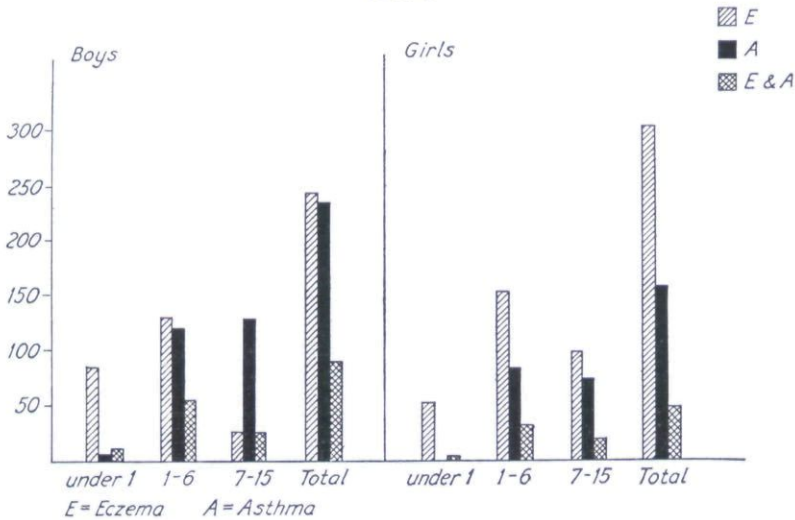
By

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The ancient Romans had already noticed that "one man's food is another man's poison", but it was not until 1868 that Salter established a causal relation between food and asthma. In 1912, Bulkley cured his own eczema of the hands with diet and in 1936 Wise found two patients with eczema to be sensitive to orange juice. In 1946, Rowe, who attached special importance to food allergies, published a report on 182 cases of atopic dermatitis of the hands, 80 (44 %) of which he considered to be caused by food allergy. In 1948, Winston and Sutton published 388 cases of atopic dermatitis and found that 30 (7.8 %) of them had food allergy. Perry (1951), in his review citing these earlier publications, criticized the methods used, i.e. strict trial diet, elimination diets, food diary, scratch and intradermal tests, pulse-dietary method used by Coca, leucopenic index, and stated that he could not find any correlation between the skin tests and the diet tests, when in collaboration with Livingood he performed both tests on 11 patients. Perry himself estimates that about 5-10 % of eczematous dermatitis seems to have a food allergy factor.

Hill (1948) had studied food allergy in children with asthma using scratch tests. Out of 100 children of 3-12 years old, the tests were positive in 35 and negative in 65. There were 218 positive scratch tests in 100 children, and 44 (20 %) of them could be proved to provoke the asthma, whereas in 16

FIG. 1



Ordinate: number of patients.

(8 %), the food which gave a positive test caused vomiting, urticaria or angioneurotic oedema.

Clein (1951) published 140 cases of milk allergy in infants, 59 of whom had eczema and 7 asthma. The others had gastrointestinal symptoms, pyloric stenosis, colic, diarrhoea, constipation, symptoms from the respiratory tract, coughing, sneezing, mucus and râles or rather indefinite symptoms such as anorexia or "very unhappy all the time" (27 cases). All these infants were quickly cured when cows' milk feeding was stopped and soy bean milk substituted.

Ratner & Untracht (1952) studied egg allergy in 500 allergic children, using scratch tests. 102 cases (20 %) gave positive reactions and to 62 of these egg was given on trial. 17 (27.4 %) showed clinical symptoms. This means that about one fourth of the positive scratch tests have clinical importance, and that about 5 % of all allergic children are hypersensitive to egg.

Walther (1954) has studied children with asthma, using skin tests, both intradermal and scratch tests. He obtained 165

positive tests on 440 children (0-13 years) and found out that egg white, fish and peas were the commonest alimentary allergens, but "cows' milk relatively seldom gives positive reactions in Norwegian children". 20 % of asthmatic children gave positive responses in skin tests for egg white and he considered 2-4 % of them to have a clinically manifest allergy. The same was true of fish.

