

# Diagnostic Value of Thrombopenia and Eosinophilia after Food Ingestion in Children with Milk and Egg Allergy

By

P. OSVÁTH and M. MÁRKUS

Department of Paediatrics, University Medical School, Szeged

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Although a large proportion of chronic diseases in early childhood is caused by food allergy, identification of the allergen often meets with difficulties. Accordingly, it would be desirable to design an *in vitro* diagnostic test, as those currently applied are either insensitive or detect other types of antibodies too. The anaphylactic reaction evokes significant changes in the blood counts of the experimental animal, and to a moderate degree in that of man. On this basis VAUGHAN [28] suggested the use of the leukopenic index, as a diagnostic means in enteral allergy. STORCK et al. [27] were the first to use thrombopenia as a diagnostic index, mainly in cases of drug allergy. The significance of eosinophilia in the demonstration of allergy is well established; in the diagnosis of food allergy it was first applied by HANSEN [13]. Although all three procedures have proved to be of limited value, the presumably less efficient enteral barrier and immunological response of children seemed to justify our attempt to test the validity of these procedures in cases of milk and egg intolerance.

## MATERIAL AND METHODS

Fifty-seven trials have been performed in 8 control individuals and in 35 children with allergy. All but four children were less than ten years old. In agreement with the observations of GOLDMAN *et al.* [11], the symptoms induced by a dietetic challenge were vomiting, diarrhoea, abdominal pain, spastic bronchitis, urticaria, eczema and anaphylaxis. During the three days preceding the diagnostic test the children had been fed a diet lacking the food allergen.

On the morning of the test day, fasting absolute blood eosinophil and platelet counts were determined, whereafter the children were given 200 ml of raw milk, or two soft-boiled eggs. After ingestion, blood samples were taken three times at one hour intervals. A decrease in the platelet count or an increase in the eosinophil count was expressed in percentage of the initial value. Accordingly, changes in the cell counts were divided into three categories (Table I). In case of an initial absolute eosinophil count under 100, or over 600/cu. mm, the relative values indicating the change were classified one category lower or higher, respectively. If, for example, the eosinophil count rose from 700 to 1100, it was considered a second degree increase instead of a first degree one, because of the high initial count.

The platelet count was determined by a direct method using benzocaine solution,

the eosinophil count was estimated by Randolph's modified method.

Data in the history, indicative of a causal relationship between ingestion of the food and the allergic symptoms, were also subdivided into three categories, according to their relative diagnostic value. Symptoms evidently originating from the introduction of the given food, were marked by 2 points while a possible causative relationship was marked by 1 point. This latter category involved symptoms as reluctance in taking the food, disgust, or irregular onset of some minor allergic signs. A zero marked cases in which no sign of allergy could be detected. All symptoms were classified, as described above, and the tables contain the sums derived from the following five data.

1. Symptoms occurring after the first ingestion of the food, or in the case of cow's milk, in the first two weeks after weaning.

2. Symptoms observed later by the parents.

3. Symptoms observed within the first 24 hours after the first ingestion of the food in the ward.

4. Symptoms having occurred during the clinical observation, and

5. Symptoms described by the parents after discharge from the hospital, or the cessation of symptoms in the course of the elimination diet.

As a rule, a final sum of 1 or 2 points indicated uncertain cases, 3 or 4 points

were characteristic of a latent case, and 5 more points of a manifest allergy.

TABLE I  
Evaluation of changes in cell counts

Grade	Platelet per cent	Eosinophil per cent
0	< -15	< +50
1	-15-24	+51-100
2	-25-34	+101-200
3	> -35	> +200

## RESULTS

A certain correlation could be demonstrated between the eosinophilia or thrombopenia, and the extent of the allergic state (Fig. 1). In the group characterized by 5 or more points, containing cases of regularly reproducible allergy, the incidence of thrombopenia exceeding 25%, or of eosinophilia over 100%, was significantly greater ( $p < 5\%$ ) than in the control group. In latent or uncertain cases of allergy the haematological reaction was practically the same as in the manifest cases.

