

BLOOD STUDIES IN ALLERGY

IV. VARIATIONS IN EOSINOPHILES FOLLOWING TEST FEEDING OF FOODS

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THE changes in the total leucocytes following the trial feeding of foods have been extensively studied since Vaughan¹ suggested the leucopenic index as a diagnostic method in food allergy. Variations in the eosinophiles have received far less attention. Squier and Madison,² in 1937, measured the eosinophile response occurring after the trial ingestion of allergenic foods by means of a white cell diluting fluid consisting of:

1 per cent eosin in water	5.0
Acetone	5.0
Distilled water	100.0

a method originally described by Dunger³ as modified by Camara and Alvarez.⁴ They reported that, following the ingestion of allergenic foods, an increase in circulating eosinophiles occurs as constantly as does a reduction of the total leucocytes and that the simultaneous counting of both eosinophiles and leucocytes increases the diagnostic accuracy of the leucopenic index. Inasmuch as Squier and Madison reported upon the use of an entirely different type of diluting fluid than that used by other investigators, this technique must be subjected to a careful study in order to understand their results.

In attempting to use this diluting fluid containing eosin, acetone, and distilled water, one immediately encounters difficulties in that the leucocytes rapidly undergo changes in the counting chamber which materially reduce their visibility. For this reason it is imperative to perform the total leucocyte count immediately after the blood is diluted in the pipette. Presumably because of this observation, both Dunger³ and von Domarus⁵ advised against attempting to enumerate the total leucocytes in similar eosin, acetone, hypotonic diluents.

A study of individual cells under high magnification (oil immersion) reveals the fact that all types of leucocytes rapidly increase in size and explode within a period of two or three minutes from the time the blood sample is mixed.⁶ The rupture of the cell membrane suddenly alters the refraction of light and accounts for the rapid fading of individual cells as observed under low magnification. This phenomenon explains the observation that one generally enumerates fewer cells in the final corner area than in the area initially counted and the fact that total leucocyte counts by this method are consistently slightly lower than parallel white cell counts with the standard acetic acid diluent even though the enumeration is started immediately after mixing and is completed with maximum speed.

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The counting chamber estimation of eosinophiles by means of this diluent also remains subject to error in that the ruptured or "ghost" cells are identified by clumps of eosin-staining granules retained in a crescent-shaped portion of the cell membrane. One encounters indeterminate forms that cannot with certainty be classified as eosinophiles. In addition, a greater absolute number of eosinophiles is usually obtained from this method than from performing parallel stained film differential counts. The latter point may not necessarily be a criticism of this method, as we have also observed higher eosinophile counts from the counting chamber than from the stained film in dealing with eosinophile values below 500 cells per cubic millimeter of blood, using a phloxine-glycol diluent in which there is no question regarding the differentiation of eosinophiles.

In data as yet unpublished, Squier⁸ agrees that the method does not give an accurate enumeration of true eosinophiles. He is of the opinion that, at least under certain circumstances, cells other than eosinophiles take an eosin stain, and he refers to eosin-staining cells rather than to eosinophiles. However, in their original communication, Squier and Madison reported a definite eosinophilia in 95.9 per cent of seventy-four ingestion tests which showed a fall in leucocytes of 1,000 cells or more, whereas an increase in eosinophiles occurred in only 2.2 per cent of eighty-eight negative cases coincident with a normal digestive leucocytosis. In their observations, the peak in the rise of the eosinophiles usually occurred thirty minutes after the ingestion of the allergenic food and remained above the initial level at the end of the ninety-minute test period.

The objections to the use of the eosin-containing hypotonic diluent under consideration refer to the quantitative enumeration of leucocytes and eosinophiles as compared with standard methods. The errors inherent in the method become less significant and might be expected to occur to a similar degree in all samples when the technique is used as advised by Squier and Madison, namely in making serial blood observations prior to and following the trial ingestion of a test food, providing the determinations are made with a short but constant time interval elapsing between the dilution of the sample and the completion of the counting and providing the work is done by a technician thoroughly familiar with this exacting routine and devoting her time exclusively to it. Under these circumstances, trial ingestion of specific foods is followed by variations in the blood findings which afford reliable evidence of the present status of allergic tolerance or intolerance. This opinion is based upon the daily use of the technique described over a period of three years during which I was associated in practice with Dr. Squier.

