

Studies on the release of histamine from basophils

2. Histamine release induced by house dust extract and anti-IgE

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Introduction

Basophils release histamine by the bridging of IgE receptors at the cell membrane with the stimulation of antigen and anti-IgE. Although the release mechanism of histamine from basophils elicited by antigen and anti-IgE is clearly different from that by the other stimulating agents (COCHRANE, D.E., et al., 1974, LICHTENSTEIN, L. M., 1975, GRANT, J.A., et al., 1977), it has been thought that the mechanism of histamine release from basophils by antigen is similar to that by anti-IgE. Recently, MARONE, G., et al., (1981) have suggested that there are some differences in the kinetics of histamine release between antigen and anti-IgE.

In this study, we examined the release of histamine from basophils of healthy and asthmatic subjects with the stimulation of antigen and anti-IgE.

Subjects and Methods

Six representative cases (two healthy and four asthmatic subjects) were selected for the study on the release mechanism of histamine from basophils. The challenge of basophils with house dust extract (42 mcg/ml) and anti-IgE (35×10^4 IU/ml, Behringwerke) was performed in a dose-res-

ponse fashion. Histamine from whole blood was assayed by an automated fluorometric technique developed by SIRAGANIAN, R. P. (1974, 1975), as described in part 1. The release was expressed as a percentage of the total histamine content in each sample. Total serum IgE was estimated by the radioimmunosorbent test (RIST). Allergen-specific IgE was assayed by the radioallergosorbent test (RAST) from Pharmacia. The results were expressed as a score.

Results

IgE-mediated release of histamine from human basophils was observed in healthy and asthmatic subjects with the in vitro stimulation of house dust extract and anti-IgE. In this article, dose-response curve of histamine release from basophils of the representative cases out of healthy and asthmatic subjects was discussed. Table 1 summarized the characteristics of the representative cases. The significantly increased release of histamine from basophils of healthy subjects was observed by anti-IgE stimulation. The dose-response curve of histamine release by anti-IgE was relatively symmetric about the concentration showing the maximal percent release. As the concentration of anti-IgE was increased above the level for optimal release the amount of histamine

Table 1. Characteristics of subjects studied

		Age	Sex	Serum IgE Skin test RAST score		
				(IU/ml)	(HD)	(HD)
Case 1.	Healthy	35	Male	145	NT	NT
" 2.	"	28	Male	92	NT	NT
" 3.	Asthma	44	Male	1338	+	3+
" 4.	"	24	Male	1910	+	1+
" 5.	"	41	Female	1100	+	-
" 6.	"	33	Male	222	+	-

NT; not done, HD: house dust.

released was promptly decreased (case 1). No significant increase in histamine release was elicited by house dust extract (Fig. 1 and 2). Case 3, an asthmatic patient with high serum IgE level and a strong positive RAST score (3+) to house dust extract, showed marked increase in the release of histamine from basophils by both anti-IgE and house dust extract (Fig. 3). In case 4, who shows 1+ of RAST score to house dust extract

and the other multiple specific allergens (ragweed, candida, alternaria and aspergillus) demonstrated by a RAST procedure, marked histamine release was caused by the addition of anti-IgE and slight increase in the release by house dust extract (Fig. 4). These findings might suggest that there is a correlation between the value of specific IgE antibody shown by RAST score and the amount of histamine released by specific IgE

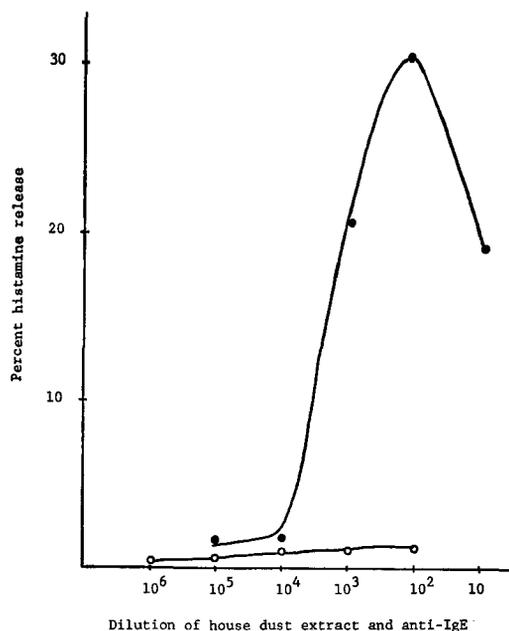


Fig. 1. Dose-response curve of histamine release from basophils; case 1, 35 years, male, healthy subject. Significantly increased release of histamine was seen by anti-IgE. No significant release to house dust extract. Anti-IgE: (●—●), House dust: (○—○).