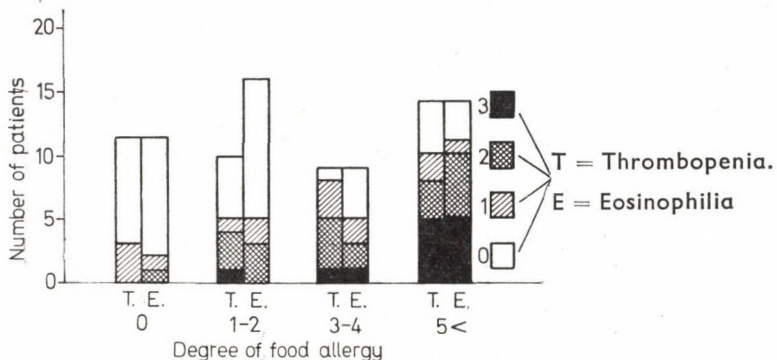


FIG. 1. Correlation between the haematological reaction and the allergic state



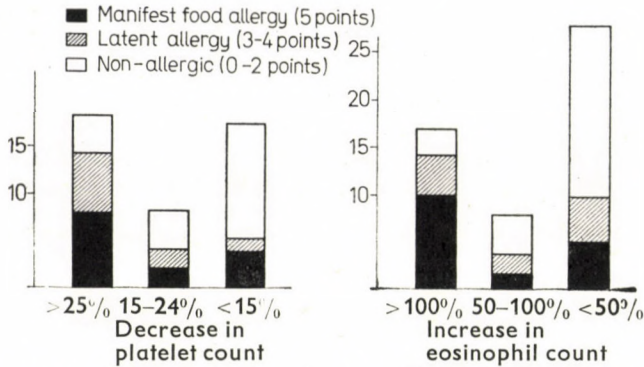


FIG. 2. Correlation between the haematological findings and the clinical symptoms

Second or 3rd degree thrombopenia or eosinophilia was accompanied by evident symptoms of allergy in one half of the cases. On the other hand, every fourth patient with negative haematological findings proved to have a marked hypersensitivity (Fig. 2). This fact is suggestive of the limited diagnostic value of any of the two tests, when applied separately.

If, however, the two types of reaction are considered simultaneously, their diagnostic value increases significantly. Thrombopenia exceeding 35% (3rd degree) together with an eosinophilia over 200% were almost always the signs of a manifest allergy,

while in cases where none of the tests attained a 2nd degree change, hypersensitivity occurred in about 10% (Fig. 3). The low specificity of a change in either the platelet count or in the eosinophil count was the result of the fact that in many cases only one of these parameters revealed significant alterations, while the other remained unaltered. Furthermore, there were two patients in whom in spite of a pronounced allergy to milk, neither eosinophilia nor thrombopenia could be demonstrated.

Repeatedly negative haematological findings were revealed in three patients with lactose intolerance, who, despite histories suggestive of milk allergy, turned out to have no intolerance to the proteins of milk.

### DISCUSSION

There is no doubt about the aetiological significance of food in allergic diseases in childhood [16]. In the majority of cases, however, it is difficult to identify the allergen, as a single dietetic challenge rarely induces

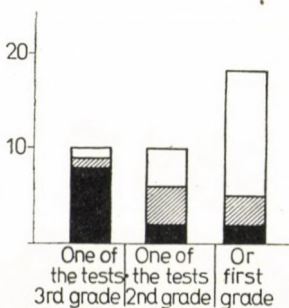


FIG. 3. Combined evaluation of the thrombopenic and eosinophilic tests



manifest clinical symptoms [5, 6, 19]. In an attempt to eliminate this difficulty in the diagnosis, we subdivided the sometimes irrelevant anamnestic and clinical data into different categories. The probability of a manifest clinical allergy was indicated by the sum derived from the weighted symptoms.

There is no agreement in literature on whether anaphylactic or "atopic" antibodies of the reagin type play a dominant role in developing the symptoms of food allergy. An alternative possibility may be the existence of several different mechanisms. This was suggested by those of our cases where only the eosinophilia was significant, as in the atopic type of allergies, while in other children only the platelet count, characteristic of anaphylactic phenomena, was reduced.