With this procedure, one obtains the postprandial leucocytosis of the compatible reaction and the neutropenia of the incompatible response as described by Vaughan,^{1, 9} Rinkel,¹⁰ Zeller,¹¹ and others. It also affords, as recently pointed out by Squier,¹² the additional measurement of an apparent increased fragility of white blood cells accompanying the incompatible food response. This is presumably due to the more rapid fading or rupturing of leucocytes associated with the allergic reaction to foods, and accounts for the greater degree of neutropenia postprandially than is found in parallel measurements with standard diluents. For instance, one may obtain preingestion total leucocyte counts with

the hypotonic diluent 10 per cent lower than with the standard diluting fluid, whereas at the peak of the blood response, following the ingestion of an allergenic food, the counts by the two methods may differ by as much as 50 per cent. This variation may or may not be accompanied by the precipitation of definite allergic symptoms, but in practice this finding generally indicates an incompatible food. Conversely, no such disparity exists between the pre- and post-ingestion parallel determinations after the feeding of a food clinically tolerated, nor have allergic symptoms been observed to follow the ingestion of a food in the presence of a leucocytosis as measured by this method.

The development of a diluting fluid containing phloxine and methylene blue dissolved in equal parts propylene glycol and water^{6, 10} permitted the accurate counting chamber differentiation and enumeration of eosinophiles in the same blood specimen used in counting the total leucocytes, with the further advantage that either procedure might be performed at varying intervals after the dilution of the blood sample. The enumeration of the eosinophiles on one side of the counting chamber (0.9 cu. mm.) proved to be a more accurate method of counting these cells than determining their number from a 200 cell stained film differential count.⁷ We also showed that total leucocyte counts by this technique agreed closely with the results of parallel counts performed with the standard acetic acid diluent, both in normal and abnormal blood.⁹ In the latter study, there were several cases of leucemia in which extremely fragile leucocytes were observed.

This method was then applied to measure the eosinophile and total leucocyte response following the trial ingestion of food. After early experiments the following technique was adopted: Cases of uncontrolled clinical allergy with unknown food sensitivities were used. The food to be tested had been included in the diet until four days prior to the test, then was completely avoided for four days and tested on the fifth. All food, medications, and tobacco were omitted five hours prior to the test. After resting in the sitting position for thirty minutes, two base line blood observations were made. An average to large serving of food was eaten within a period of five minutes, and repeated blood observations were made twenty, forty, and sixty minutes following the completion of the test meal. If symptoms had not been produced within the first hour after test feeding, a second serving was fed, and the patient was kept under clinical observation for an additional thirty minutes. A small group of cases was studied similarly except that blood counts were made for prolonged intervals after a single feeding. Another group including normal persons was followed; in this case blood counts were made for an hour after each of the two feedings.

Each blood observation per case was made by the same technician, employing the same pipette and counting chamber; it included the enumeration of the eosinophiles in the ruled area of the two sides of the counting chamber (1.8 cu. mm.) and the total leucocytes of the eight squares or the four corner areas on both sides of the counting chamber. The average of the preingestion counts was taken as the base line, and only in this respect did the technique differ from

that recently advocated by Rinkel.¹⁵ In the graphic representation of results, a square equals 100 eosinophiles and 1,000 leucocytes. We have found that it is advantageous to express the change occurring in the total leucocyte count in terms of the percentage variation from the basal observations, a type of representation which will be employed in future communications.¹⁶ However, in the present study variations in the leucocytes from the base line level will be represented in absolute figures inasmuch as it is desirable to show the absolute variation occurring in the eosinophile counts.

The individual food tests were classified as compatible, incompatible, or indeterminate, dependent upon variations in the total leucocyte counts. Although the interpretation of these reactions will be discussed in detail elsewhere,¹⁶ it may be stated that an incompatible response is characterized by a postingestion neutropenia of 10 per cent or greater as compared with the average of the two preingestion counts and that a compatible response is associated with a postprandial increase in total leucocytes.

THE EOSINOPHILE RESPONSE IN ALLERGIC INDIVIDUALS DURING THE
FIRST HOUR FOLLOWING TRIAL INGESTION

The first 75 compatible and 75 incompatible tests were selected for analysis. Symptoms were produced following trial feeding in 47 or 62.7 per cent of the first group. Allergic symptoms were not accentuated or reproduced in the remaining 28 cases (37.3 per cent) or in any of the 75 determinations associated with a digestive leucocytosis.

TABLE I. THE MEAN NUMBER OF EOSINOPHILES PER CUBIC MILLIMETER OF BLOOD IN PRE- AND POSTINGESTION DETERMINATIONS OF 75 INCOMPATIBLE AND 75 COMPATIBLE INDIVIDUAL FEEDING TESTS

	AVERAGE NUMBER OF EOSINOPHILES PER CUBIC MILLIMETER OF BLOOD			
	PREINGESTION	POSTINGESTION		
	AVERAGE OF TWO DETERMINATIONS	20 MINUTE	40 MINUTE	60 MINUTE
Incompatible	290.8	273.1	280.2	281.5
Compatible	287.1	280.9	279.6	292.3

The mean pre- and postingestion eosinophile values, as shown in Table I, are in close agreement in spite of the fact that the average postingestion total leucocyte counts were below the fasting levels in the incompatible group and above the basal levels in the compatible tests.