FIG. 2

*Positive intracutaneous reactions in 1050 children with asthma and eczema.*

|                    |      |              |     |
|--------------------|------|--------------|-----|
| Cocoa .....        | 468  | Carrot ..... | 163 |
| Egg .....          | 432  | Mutton ..... | 160 |
| Milk .....         | 405  | Pork .....   | 148 |
| Wheat .....        | 250  | Coffee ..... | 138 |
| Codfish .....      | 227* | Tomato ..... | 134 |
| Pea .....          | 215  | Tea .....    | 128 |
| Rye .....          | 215  | Apple .....  | 88  |
| Oats .....         | 188  | Orange ..... | 70  |
| Beef .....         | 186  | Onion .....  | 57  |
| Baltic sprat ..... | 163* |              |     |

\* Codfish was not tested in 9 cases and Baltic sprat in 12 cases.

To gain some idea of food allergies in Finnish children with asthma and eczema, we went through all the case-reports of the children up to 15 years who had been admitted to the Hospital for Allergic Diseases in Helsinki during the years 1947-1956. We studied the results of skin tests, leucopenic index, general and local reactions to provocation and clinical experiences.

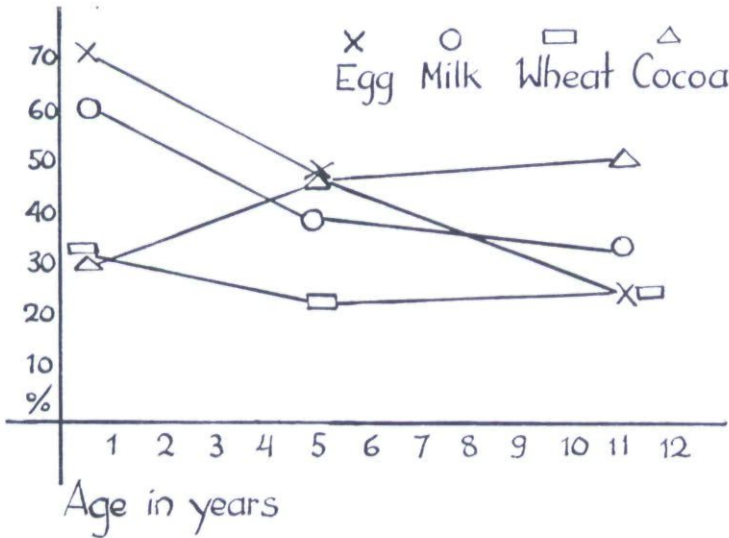
Our material consists of 1076 children, 581 boys and 495 girls. 404 had asthma, 439 had eczema and 133 had both asthma and eczema. 154 were under 1 year, 526 were 1-6 years and 360 7-15 years of age.

Fig. 1 shows the composition of the material according to age, sex and diagnosis.

Among these 1076 children there were 98 (9 %), who, in the repeated examinations made during their stay in the hospital, never had an eosinophil cell count over 4 %. It is a recognised fact that the eosinophily of allergic persons tends to

FIG. 3

*Percentage of positive intracutaneous reactions on egg, milk, wheat and cocoa in different age groups.*



drop when there is an infection and a rise of the sedimentation rate, and to appear again when the B.S.R. has become normal.

All the patients were examined by intracutaneous skin tests. Extracts of Finnish allergens were prepared in the hospital's own laboratory, and before use they were checked on 10 so-called "normal" subjects. Every patient was tested with egg, milk, cereals, meat, fish, cocoa, coffee, tea, fruit and vegetables. Tests were made, especially with the small children, in several groups according to the reactions. Special precautions were taken when testing with fish, it was omitted if there was a history of hypersensitivity to fish, or if the child showed a strong reaction to one fish, then the other was omitted. Thus 9 children were not tested with codfish and 12 not tested with Baltic sprat.

