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Abstract

IgE-mediated histamine release from whole blood was analyzed in 44 patients with bronchial asthma by observing maximum present release and dose-response curves of histamine release induced by anti-IgE and house dust extract. The maximum histamine release from whole blood induced by anti-IgE correlated with total serum IgE levels. There was a close correlation between allergen-induced release from whole blood and the serum levels of specific IgE antibodies. In the maximum histamine release from whole blood induced by both anti-IgE and allergen, the interaction with a serum factor was not clearly recognized. Effect of a serum factor was shown in the dose-response curves of anti-IgE-induced histamine release, but not in those of allergen-induced histamine release. The dose-response curves caused by anti-IgE showed that basophils from cases with a high serum IgE level require much more anti-IgE to produce maximum histamine release than basophils from cases with a low serum IgE level. The results showed that IgE molecules contained in the serum participate in anti-IgE-induced histamine release from whole blood.

KEYWORDS: histamine release, whole blood, serum factor, allergen, anti-IgE

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EFFECT OF A SERUM FACTOR ON IgE-MEDIATED HISTAMINE RELEASE FROM WHOLE BLOOD

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Abstract. IgE-mediated histamine release from whole blood was analyzed in 44 patients with bronchial asthma by observing maximum percent release and dose-response curves of histamine release induced by anti-IgE and house dust extract. The maximum histamine release from whole blood induced by anti-IgE correlated with total serum IgE levels. There was a close correlation between allergen-induced release from whole blood and the serum levels of specific IgE antibodies. In the maximum histamine release from whole blood induced by both anti-IgE and allergen, the interaction with a serum factor was not clearly recognized. Effect of a serum factor was shown in the dose-response curves of anti-IgE-induced histamine release, but not in those of allergen-induced histamine release. The dose-response curves caused by anti-IgE showed that basophils from cases with a high serum IgE level require much more anti-IgE to produce maximum histamine release than basophils from cases with a low serum IgE level. The results showed that IgE molecules contained in the serum participate in anti-IgE-induced histamine release from whole blood.

Key words : histamine release, whole blood, serum factor, allergen, anti-IgE.

The whole blood method for the determination of the amount of histamine release has some advantages over the washed leucocyte method. The former is easier to perform and is a better index of the *in vitro* immediate allergic reaction. Siraganian and Brodsky (1) reported that histamine release from whole blood correlated well with the release from washed leucocytes. We previously reported that the determination of histamine release from whole blood of atopic asthmatics is valuable for the clinical study of allergy (2). When whole blood is used to determine the amount of histamine release from basophils, the release of histamine is affected by the interaction of several serum factors such as total IgE, specific IgE and blocking antibodies. There is no definite information about the effects of serum factors on histamine release from whole blood.

In the present study, effects of a serum factor on the release of histamine from whole blood upon addition of anti-IgE and house dust extract were observed by both maximum percent release and dose-response curves.

SUBJECTS AND METHODS

Forty-four patients with bronchial asthma, who showed positive skin reaction to house dust, were selected. Their ages were from 16 to 71 years, with a mean of 40 years.

The amount of histamine released from whole blood was measured by an automated histamine analysis system (3), as described in our previous study (2). The results were expressed as a percentage of the total histamine content of the blood. Two different concentrations of anti-IgE (Behringwerke; E_2 ; $\times 10^2$, E_1 ; $\times 10^1$ dilution) and house dust extract (Torii Co. 40.0 $\mu\text{g}/\text{ml}$; H_2 ; $\times 10^3$, H_1 ; $\times 10^2$ dilution) were used as stimulating agents.

Serum IgE and specific IgE antibodies were measured by the RIST and the RAST method from Pharmacia.