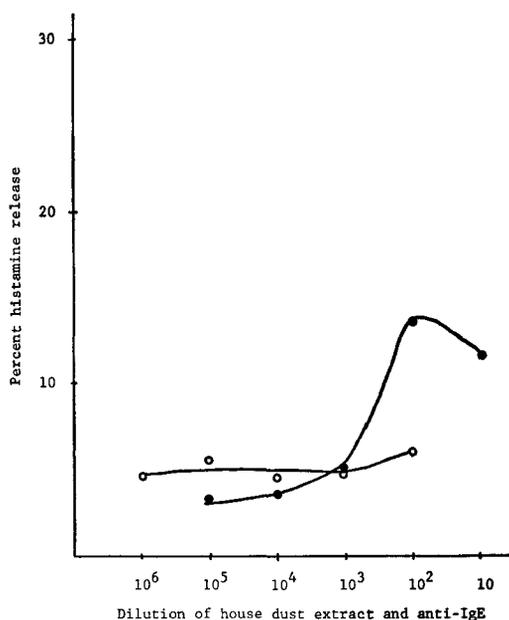


Fig. 2. Histamine release from basophils; case 2, 28 years, male, healthy subject. A slightly increased release of histamine was elicited by anti-IgE. No significant release to house dust extract. Anti-IgE: (●—●), House dust extract: (○—○).

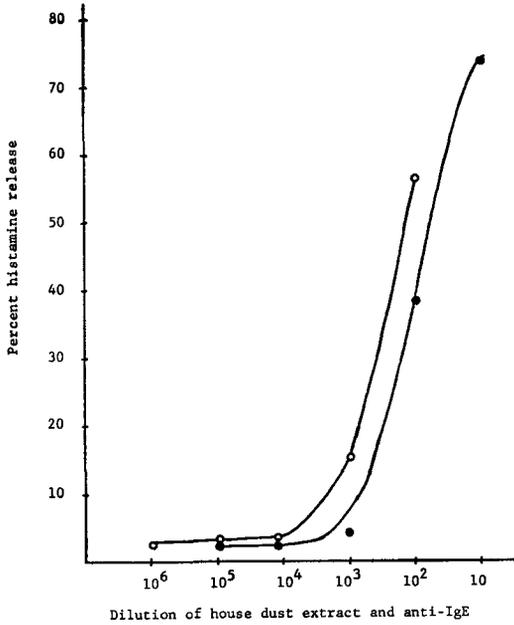


Fig. 3. Histamine release from basophils; case 3, 44 years, male, bronchial asthma. Marked increase in the release of histamine was elicited by both anti-IgE and house dust extract. House dust extract: (○—○), Anti-IgE: (●—●).

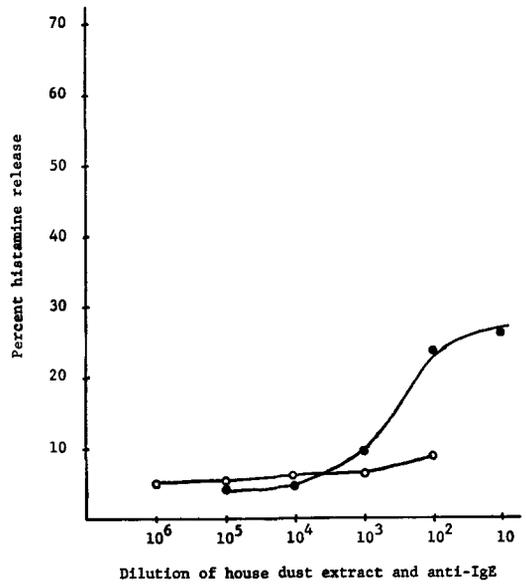


Fig. 5. Histamine release from basophils; case 5, 41 years, female, bronchial asthma. Significant increase in histamine release was induced by anti-IgE. No significant release to house dust extract. Anti-IgE: (●—●), House dust extract: (○—○).

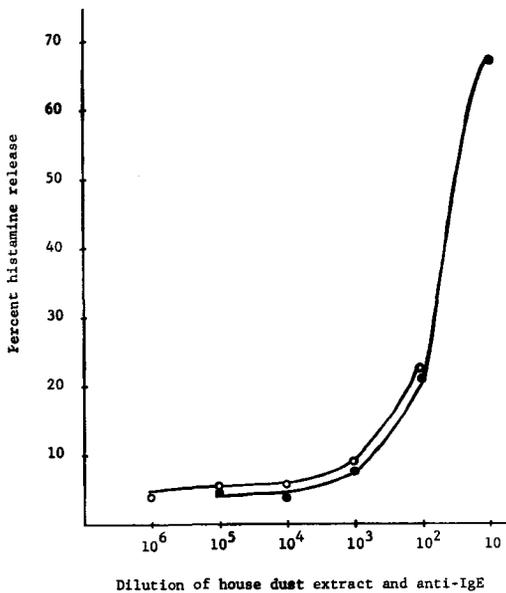


Fig. 4. Histamine release from basophils; case 4, 24 years, male, bronchial asthma. Markedly increased histamine release by anti-IgE, and slight increase to house dust extract were observed. Anti-IgE: (●—●), House dust extract: (○—○).