When evaluating the test results, we omitted 26 children who reacted positively to almost every food (at least 15 out of 19 foods tested). We considered the positive reactions in

these cases to show a generally high reactivity of the skin rather than any specific hypersensitivity to food. These cases were equally distributed over the material, irrespective of sex, age or diagnosis.

Of the remaining 1050 children, 152 (14 %) showed a totally negative response to every food tested and 899 (86 %) reacted positively to one or more. 168 (16 %) reacted positively to one food only, 57 to cocoa, 35 to egg, 19 to milk, 11 to wheat, 10 to codfish.

FIG. 4

*Percentage of positive intracutaneous reactions to cocoa, egg, milk, wheat, codfish and pea in 1050 children with asthma and eczema according to diagnosis.*

| Diagnosis    | Number of cases | Positive intracutaneous reactions % |     |      |       |         |     |
|--------------|-----------------|-------------------------------------|-----|------|-------|---------|-----|
|              |                 | Cocoa                               | Egg | Milk | Wheat | Codfish | Pea |
| <i>Boys</i>  |                 |                                     |     |      |       |         |     |
| A & E .....  | 84              | 42                                  | 65  | 52   | 38    | 30      | 24  |
| E .....      | 236             | 37                                  | 58  | 43   | 27    | 27      | 18  |
| A .....      | 245             | 45                                  | 32  | 37   | 21    | 20      | 21  |
| <i>Girls</i> |                 |                                     |     |      |       |         |     |
| A & E .....  | 42              | 64                                  | 45  | 48   | 24    | 33      | 26  |
| E .....      | 290             | 45                                  | 40  | 32   | 22    | 15      | 27  |
| A .....      | 153             | 50                                  | 24  | 38   | 20    | 20      | 19  |

Fig. 2 shows the number of positive intracutaneous reactions to the various foods. Altogether 20034 tests were performed, and 3800 of them (19 %) gave a positive result.

As was already mentioned, codfish was not tested in 9 cases nor Baltic sprat in 12 cases, and there is good reason to presume that these cases would have given positive reactions to fish. But the order of the foods in fig. 2 would still remain unchanged, even if the presumably positive fish tests were added.

Examining the results, we noticed that boys gave a greater number of positive reactions than girls. In different diagnostic groups the greatest number of positive reactions was found in

the children who had both asthma and eczema, next came the group with eczema, and the children with asthma had fewest positive reactions to foods. Fig. 4 shows the percentage of positive reactions to those 6 common foods that had the highest number of positive reactions in the different diagnostic groups.

FIG. 5

*Percentage of positive intracutaneous reactions to cocoa, egg, milk, wheat, codfish and pea in 1050 children with asthma and eczema according to age.*

| Age          | Number of cases | Positive intracutaneous reactions % |     |      |       |         |     |
|--------------|-----------------|-------------------------------------|-----|------|-------|---------|-----|
|              |                 | Cocoa                               | Egg | Milk | Wheat | Codfish | Pea |
| <i>Boys</i>  |                 |                                     |     |      |       |         |     |
| - 1 .....    | 97              | 28                                  | 68  | 61   | 29    | 24      | 20  |
| 1- 6 .....   | 297             | 44                                  | 54  | 38   | 24    | 27      | 20  |
| 7-15 .....   | 171             | 44                                  | 27  | 36   | 28    | 21      | 27  |
| <i>Girls</i> |                 |                                     |     |      |       |         |     |
| - 1 .....    | 49              | 29                                  | 71  | 59   | 33    | 16      | 20  |
| 1- 6 .....   | 254             | 48                                  | 39  | 35   | 20    | 17      | 16  |
| 7-15 .....   | 182             | 56                                  | 20  | 29   | 20    | 20      | 23  |