RESULTS

Correlation between anti-IgE-induced histamine release and serum IgE levels. Anti-IgE-induced histamine release from whole blood of all the asthmatics studied here correlated with serum IgE levels. The maximum percent release, however, varied greatly from 6.2 % to 47.5 % in the cases with a serum IgE level of less than 300 IU/ml (Fig. 1). Less histamine release from basophils was caused by anti-IgE only in the cases with less than a 300 IU/ml serum IgE level. A significant difference in the maximum percent release induced by anti-IgE was present between the cases with 0-300 IU/ml and those with 301-500 IU/ml serum IgE ($p < 0.01$). In all the cases with over 1000 IU/ml serum IgE, basophils released a

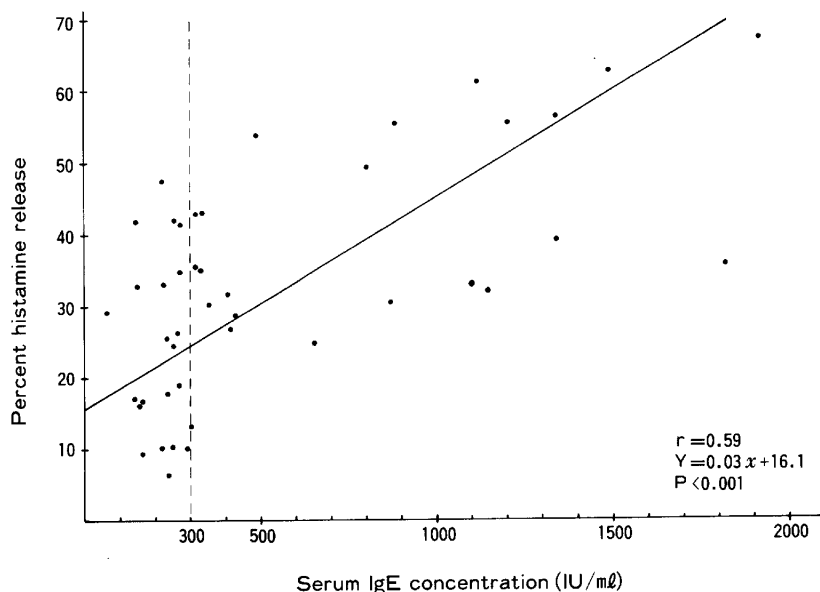


Fig. 1. Correlation between maximum percent histamine release induced by anti-IgE and serum IgE levels in patients with bronchial asthma.

Effect of a Serum Factor on Histamine Release

TABLE 1. SERUM IgE LEVELS AND ANTI-IgE-INDUCED HISTAMINE RELEASE FROM WHOLE BLOOD

SerumIgE (IU/ml)	No of cases	Percent histamine release			
		Mean $\pm$ SEM	Number of cases		
			< 20 %	20-30 %	30 % <
0-300	22	23.8 $\pm$ 2.7*	11 (50.0%)	4 (18.2%)	7 (31.8%)
301-500	9	38.4 $\pm$ 2.8*	0 (0 %)	2 (22.2%)	7 (77.8%)
501-1000	4	40.0 $\pm$ 7.4	0 (0 %)	1 (25.0%)	3 (75.0%)
> 1001	9	48.7 $\pm$ 5.0	0 (0 %)	0 (0 %)	9 (100%)

p < 0.01 compared with the 0-300 IU/ml group (t-test)