The eosinophile counts in a representative group of cases with unquestioned evidence of clinical sensitivity are shown in Table II. In each instance the total leucocyte count showed a postprandial leucopenia of 10 per cent or greater. These cases are listed in the order in which allergic manifestations developed after a single feeding; those patients in whom symptoms did not occur during the first hour received a second feeding. The evidence of clinical sensitivity in those who failed to develop symptoms following the test was based upon allergic intolerance as a result of cumulative feeding. The preponderance of the relatively high eosinophile counts is deliberate. Cases with counts below 100 cells

TABLE II. EOSINOPHILES EXPRESSED IN ABSOLUTE VALUES AND IN PERCENTAGE OF THE TOTAL LEUCOCYTE COUNT PRIOR TO AND FOLLOWING THE INGESTION OF ALLERGENIC FOODS

NO.	CASE	FOOD	EOSINOPHILES PER CUBIC MILLIMETER OF BLOOD										CLINICAL REACTIONS	
			PREINGESTION					POSTINGESTION						
			PER CUM.MM.		PER CENT		20 MIN.		40 MIN.		60 MIN.			
PER CUM.MM.	PER CENT	PER CUM.MM.	PER CENT	PER CUM.MM.	PER CENT	PER CUM.MM.	PER CENT	PER CUM.MM.	PER CENT	ONSET	DESCRIPTION AND DURATION			
1	B. B.	Milk	333	5.7	322	5.7	377	7.0	521	6.4	366	4.9	3 min.	Abdominal cramps throughout test
2	G. E.	Wheat	660	9.0	644	9.1	455	7.4	710	9.2	810	9.2	5 min.	Severe coughing 5 minutes
3	L. T.	Wheat	455	5.2	522	6.2	522	7.3	610	8.8	488	5.4	5 min.	Coughing throughout test
4	H. M.	Wheat	344	4.0	444	5.5	244	3.1	333	4.8	355	4.2	8 min.	Sneezing, rhinorrhea throughout test
5	L. P.	Milk	377	3.7	377	3.7	355	3.8	433	5.1	288	2.9	10 min.	Abdominal distress throughout test
6	E. S.	Wheat	311	4.1	288	4.1	266	5.0	288	5.7	288	4.5	10 min.	Nasal stuffiness throughout test
7	H. L.	Wheat	610	6.4	655	6.9	721	7.9	644	7.9	744	7.5	15 min.	Stuffy nose Coughing throughout test
8	H. L.	Milk	444	4.1	466	4.3	400	4.1	566	5.8	533	5.2	20 min.	Nasal stuffiness throughout test
9	K. R.	Wheat	1154	14.2	1088	13.6	1088	13.9	821	12.2	844	11.4	20 min.	Sneezing throughout test
10	J. B.	Wheat	122	1.6	122	1.6	67	0.7	89	1.5	89	1.4	24 min.	Severe head pain throughout test
11	R. H.	Rye	299	2.9	277	2.6	333	3.1	433	6.2	344	4.5	25 min.	Nasal stuffiness 10 minutes
12	H. E.	Milk	2586	20.0	2508	19.9	2175	19.1	2342	21.1	1898	16.0	30 min.	Asthma throughout test
13	D. C.	Egg	189	1.7	211	1.9	178	1.8	200	2.1	222	2.2	40 min.	Sneezing, coughing 3 minutes
14	R. H.	Egg	400	5.7	444	5.8	289	4.8	289	4.7	311	4.1	5 hr.	Urticaria
15	A. S.	Milk	177	1.8	166	1.8	100	1.3	277	2.8	211	1.9	60 min.	Rhinorrhea
16	A. S.	Orange	155	2.3	144	2.6	100	1.7	55	0.7	144	2.1	70 min.	Headache
17	M. T.	Milk	111	1.5	89	1.4	44	0.6	0	0	111	1.1	4 hr.	Flare of eczema
18	R. H.	Chicken	444	6.6	366	5.5	266	4.5	532	6.7	710	8.8	2 hr.	Headache, fatigue
19	H. S.	Beef	222	2.5	222	2.4	355	4.6	333	4.0	311	3.8	4 hr.	Flare of eczema
20	T. C.	Wheat	510	7.1	499	7.3	566	9.1	511	9.3	488	7.1	2 hr.	Dizziness
21	J. K.	Beef	222	2.8	189	2.5	200	3.2	200	2.8	177	2.3	3 hr.	Severe headache
22	J. K.	Wheat	244	3.3	233	3.4	233	3.2	233	4.2	166	2.8	4 hr.	Itching lips, coughing
23	H. L.	Egg	488	4.3	533	4.8	932	8.7	943	10.0	677	6.0	7 hr.	Giant hives
24	R. H.	Orange	388	3.9	388	3.9	377	5.8	333	4.7	275	3.8	7 hr.	Urticaria
25	R. H.	Wheat	533	5.4	444	4.9	264	4.9	155	2.9	311	4.2	7 hr.	Rhinitis from cumulative feeding

