

## Studies on the release of histamine from basophils.

### 3. Correlation between basophil reactivity to anti-IgE and blood eosinophilia.

Yoshiro TANIZAKI, Haruki KOMAGOE, Michiyasu SUDO,

Masaaki MIFUNE and Hiroshi MORINAGA

Department of Medicine, Okayama University  
Medical School, Misasa Branch Hospital

Saburo NAKAGAWA, Hikaru KITANI and Ikuro KIMURA

2nd Department of Medicine, Okayama University Medical School

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#### Introduction

Blood eosinophilia is common in immediate allergic diseases. Mast cells and basophils, when these cells are activated by specific allergen and anti-IgE, release histamine, SRS-A, PAF (platelet activating factor) and ECF-A (eosinophil chemotactic factor of anaphylaxis). Thus, there is a close correlation between IgE-mediated reaction and blood eosinophilia. While, IgE-mediated histamine release from basophils is one of the parameters representing immediate hypersensitivity (PRUZANSKY, J.J. et al., 1967, LICHTENSTEIN, L. M., et al. 1964) In the present study, relationship between anti-IgE-induced histamine-release from basophils and blood eosinophilia was discussed in patients with bronchial asthma.

#### Subjects and Materials

14 patients with bronchial asthma were selected in the present study. All of them showed blood eosinophilia of more than 8%. The subjects were divided into two groups; group I and group II. Group I comprised asthmatic subjects with positive skin test to house dust and/or the other allergens, and positive radioimmunosorbent test (RAST) to house dust. On the other hand, group II comprised asthmatic cases with negative skin

Table 1. Asthmatic subjects classified by skin test and RAST score to house dust

	Skin test	RAST (HD)	Blood eosinophils
Group I	+*	+	8% ↑
Group II	-	-	8% ↑

\* positive skin reaction to house dust and/or the other allergens. HD ; house dust

test to various allergens and negative RAST to house dust (Table 1).

Group I included 8 asthmatic subjects (5 females and 3 males, their ages varied from 16 to 52 years with a mean of 31.1 years). The mean age at onset in group I was 18.2 years (range ; 4-44 years), and the mean blood eosinophil count 10.3%. Group II had 6 cases (5 females and one males, their ages varied from 22 to 70 years with a mean of 53.0 years). The mean age at onset (44.8years)in group II was much higher than that in group I. The mean eosinophil count in group II was 14.3%, and also higher than that in group I (table 2).

Histamine release from basophils of asthmatic subjects was examined using whole blood, as previously described (TANIZAKI, Y., et al., 1983).

Table 2. Characteristics of asthmatic subjects studied.

	No of cases	Age	Sex	Age of onset	F.H.	Blood eosinophils (%)
Group I	8	31.1 (16-52)	F; 5 M; 3	18.2 (4-44)	6/8	10.3 (8-16)
Group II	6	53.0 (22-70)	F; 5 M; 1	44.8 (17-58)	1/6	14.3 (8-23)

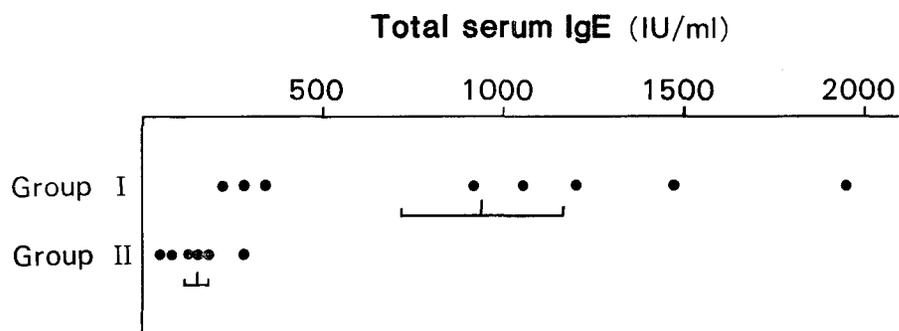


Fig. 1. Serum IgE levels in each group.