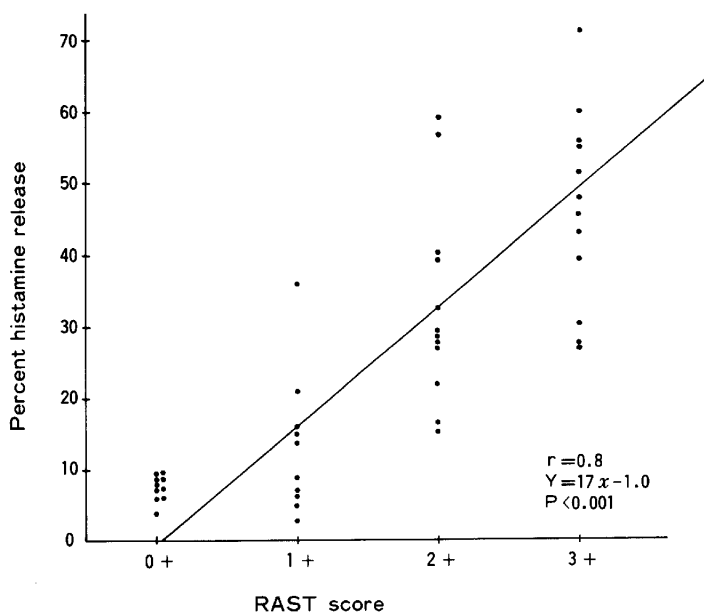


Fig. 2. Correlation between maximum percent histamine release induced by house dust extract and RAST scores.

large amount of histamine (more than 30 %) upon addition of anti-IgE (Table 1).

Correlation between house dust-induced histamine release and RAST scores. The release of histamine induced by house dust extract correlated with RAST scores to house dust, with a correlation coefficient of $r=0.8$. Basophils from cases with a RAST score of 0+ did not release a significant amount of histamine upon addition of house dust extract. There was a statistically significant difference in histamine release induced by house dust extract between the cases with a RAST score of 1+ and 2+ ($p<0.01$). A large amount of histamine was released in the cases with a RAST score of 3+ when their basophils were incubated with house dust extract (Fig. 2).

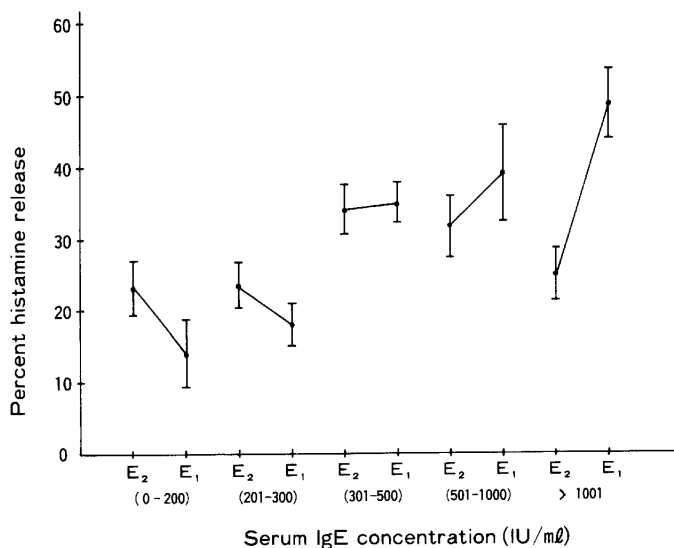


Fig. 3. Dose-response curves of histamine release from whole blood induced by two different concentrations— low (E_2 : $\times 10^2$ dilution) and high (E_1 : $\times 10^1$ dilution)—of anti-IgE and total serum IgE levels. Horizontal bars represent the mean $\pm$ SEM.

Dose-response curves of histamine release elicited by anti-IgE and house dust extract. Different concentrations, low (E_2) and high (E_1), of anti-IgE caused different amounts of histamine release from whole blood. In the cases with a low serum IgE level (less than 300 IU/ml), a large amount of histamine was released by the low concentration of anti-IgE (E_2) than by the high concentration of anti-IgE (E_1). On the other hand, maximum histamine release was elicited by the high concentration of anti-IgE in the cases with a high serum IgE level (more than 500 IU/ml). This phenomenon in which maximum release was elicited by a low anti-IgE concentration in the cases with a low serum IgE level and by a high anti-IgE in the cases with a high serum IgE might be due to the interaction of IgE molecules contained in the serum (Fig. 3).

Histamine release was induced by two different concentrations, low (H_2) and high (H_1), of house dust extract. In all cases, basophils released more histamine with the high concentration of house dust extract (H_1) than with the low concentration of house dust extract (H_2). The dose-response slope from H_2 to H_1 became higher in accordance with higher RAST scores. No effect of a serum factor on the dose-response curves of histamine release from basophils was seen when the whole blood of asthmatics was incubated with house dust extract (Fig. 4).