per cubic millimeter, although frequently encountered, were not included because the small number of cells permitted relatively less accurate eosinophile determinations.

Although one may note marked differences between individual tests, the evidence presented leads to the conclusion that the trial ingestion of allergenic foods is not associated with constant variations in the blood eosinophiles as observed during the first hour after feeding. Neither was there any constancy of the eosinophile response in allergic individuals during the first hour following trial feeding of clinically proved compatible foods which might be employed to characterize a negative response.

These findings may appear at variance with the early report of Squier and Madison² although such is actually not the case, as the eosin containing hypotonic diluent they employed does not permit a quantitative measurement of true eosinophiles. Squier⁸ is of the further opinion, with which the author concurs, that there is a rough parallelism between the number of eosinophile-like cells and the increased fragility of leucocytes occurring after the ingestion of allergenic foods as measured by his technique.

THE EOSINOPHILE RESPONSE IN ALLERGIC INDIVIDUALS FOLLOWED FOR SEVERAL
HOURS AFTER THE SINGLE FEEDING OF AN ALLERGENIC FOOD

A smaller group of cases was studied by obtaining total leucocyte and eosinophile counts at frequent intervals for two hours and then hourly for as long as ten hours following test feeding; otherwise the technique was identical with that previously described. Striking changes in eosinophiles were observed in a few cases which developed sharp but transient allergic symptoms following trial ingestion; these consisted of an initial diminution of eosinophiles concurrent with the acute reaction, followed by a delayed eosinophilia which developed after the acute reaction had subsided. The various phases of this response are usually not observed during the first hour after trial feeding although Case 2 in Table II is a good example. Delayed reactions of this type are illustrated by repeated observations in a single case shown in Fig. 1 and Table III.

TABLE III. VARIATIONS IN EOSINOPHILES FOLLOWING THE SINGLE FEEDING OF AN ALLERGIC FOOD, MILK

TIME OF TEST	EOSINOPHILES (PER CU. MM.)	EOSINOPHILES (%)	SYMPTOMS
<i>Prior to Feeding</i>			
20 minutes	89	1.3	None
5 minutes	89	1.3	None
<i>After Feeding</i>			
20 minutes	122	1.8	None
40 minutes	189	2.7	None
60 minutes	277	4.2	Coughing
80 minutes	178	2.9	Mild asthma
100 minutes	155	2.4	Mild asthma
2 hours	400	6.2	Symptom free
3 hours	422	6.0	Symptom free
4 hours	433	6.3	Symptom free
5 hours	400	5.1	Symptom free
6 hours	488	6.4	Symptom free
7 hours	444	6.2	Symptom free

This patient, M. K., aged 43 years, with a diagnosis of bronchial asthma, had been subject to violent paroxysms of coughing for six weeks prior to his first visit in early July, 1943. Severe attacks of coughing and dyspnea occurred regularly soon after the evening meal, which invariably contained two eggs. The severity of his symptoms may be judged by the fact that he lost 20 pounds during a period of six weeks and that, upon three different occasions, loss of consciousness followed a paroxysm of coughing and dyspnea. The avoidance of eggs resulted in complete relief of symptoms and, prior to prolonged avoidance, each subsequent attempt to eat eggs was followed by a recurrence of coughing and dyspnea. The initial feeding test with eggs, in October, 1943, was performed after four days of specific avoidance.