FIG. 6

*Leucopenic index.*

| Age       | Milk  |      | Wheat |      | Oats  |      | Rye   |      | Codfish |      |
|-----------|-------|------|-------|------|-------|------|-------|------|---------|------|
|           | Total | Pos. | Total | Pos. | Total | Pos. | Total | Pos. | Total   | Pos. |
| - 1 ....  | 87    | 46   | 25    | 14   | 5     | 3    | -     | -    | 3       | 2    |
| 1- 6 .... | 143   | 80   | 37    | 16   | 11    | 4    | 7     | 4    | 7       | 2    |
| 7-15 .... | 37    | 24   | 11    | 7    | 7     | 3    | 1     | 1    | 1       | -    |
| Total ... | 267   | 150  | 73    | 37   | 23    | 10   | 8     | 5    | 11      | 4    |

Comparing the results in different age groups, we noticed that the youngest children had the highest number of positive reactions, and that the relative number fell with increasing age. Egg and milk gave particularly numerous positive reactions in children under 1 year of age; in older children the

percentage fell, whereas cocoa, for instance, gave fewer positive reactions during the first year and more in the older children. Fig. 5 and the graphic fig. 3 illustrate these facts.

In many earlier publications attention has been paid to the positive reactions to egg in infants under 1 year old, because they occur in children who have never eaten egg. The explanation appears to be that penetration through the placenta by allergens allows subsequent intrauterine sensitization of the foetus. Breastfed infants may also become sensitized by breast-milk to allergens included in mother's diet.

FIG. 7

*Comparison of results of intracutaneous test and leucopenic index with milk.*

|                       |      |               |                |      |
|-----------------------|------|---------------|----------------|------|
| Intracut. test .....  | Pos. | Neg.          | Pos.           | Neg. |
| Leucop. index .....   | Pos. | Neg.          | Neg.           | Pos. |
| Number of cases ..... | 134  | 10            | 107            | 16   |
|                       |      | 144           | 123            |      |
|                       |      | Results agree | Results differ |      |

*Comparison of results of intracutaneous test and leucopenic index with wheat.*

|                       |      |               |                |      |
|-----------------------|------|---------------|----------------|------|
| Intracut. test .....  | Pos. | Neg.          | Pos.           | Neg. |
| Leucop. index .....   | Pos. | Neg.          | Neg.           | Pos. |
| Number of cases ..... | 34   | 2             | 34             | 3    |
|                       |      | 36            | 37             |      |
|                       |      | Results agree | Results differ |      |

In our material it seems that milk gives more positive reactions than is generally reported in the literature. According to the statistics by Rinkel milk takes third place after corn and wheat but before egg. Epstein and Palecek (1951), who have studied infants with eczema using scratch tests, state that milk takes fourth place after egg, wheat and potatoes. Hill reckons that 1/5 of the positive scratch tests in asthmatic children are clinically important, and he has provoked allergic symptoms with egg white, fish, peanuts, walnuts and cocoa. Walther in

his Norwegian material considers egg, fish and peas to be the commonest food allergens but rarely milk.

Cows' milk is a major constituent of the diet of children in Finland. For infants under 9 months it is brought to the boil, when their formula is prepared, but older children mostly drink fresh unheated milk. The use of powdered, condensed or evaporated milk is very seldom met with.

There have been some earlier publications concerning food allergies in Finland. Kauppinen, studying results of intracutaneous tests in 330 children with eczema, found the greatest number of positive reactions to egg white, followed by milk, cocoa, egg yolk and wheat. Pätälä considered the high consumption of unpasteurized milk a possible cause of eczema. Pirilä reporting on Besnier's Prurigo in Finland, came to the conclusion that foods may not have great etiological significance. Brummer could not find evidence of food allergy in patients with gastrointestinal symptoms.