DISCUSSION

IgE-mediated histamine release has been extensively studied using washed leucocytes (4-6). It has been reported that anti-IgE-induced release of histamine

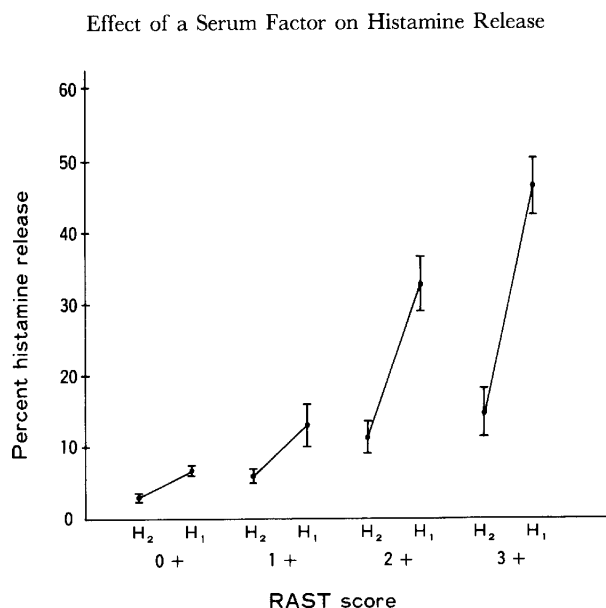


Fig. 4. Dose-response curves of histamine release from whole blood induced by two different concentrations— low (H_2 : $\times 10^3$ dilution) and high (H_1 : $\times 10^2$ dilution)—of house dust extract and RAST scores. Horizontal bars represent the mean $\pm$ SEM.

from washed leucocytes of hypersensitive individuals correlates with their serum IgE levels (7, 8). Assem *et al.*, however, reported that the correlation between total serum IgE and histamine release from washed leucocytes induced by anti-IgE was generally poor (9). Serum IgE levels of allergic subjects were variable, but their basophils showed a consistently high response to anti-IgE. On the other hand, allergen-induced histamine release from washed leucocytes correlated with the levels of serum specific IgE antibodies (10).

In the present study, it was found that anti-IgE-induced histamine release from whole blood correlates to a certain extent with the levels of total serum IgE. However, in the cases with a low concentration of serum IgE (less than 300 IU/ml), the release of histamine from whole blood by addition of anti-IgE varied greatly, as described by Radermecker (11), who used whole blood in his experiment on histamine release. The results obtained here revealed that allergen-induced histamine release from whole blood correlated well with the levels of serum specific IgE antibodies. This result is similar to that of Lichtenstein, *et al.* (10).

Several factors, such as total serum IgE, specific IgE antibodies and the reactivity of target cells, participate in IgE-mediated reactions. Observing the histamine release from whole blood might be better for estimating the severity of *in vivo* IgE-mediated reactions. When whole blood is used in experiments on IgE-mediated histamine release, the release is affected by the interaction of several

serum factors. Siraganian and Brodsky (1) reported that histamine release from whole blood generally correlates with release from washed leucocytes. When the cells are incubated with allergen, however, maximum histamine release from whole blood is usually less than the release from washed leucocytes. In the present study, it was also observed that the dose-response curves of allergen-induced histamine release from whole blood depends on the concentration of serum specific IgE antibodies. There is, however, no available information about the interaction of serum factors in dose-response curves of anti-IgE-induced histamine release. The dose-response curves of histamine release produced by anti-IgE were different from those induced by allergen. Basophils from the cases with a high concentration of serum IgE require much more anti-IgE to cause maximum histamine release, perhaps because of the interaction of IgE molecules contained in their serum. As described above, an interaction of serum specific IgE antibodies in allergen-induced release from whole blood was not shown. Further study is necessary to understand the participation of blocking antibodies in allergen-induced histamine release from whole blood.

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