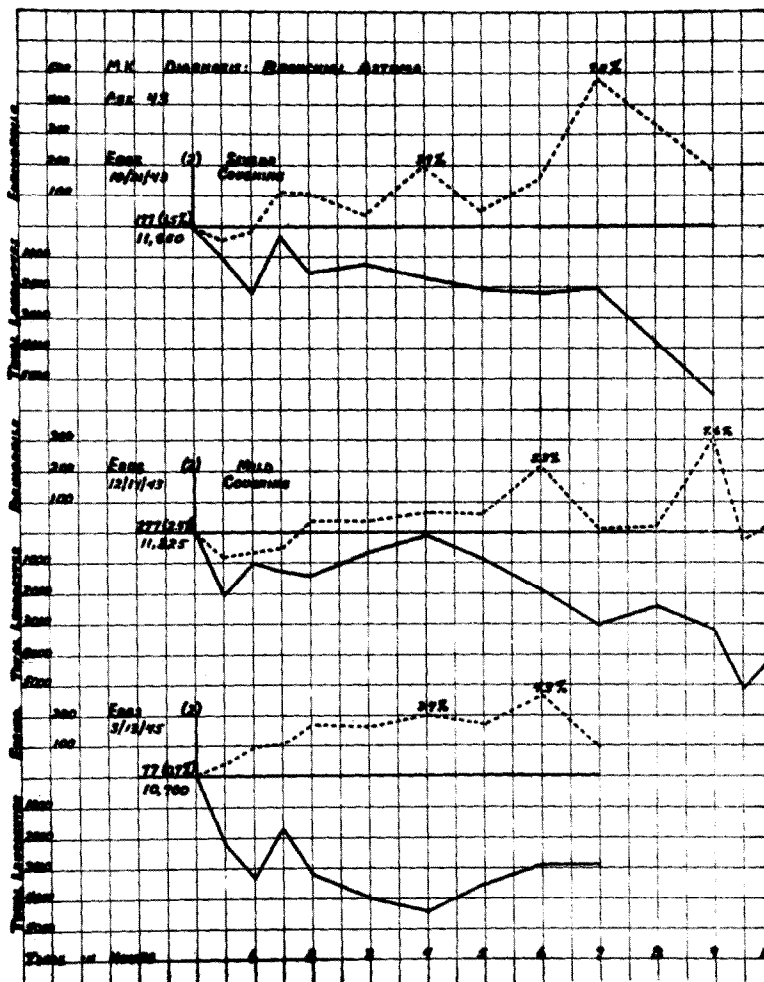


Fig. 1.—Repeated individual feeding tests with eggs in an egg-sensitive patient, showing a delayed eosinophilia and neutropenia.

As may be noted, the initial diminution of eosinophiles and total leucocytes coincided with an acute paroxysm of coughing; this was followed by a delayed eosinophilia and an eventual neutropenia of 5,000 cells. Differential counts by the stained film and counting chamber techniques showed that the reduction of total leucocytes was due entirely to a decrease in polymorphonuclear leucocytes.

After six weeks of complete egg avoidance, during which time he regained 12 of the 20 pounds that he had lost, eggs were returned in a single meal and tolerated. A second

individual feeding test four days later was associated with transient coughing and blood findings similar to those in the first test. It is of interest that the eosinophile response, although of similar pattern, developed more slowly in the second test.

With the complete avoidance of eggs he remained symptom free until the sudden recurrence of coughing, dyspnea, and orthopnea in late May, 1944. During this interval he had doubled his milk intake by drinking six to eight glasses per day. After noting that an attack of asthma and increased phlegm in the throat followed the ingestion of two glasses of milk taken while fasting, milk was eliminated for four days, and the patient was tested on the fifth day. He developed an acute paroxysm of coughing beginning fifty minutes after ingestion which persisted for an hour. The changes in the eosinophile values are shown in Table III. It is of interest that, although the eosinophiles showed an initial increase from the base line level of 89 per cubic millimeter of blood prior to the onset of symptoms, the total number dropped off significantly during the period of allergic reaction. The eosinophiles then rose sharply with the subsidence of coughing, eventually reaching a peak of 488 per cubic millimeter at six hours.

With the avoidance of both eggs and milk, he has remained symptom free except for coughing after eating ice cream in November, 1944. In recent months both eggs and milk have been clinically tolerated in cooking when used once a week.

Two eggs were eaten five days prior to the final egg test in March, 1945, the result of which is shown in the third graph of Fig. 1. Symptoms did not occur after either the preparatory or the test feedings, presumably because of some acquired tolerance as a result of prolonged avoidance. The progressive increase in eosinophiles in the absence of symptoms is in contrast to the two previous egg tests and the milk test in which transitory decreases in eosinophiles were associated with the production of allergic symptoms. The eventual eosinophilia in these observations is particularly striking in view of the coincident neutropenia.

The constant pattern of the total leucocyte response should be emphasized. Although the variations occurred at different time intervals with the three egg feeding tests, each was characterized by an initial sharp neutropenia, then a compensatory upswing, and eventually a progressive neutropenia.

THE EOSINOPHILE RESPONSE IN NORMAL AND ALLERGIC INDIVIDUALS FOLLOWING REPEATED FEEDINGS

Fifteen normal, nonallergic persons, either medical students or younger members of the hospital staff, were subjected to the test technique as originally described, with the exception that eosinophile and total leucocyte counts were obtained twenty, forty, and sixty minutes after each of two successive feedings. The eosinophile values for this group are shown in Table IV.