Histamine released from basophils was assayed by an automated fluorometric histamine analysis system (SIRAGANIAN, R. P., 1974). The results were expressed as a percent release of the total histamine content.

Skin test was performed by intradermal injection (0.02 ml) of allergens. The reaction was evaluated at 15 minutes.

Serum IgE levels were estimated by the radioimmunosorbent test (RIST) (Pharmacia). Serum specific IgE to house dust was measured by the radioallergosorbent test (RAST) (Pharmacia).

### Results

Serum IgE levels in the two groups were compared. Serum IgE levels in group I varied widely from low to high levels. On the other hand, serum IgE levels in group II was generally low. Thus, the serum IgE levels in group I were much higher than those in group II. A statistically significant difference was present between the two groups ( $p < 0.05$ ) (Fig. 1).

Maximum percent histamine release from basophils induced by anti-IgE was  $50.7 \pm 5.0\%$  (mean  $\pm$  SEM) in group I and  $10.5 \pm 1.7\%$  in group II, respectively. The release of histamine in group

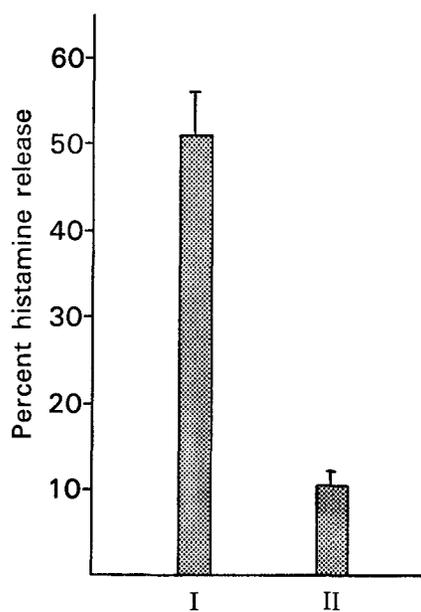


Fig. 2. Maximum percent histamine release induced by anti-IgE in each group.

I was higher than that in group II. There was a statistically significant difference between the two groups ( $p < 0.01$ ) (Fig. 2).

The dose-response curves of anti-IgE-induced histamine release were different between the two

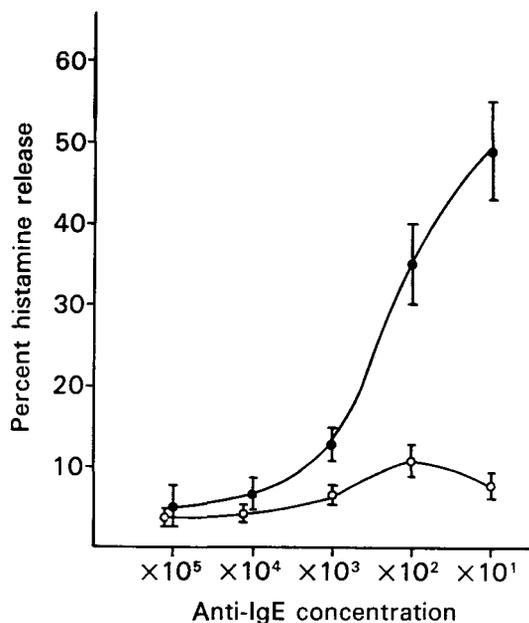


Fig. 3. Dose-response curve of anti-IgE-induced histamine release in each group: group I (●—●), group II (○—○).

groups. The dose-response curve of histamine release in group I showed consistent increase as the anti-IgE concentrations increased. While, the dose-response curve of histamine release in group II was very low and symmetric at the concentration causing the maximum percent release. The curve in group I was much higher than that in group II. The results suggested that basophils from the subjects in group I react to anti-IgE dose-dependently. While, basophils from the cases in group II hardly react to anti-IgE. This demonstrates no participation of IgE in blood eosinophilia of group II (Fig. 3).