Earlier, in another connection, we studied the relation between breast feeding and sensitivity to cows' milk, as well as the expression of allergic symptoms in children. As is seen in fig. 9, in those children, who had been breastfed for less than 3 months, there were 56.7 % with positive skin reactions to cows' milk, but the percentage was only 35.1 in the children who had been breastfed up to 6 months. In 207 allergic children we found that in 159 (70 %) their first outbreak of eczema had coincided with the commencement of cows' milk feeding.

In 1933 Vaughan had published his studies on the leucopenic index. He discovered that in allergic persons the leucocyte count dropped after a meal of allergenic food, and he used counting of leucocytes to diagnose food allergy. The method has been very sharply criticized and its value has been doubted. It is still in use in our hospital as a diagnostic aid, because the studies by Eriksson-Lihr and Pettay have shown that positive leucopenic index tests are due to a reduction in the number of lymphocytes, the "alarm reaction", the allergenic food acting as a stress causing increased secretion from the adrenal cortex.

Besides counting the leucocytes we have tried to observe whether any other reactions, local or general, are elicited by the food. These tests have been performed in cases in which skin tests or clinical symptoms have indicated food allergy.

Fig. 6 shows the results of the leucopenic index tests. They were most frequently done on milk, then followed wheat, oats, codfish and rye. About 50–60 % were considered to be positive, i.e. those cases, where the leucocyte count was reduced by 1000 or more cells.

FIG. 8  
*Hyposensitization.*

| Age       | Milk | Egg | Wheat | Barley | Oats | Rye | Fish | Orange | Total number hyposens | % of cases |
|-----------|------|-----|-------|--------|------|-----|------|--------|-----------------------|------------|
| — 1 ....  | 40   | 5   | 3     | —      | 2    | 2   | 3    | —      | 49                    | 34         |
| 1– 6 .... | 92   | 16  | 2     | 1      | 1    | 1   | —    | —      | 100                   | 18         |
| 7–15 .... | 26   | 1   | 6     | —      | 3    | 3   | 1    | 1      | 33                    | 9          |
| Total ... | 158  | 22  | 11    | 1      | 6    | 6   | 4    | 1      | 182                   |            |

| Diagn.   | Milk | Egg | Wheat | Barley | Oats | Rye | Fish | Orange | Total number hyposens | % of cases |
|----------|------|-----|-------|--------|------|-----|------|--------|-----------------------|------------|
| A & E .. | 35   | 7   | 5     | 1      | 4    | 4   | 2    | 1      | 44                    | 35         |
| E .....  | 95   | 12  | 4     | —      | —    | —   | 1    | —      | 106                   | 20         |
| A .....  | 28   | 3   | 2     | —      | 2    | 2   | 1    | —      | 32                    | 8          |

We have compared the results of skin tests and of leucopenic index in those cases in which the two tests were done on the same patient. Both were done with milk in 267 cases. As is seen in Fig. 7, the results agreed in 144 cases and differed in 123 cases. In the case of wheat the leucopenic index was determined in 73 cases and the results agreed in 36 cases with the results of the skin tests and differed in 37 cases.

In this respect there was no difference between the age groups. In 90 children under 1 year of age the results agreed in 47 and differed in 43 cases.

It is commonly believed that allergenicity of milk depends on

its proteins, but in some cases we have been able to prove butter to be the irritating factor. The eczema has become worse when butter is eaten, has disappeared when margarine is substituted for butter, and has appeared again after addition of butter to the diet. In one case the leucopenic index was found to be positive after butter and negative after margarine.

Taking into account the extent of the material and the number of positive skin tests, severe generalized symptoms have been few, all of them in children who have reacted to many foods. In 4 children symptoms of shock occurred in connection with skin tests or leucopenic index tests.