It is evident that there is not a significant or constant variation in the eosinophile values following either feeding, although there is a slight diminution of the mean values at the twenty-minute observation in each series. The variations in the total leucocyte counts will be reported as controls in another publication; in the majority of instances the total white blood count either showed no change or showed a postprandial increase over the fasting level. Two cases showed a decrease of 300 and 400 cells in the respective initial twenty-minute counts.

In a group of allergic patients studied similarly, there were no constant variations in the eosinophiles following the ingestion of double doses of either compatible or incompatible foods. One case, showing an interesting variation in the eosinophiles after the second feeding coincident with a sharp clinical reaction, will serve as an illustration of a type of reaction sometimes encountered.

W. S., a man, aged 63 years, had been subject to perennial allergic rhinitis for fifteen years, complicated by nasal polyposis and frequent sinus infections. He had had almost continuous asthma since its inception in 1942. When first seen he had been hospitalized for ten weeks with asthma of sufficient severity to require special nursing care and intermittent oxygen therapy. One feature of his hospital routine had been the daily intake of three or four egg-nogs as part of a high caloric diet. Although he was dust sensitive clinically and by skin test, dust avoidance and hyposensitization for a period of two years had failed to relieve his asthma.

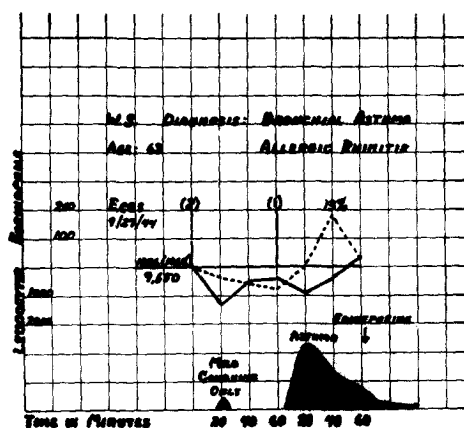


Fig. 2.—Individual feeding test with egg in an egg-sensitive asthmatic patient. The second feeding precipitated a sharp attack of asthma which was followed by eosinophilia.

While in the hospital he was placed on a synthetic diet of the type advocated by Olmsted, Harford, and Hampton.¹⁷ Improvement in the asthma was noted on the third day and progressed to the point that he was asthma-free prior to an egg feeding test on the sixth day of the special diet. The record of the blood findings and symptoms is shown graphically in Fig. 2. Although he coughed a few times twenty minutes after the first dose, the patient did not regard this as significant. Coughing recurred ten minutes after the second dose and rapidly progressed into a violent attack of asthma. The severity of the attack had subsided materially by the time of the second forty-minute count, although he still had sufficient asthma at the completion of the hour to warrant the administration of epinephrine. While avoiding eggs, potato, and lamb he has remained free from troublesome asthma for over six months. The latter two foods were returned and have been tolerated in moderation. The rhinitis did not come under control with diet management and the continuation of his program of dust avoidance for a trial period of two months. He has been made more comfortable in this respect with house dust hyposensitization.

This patient developed the initial decrease in eosinophiles as previously described. The sharp increases in these cells from a level of 955 (10.3 per cent) prior to the second feeding to a peak of 1,210 (13 per cent) following the most acute phase of his asthma is of particular interest in view of the severity of the clinical response. It is a common experience to precipitate acute allergic symptoms within a few minutes following the repeated feeding of a food which was

TABLE IV. EOSINOPHILES EXPRESSED IN ABSOLUTE VALUES AND IN PERCENTAGE OF THE TOTAL LEUCOCYTE COUNT PRIOR TO AND FOLLOWING THE INGESTION OF FOOD IN NORMAL, NONALLERGIC INDIVIDUALS