### Discussion

It is well known that IgE-mediated immediate hypersensitivity plays an important role as one of the reactions causing bronchial asthma. In this condition, blood eosinophilia was popularly observed in patients with bronchial asthma. In clinical observations, both basophilia and eosinophilia are seen in the pre-attack stage of bronchial asthma (KIMURA, I., et al., 1973). Migration of basophils and eosinophils into the sputum of

asthmatics was also observed during an attack stage (KIMURA, I., et al., 1975). These findings suggest that there is a close correlation between basophils and eosinophils in atopic bronchial asthma.

Eosinophil chemotactic factor of anaphylaxis (ECF-A), which exists in the preformed state in basophils and mast cells (GOETZL, E. J., et al., 1975), is released from these cells after interaction between antigen and cell-bound IgE. The results obtained here demonstrated that blood eosinophilia and IgE-mediated reaction (expressed by histamine release by anti-IgE) coexisted in the cases of group I, showing a correlation between the two blood cells. On the other hand, the subjects classified into group II are called 'intrinsic' asthma. The cases in group II showed blood eosinophilia, but not significant increase in the release of histamine induced by anti-IgE.

It was speculated that release of other chemical mediators such as SRS-A and ECF-A was elicited by stimulation with anti-IgE. That is, participation of IgE-mediated immediate reaction was not clear in the cases in group II. The results revealed that blood eosinophilia is not elicited by antigen interaction with cell-bound IgE. It was found from the present study that blood eosinophilia observed in patients with bronchial asthma is elicited by different mechanisms; One is IgE-mediated immediate reaction, and another is unknown, but not IgE-mediated one. Further study is necessary to analyze mechanism causing blood eosinophilia in 'intrinsic' asthma.

### Summary

Histamine release from basophils induced by anti-IgE was examined in 14 asthmatic subjects with blood eosinophilia. The subjects were divided into two groups; group I (with blood eosinophilia, positive skin test and positive RAST to house dust) and group II (with blood eosinophilia, negative skin test to various allergens and negative RAST to house dust).

1. Serum IgE levels in group I were much higher than those in group II.
2. Maximum percent histamine release induced

by anti-IgE was much higher in group I than in group II.

3. Dose-response curve of anti-IgE-induced histamine release in group I showed consistent increase as anti-IgE concentrations increased. while, dose-response curve in group II was very low.

These findings suggested that blood eosinophilia in group I might be elicited relating to IgE-mediated reaction. However, mechanism causing eosinophilia in group II was not clear in the present study.

#### Acknowledgement

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#### 好塩基球からのヒスタミン遊離に関する研究.

#### 3. 抗ヒト IgE に対する好塩基球の反応性と末梢血好酸球増多

谷崎勝朗, 駒越春樹, 周藤真康. 御般政明, 森永 寛, 中川三郎\*, 貴谷 光\*, 木村郁郎\*

岡山大学医学部附属病院三朝分院内科

\* 岡山大学医学部第2内科

末梢血好酸球増多を示す気管支喘息14症例について, 抗ヒト IgE による好塩基球からのヒスタミン遊離を検討した. ハウスダストに対する皮内反応および RAST が陽性を示す症例群 (group I) では, 血清 IgE 値が高く, また抗ヒト IgE による Max. %ヒスタミン遊離も高く (50.7±5.0%), その dose-response curve は抗ヒト IgE 添加濃度が高くなるにつれて上昇する傾向を示した. 一方種々のアレルゲンエキスに対する皮内反応が陰性で, かつ RAST も陰性を示す症例群 (group II) では, 血清 IgE 値が低く, また抗ヒト IgE による Max. %ヒスタミン遊離も低く (10.5±1.7%), その dose-response curve は全般的に低く, 抗ヒト IgE 添加濃度が高いところではむしろ抑制される傾向を示した.