FIG. 9

*Incidence of breast feeding and sensitivity to milk in 500 allergic children.*

| Duration of<br>breast feeding<br>months | Number of<br>cases | %    | Average<br>breast<br>feeding | Milk-<br>sensitive | %    |
|-----------------------------------------|--------------------|------|------------------------------|--------------------|------|
| -3 .....                                | 305                | 61.0 | 63.0                         | 173                | 56.7 |
| 3-6 .....                               | 121                | 24.2 | 22.0                         | 52                 | 43.0 |
| Over 6 ...                              | 74                 | 16.8 | 15.0                         | 26                 | 35.1 |

Milder symptoms such as itch or whistling breath have occurred in connection with the tests, but as several foods were generally tested simultaneously, it is difficult to ascribe these to any particular food.

Gastrointestinal symptoms rarely occurred in our material. In those cases that have displayed such symptoms during hospitalization, they have mostly been due to infections. As soon as the infection has been cured, it has been possible to resume the usual diet, without recurrence of the symptoms.

182 patients (17 %) have been hyposensitized to foods, food allergy in these cases being considered to have some clinical importance. Fig. 8 shows that cows' milk was the commonest allergenic food; there were 158 cases hyposensitized to milk, 22 to egg. 14 children were hyposensitized to more than 1 food. Both milk and egg were given by mouth in increasing amounts during the hyposensitization. Cereals were

given subcutaneously. Other foods, such as fish, cocoa or peas were totally omitted from the diet, if they were suspected to be allergenic in any particular case.

As regards the diagnosis, it was noted that relatively the largest number of cases were hyposensitized in the group with both asthma and eczema (35 %), less in the group with eczema only (20 %), and least in the group having asthma only (8 %).

To determine the role of food allergies in each individual case, as accurate and detailed a case history as possible was first sought. The information gained was then compared with the results of the skin tests. If any food was especially suspected, a portion of it was given to the patient on trial, and the leucocyte counts and clinical symptoms were checked. As everybody, who has been engaged in these questions, knows, the history is more often than not vague, diffuse, irrelevant and not wholly reliable. The skin tests produce many positive reactions that have no clinical significance, since allergies already overcome or only to appear in future may present positive results. A decrease in the leucocyte count provoked by a special food shows the reaction of the organism at the moment of testing. If some clinical symptom can be seen after provocation, it will, of course, definitely prove the relationship. But in many cases the methods will fail, and then it is clinical observation that will give the most reliable insight into the food allergies.

#### SUMMARY

In the period 1947-1956 the Hospital for Allergic Diseases in Helsinki admitted 1076 children of 0-15 years, 381 boys and 495 girls. 404 had asthma, 539 had eczema and 133 both asthma and eczema; 154 children were under 1 year of age, 562 from 1 to 6 and 360 from 7 to 15 years old.

All the patients were tested intracutaneously with various foods.

26 children gave positive reactions to almost every food tested.

152 children (14 %) out of 1050 gave negative reactions to all foods tested and 899 (86 %) gave positive reactions to one or more foods. 168 (16 %) reacted positively to one food only. About 20,000 intracutaneous skin tests were performed and 3800 (19 %) of them were positive.

The foods giving the greatest number of positive skin reactions were in the order: cocoa, egg, milk, wheat, codfish, rye.

There were a larger number of positive skin reactions in boys than in girls.

In children who had both asthma and eczema positive skin-reactions to foods were found more frequently than in children who suffered from asthma alone.

The number of positive skin reactions to foods diminished with increasing age. This decrease was especially conspicuous with egg and milk after the first year of age.

The leucopenic index was checked after provocation tests with suspected foods in 386 cases and it was considered positive in 213. It was positive to milk in 150 out of 267 cases, and to wheat in 37 out of 73.

Severe generalized symptoms were rare (4 cases).

Gastrointestinal symptoms due to food allergy were uncommon in the material.

In 182 patients (17 %) food allergy was considered to be of clinical importance and they were hyposensitized, most of them, 158, to milk. The percentage of hyposensitized children was highest in the group with both asthma and eczema (35 %), and lowest in the group with asthma (8 %).

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