		EOSINOPHILES PER CUBIC MILLIMETER OF BLOOD																	
CASE	FOOD	PREINGESTION						POSTINGESTION											
		20 MIN.			40 MIN.			60 MIN.			20 MIN.			40 MIN.			60 MIN.		
		PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CU. MM.	PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CU. MM.	PER CENT	PER CENT
M.	Orange	178	2.4	166	2.1	200	2.7	255	3.3	255	3.3	178	2.2	211	2.8	200	2.7		
	Tomato	144	1.7	122	1.4	144	1.7	144	1.8	144	1.6	144	1.6	188	2.2	155	1.9		
W.	Wheat	155	3.4	178	3.2	89	1.5	144	2.6	166	2.8	100	2.1	133	2.8	155	3.3		
	Eggs	122	2.5	89	1.9	89	1.5	44	0.9	89	1.6	78	1.5	89	1.7	89	1.8		
S.	Orange	289	3.4	289	3.6	277	3.4	355	4.4	333	4.0	322	3.7	388	4.7	322	3.9		
	Potato	322	3.7	322	3.9	277	3.1	344	4.0	344	3.9	255	3.0	277	3.2	344	4.0		
D.	Milk	78	0.9	89	1.0	89	1.0	144	1.4	133	1.4	100	1.1	155	1.6	100	1.0		
	Eggs	233	2.6	211	2.5	222	2.1	233	2.5	311	3.1	266	2.5	222	2.1	222	2.2		
R.	Potato	144	2.1	122	1.7	100	1.5	111	1.7	111	1.4	100	1.4	111	1.5	144	2.1		
	Orange	89	1.5	89	1.4	89	1.5	78	1.3	100	1.5	89	1.9	89	1.4	89	1.4		
L.	Tomato	100	1.3	67	0.9	67	0.8	78	1.0	78	0.9	89	1.2	78	1.0	89	1.1		
	Potato	67	0.8	67	0.8	56	0.6	78	0.9	67	0.8	89	0.8	56	0.6	67	0.8		
Di.	Orange	255	3.4	222	3.1	266	3.4	233	3.0	178	2.5	189	2.6	211	2.8	200	2.7		
N.	Potato	122	1.7	178	2.4	233	3.4	189	2.4	233	3.1	244	3.0	189	2.5	255	3.2		
Ra.	Orange	155	1.8	178	2.2	144	1.5	189	2.3	155	1.8	189	2.2	200	2.4	200	2.4		
Mean		163.5		159.1		156.1		175.4		179.8		163.5		173.2		175.4			

either tolerated without symptoms or resulted in equivocal manifestations in the initial fasting dose. From evidence in other cases, a blood response of this type is not an uncommon finding; variations of this type are less apparent when the number of eosinophiles is within normal limits. Under these circumstances there may be no significant variation in the eosinophiles in spite of the production of acute allergic symptoms.

DISCUSSION

The postingestion eosinopenia occurring simultaneously with the production of acute allergic symptoms, followed by a delayed eosinophilia as the symptoms subside, is identical with the hematological and clinical response recently observed in cases of drug allergy.¹² A similar "S" type of eosinophile curve, characterized by an early decrease in cells coincident with allergic symptoms and a delayed eosinophilia, was observed to follow the trial ingestion of specific sulfonamides in cases of known sensitivity. It should be mentioned, although this phase will be discussed in detail elsewhere, that the total leucocytes also show a similarity of response following the trial ingestion of foods and drugs (sulfonamides). In general the hematological changes are less abrupt and show less extensive "swings" following the ingestion of specific foods, an observation in keeping with the fact that the precipitated clinical reactions of food testing by trial ingestion are less violent than those observed in cases of drug sensitivity. The two cases of food sensitivity reported in detail in the present study are characterized by a high degree of specific sensitivity. It is advantageous to observe the pattern of hematological response in such instances, for less evident variations from this pattern might be expected to occur in cases with lesser degrees of sensitivity or in patients with lower eosinophile counts.

This type of blood response appears reasonable if one thinks of the blood as a carrier of eosinophiles between the points of origin and the points of need. In view of the well-substantiated observations that eosinophiles tend to collect at the shock organ site early in the process of an allergic reaction,¹³ one might assume that this localization is associated with a reduction of the number in the peripheral blood. One might further speculate that, in response to a demand for eosinophiles, these cells would be released into the blood stream either from the bone marrow or possibly other reservoirs. The work of Kline, Cohen, and Rudolph¹⁴ indicates that the eosinophile apparently fulfills its function early in the course of the acute allergic reaction. They found the eosinophile to be the first cell type to arrive at the site of induced ragweed wheals in ragweed-sensitive persons and the first to leave the site of reaction as determined by serial biopsies. As symptoms of the food or drug reaction abate and the demand subsides, a temporary excess of eosinophiles might conceivably develop in the peripheral blood; these might come either from the subsiding allergic reaction site or as a result of the continued increased supply in the presence of a lessened demand. Of course, both factors and possibly others may be operating.

The evidence obtained from sharp food and drug reactions appears to substantiate this theory. It should be emphasized, however, that there are no significant variations in the levels of eosinophiles during the first hour following

the trial ingestion of foods. The initial diminution of these cells most clearly observed in certain acute allergic reactions, has been observed to occur to the same degree in reactions to foods which are clinically compatible, and suggestive changes of the same type may be found in some normal, nonallergic persons following trial ingestion of foods. There seems to be no suggestion that one may follow the eosinophiles and obtain evidence of diagnostic importance from variations during the first hour following trial feeding. There is a suggestion that certain allergic individuals develop a delayed increase in eosinophiles postprandially as a part of the reaction of specific allergic intolerance and that this response may take the form of a smooth curve in the event that allergic symptoms are not precipitated. How often this type of response occurs is speculative, but that it does occur there can be little doubt. The delayed eosinophilia, occurring after acute allergic symptoms have begun to subside, remains the most striking quantitative variation in the blood eosinophiles that has been observed.