The correlation between eosinophilia and the allergic phenomena of atopic type is well established. In such cases eosinophilia is probably evoked by the soluble complex formed by the foreign protein and the antibody [4, 21].

Thrombopenia is a common finding in experimental anaphylaxis [17, 19]. The formation of platelet aggregates at the site of sensibilization has been established by microcinematography [20] and electronmicroscopy [2]. According to SALMON et al. [22] the phenomenon plays a principal role in the pathomechanism of anaphylaxis. The thrombopenia test was used by STORCK et al. [26, 27] in adults for the diagnosis of food allergy. A 15% decrease in the platelet count occurred

in the control group while a 30% decrease in allergic patients, although negative reactions also occurred in this latter group. We modified the procedure by prolonging the test period from 90 to 180 minutes. According to our results, in almost every case where in spite of the food allergy the platelet count remained normal, a significant eosinophilia could be detected. Therefore the combined use of the two tests is suggested. If, however, both the eosinophil and the platelet counts remain unaltered, which is an exceptional finding in patients with food allergy, it may be the result of a delayed hypersensitivity, a hindered gastro-intestinal passage, or of the insufficient reaction of the bone marrow.

Food allergy is presumably induced locally, by antibody forming cells in the enteral mucosa [8, 9]. Several types of diagnostic test have been suggested for the demonstration *in vitro* of hypersensitivity. It occurs only in extremely grave cases that the serum precipitates the antigen [12], while passive haemagglutination is a too sensitive procedure, yielding a positive result in a large number of asymptomatic cases [1, 14, 15, 24, 25]. COOMBS et al. [7] performed passive haemagglutination by using anti IgA globulin, thus rendering the method more reliable. DÖLEN and AAS [10] obtained unfavourable results with the diagnostic use of the basophile leukocyte degranulation in cases of intolerance to fish. The method based on passive cutaneous anaphylaxis seems to offer better results: a positive



reaction could be obtained in 65% of the sera of children with milk intolerance [6, 22].

As to diagnostic tests *in vivo*, cutaneous reactions agreed with clinical findings in 20 to 50% of the cases [13, 14, 21, 25, 28]. Our data regarding the simultaneous incidence of eosinophilia and thrombopenia in allergic patients, offer a better coincidence: a positive result was found in every four out of five cases, though there still occurred discrepancies with clinical findings. The method giving the best results is still the repeated induction of clinical symptoms.

Since malnutrition may occur with the classical chronic elimination diet, and a new, provoking food can be introduced only every 3rd or 5th day [19] it is of practical importance to observe the platelet and eosinophil counts. Furthermore, there are chronic diseases such as enterocolitis, eczema, or bronchitis, where the beneficial effects of an elimination diet are even more delayed; the onset of anatomical restitution may take several weeks.

In such chronic cases and in patients with a latent allergy to a common food allergen, the combined eosinophilia and thrombopenia test is especially useful in giving preliminary information. Consequently, an appropriate diet can be prescribed, but the final evidence of the existence of a

food allergy will be provided only by the effect of the diet.

#### SUMMARY

The eosinophil and platelet counts were examined in children with milk or egg allergy, and in a control group. Blood samples were taken before food ingestion, and in the consecutive three hours at one hour intervals. In children with manifest allergy, an increase in the eosinophil count, or a decrease in the platelet count, exceeding 100 and 25% respectively, occurred in a significantly larger number than in the control group. The changes of the same parameters when exceeding 200 or 35%, respectively, were suggestive of a manifest allergy in 80% of the cases. Since in a number of patients only one of the parameters had changed, the combined use of the two tests seems to be of a greater diagnostic value.

The demonstration of haematological changes in food allergy cannot replace the diagnostic test of repeated challenges with the allergen. It is, however, a valuable means for shortening the necessary period of hospitalization, and in drawing attention upon the presence of an allergen in the food, in the case of a chronic allergic disease.

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Dr. P. OSVÁTH  
Gyermekklinika  
Szeged, Hungary