SUMMARY

1. Observations of the eosinophiles in the peripheral blood following trial ingestion of food are reported in allergic and normal persons.

2. The eosinophiles were enumerated in the counting chamber by means of a white blood cell diluting fluid containing phloxine and methylene blue dissolved in equal parts propylene glycol and water.

3. Certain allergic individuals who develop acute symptoms following the trial ingestion of food show a decrease of eosinophiles coincident with the clinical reaction and, as the symptoms subside, develop a delayed eosinophilia.

4. This response is similar to that observed following trial ingestion of allergenic drugs in cases of known sensitivity. It is seen most clearly in cases of acute reactions of short duration, and the entire response is not commonly observed during the first hour after feeding.

5. This is by no means a constant finding following the ingestion of an allergenic food; it occurs more clearly in some allergic individuals than in others.

6. Single or repeated feedings in normal persons or the ingestion of compatible foods in allergic patients are not followed by a characteristic or constant variation in the level of eosinophiles.

REFERENCES

1. Vaughan, W. T.: Food Allergens. III. The Leucopenic Index, Preliminary Report, *J. ALLERGY* 5: 601, 1934.
2. Squier, T. L., and Madison, F. J.: The Hematologic Response in Food Allergy; Eosinophilia in the Leucopenic Index, *J. ALLERGY* 8: 250, 1937.
3. Dunger, R.: Eine einfache Methode der Sählung der eisinophilen Leukozyten und der praktische Wert dieser Untersuchung, *München. med. Wchnschr.* 57: 1942, 1910.
4. Camara, P., and Alvarez, J. G.: Investigaciones sobre la langre "in vitro," *Arch. cardio. y hemat.* 13: 315, 1932.
5. von Domarus, A.: Die Bedeutung der Kammerzählung der Eosinophilen für die Klinik, *Deutsches Arch. f. klin. Med.* 171: 333, 1931.
6. Randolph, T. G.: Blood Studies in Allergy. I. The Direct Counting Chamber Determination of Eosinophiles by Propylene Glycol Aqueous Strains, *J. ALLERGY* 15: 89, 1944.
7. Randolph, T. G., and Stanton, C. L.: A Comparison of Differential Counts From the Stained Film and Counting Chamber Using a Propylene Glycol Aqueous Stain, *Am. J. Clin. Path.* 15: 17, 1945.

8. Squier, T. L.: Personal communication.
9. Vaughan, W. T.: Further Studies on the Leucopenic Index in Food Allergy, *J. ALLERGY* 6: 78, 1934.
10. Rinkel, H. J.: The Leucopenic Index in Allergic Diseases, *J. ALLERGY* 7: 356, 1936.
11. Zeller, M.: The Leucopenic Index in Intractable Asthma, *Illinois M. J.* 69: 54, 1936.
12. Squier, T. L.: Hematologic Manifestations of Hypersensitive States, *Virginia M. Monthly* 72: 67, 1945.
13. Randolph, T. G.: Enumeration and Differentiation of Leucocytes in the Counting Chamber With Propylene Glycol Aqueous Stains, *Proc. Soc. Exper. Biol. & Med.* 52: 20, 1943.
14. Mallery, O. T., Jr., and Randolph, T. G.: The Effect in Vitro of Propylene Glycol on Leucocytes, *J. Lab. & Clin. Med.* 29: 203, 1944.
15. Rinkel, H. J.: Food Allergy. II. The Technique and Clinical Application of Individual Food Tests, *Ann. Allergy* 2: 504, 1944.
16. Randolph, T. G., and Rawling, F. F. A.: Blood Studies in Allergy. V. Variations in Total Leucocytes Following the Test Feeding of Foods. (In preparation.)
17. Olmsted, W. H., Harford, C. G., and Hampton, S. F.: Use of Synthetic Diet for Food Allergy and Typhoid, *Arch. Int. Med.* 73: 341, 1944.
18. Randolph, T. G., and Rawling, F. F. A.: Blood Studies in Allergy. III. Cellular Reactions in Sulfonamide Sensitivity, *J. ALLERGY* 16: 17, 1945.
19. Kline, B. S., Cohen, M. B., and Rudolph, J. A.: Histologic Changes in Allergic and Non-Allergic Wheals, *J. ALLERGY* 3: 531, 1932.