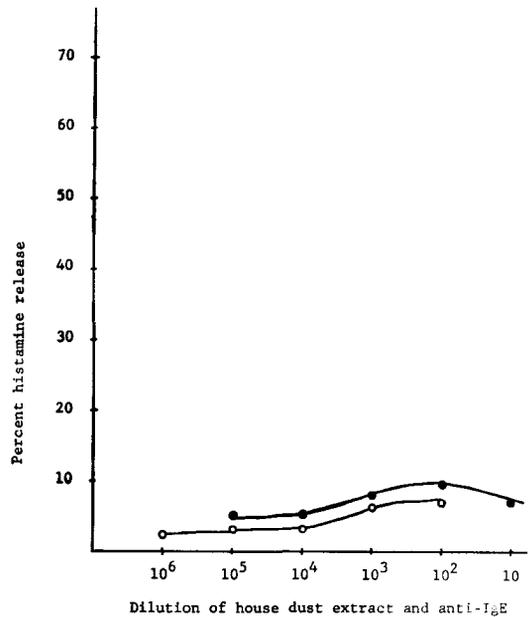


Fig. 6. Histamine release from basophils; case 6, 33 years, male, bronchial asthma. No significant release was elicited by both anti-IgE and house dust extract. Anti-IgE: (●—●), House dust extract: (○—○).

antibody. Case 5, who shows negative RAST to house dust and positive RAST to ragweed allergen with high serum IgE level, revealed significantly increased release of histamine from basophils by anti-IgE, while no increase in the release by house dust extract (Fig. 5). In case 6, with negative RAST to house dust and with normal serum IgE level, no significant increase in the release of histamine was induced by both anti-IgE and house dust extract (Fig. 6).

Discussion

In this study, it was demonstrated that house dust extract causes the release of histamine only from basophils of asthmatic subjects who are sensitive to house dust, while anti-IgE stimulation elicited histamine release from basophils of both healthy and asthmatic subjects. It has been thought that there is no positive correlation between the release of histamine with anti-IgE and serum IgE levels. A correlation was present between allergen-specific IgE and allergen-induced histamine release (case 3 and 4).

Recently, MARONE, G. et al. (1981) reported that antigen-induced histamine release from basophils differs from the release by anti-IgE in several points;

- 1) Antigen causes the release of histamine over a broader concentration range than does anti-IgE.
- 2) The release pattern of antigen is not so susceptible to excess inhibition as anti-IgE.
- 3) The release process caused by antigen has a shorter lag phase and a more rapid rate than that by anti-IgE.
- 4) All agents activating adenylate cyclase are significantly more effective against antigen-induced release than against that caused by anti-IgE.
- 5) Indomethacin potentiates antigen-induced release, but not anti-IgE-induced release. Our data also showed that a limited concentration of anti-IgE could induce significantly increased release of histamine (case 1 and 2).

It is of interest that there is a patient with bronchial asthma whose basophils do not release histamine significantly in response to anti-IgE and antigen. This result here differs from that

reported by ASSEM, E.S.K. et al. (1981), who has described that allergic patient basophils show a consistently high response to anti-IgE. The increased basophil reactivity in asthmatic subjects has also been reported by CONROY, M. C. et al., (1977), who termed it 'releasability'. This difference in basophil reactivity of asthmatics to anti-IgE might be explained by two differences in the methods. Firstly, they utilized washed cells in the experiments for histamine release, while we used whole blood. Secondly, they observed the release of histamine from basophils after 60 minutes' incubation with anti-IgE, while we incubated whole blood with anti-IgE for 15 min. According to the data demonstrated by MARONE et al., the release process caused by anti-IgE has a longer lag phase than that by antigen. It might be possible to speculate that low reactive basophils from some asthmatics release no significant amount of histamine by 15 minutes' incubation. Sixty minutes' incubation seems to be enough for any basophils to release histamine by both anti-IgE and antigen. From our small data we could not neglect the other possibility to explain the different results for basophil reactivity to anti-IgE. Further study should be performed for low reactivity of basophils from asthmatics to anti-IgE.

Summary

IgE-mediated release of histamine from whole blood was examined in two healthy and four asthmatic subjects by dose-dependent fashion. The significantly increased amount of histamine was released from basophils of both healthy and asthmatic subjects by a limited concentration of anti-IgE. Antigen (house dust) caused histamine release only from basophils of asthmatics who are sensitive to house dust. Basophils from one patients with asthma released no significant amount of histamine by anti-IgE.

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好塩基球からのヒスタミン遊離に関する研究.

2. ハウスダスト抗原および抗ヒト IgE によるヒスタミン遊離

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好塩基球からの IgE-mediated histamine release の機序を, 健康人(2名)および気管支喘息(4例)それぞれの代表例で比較検討した. 抗ヒト IgE の添加濃度別検討では, 健康人および外因性喘息例いずれも有意のヒスタミン遊離の増加をしめしたが, Max. % histamine release をひきおこす抗ヒト IgE の濃度は比較的限られた範囲内にある傾向がみられた. 一方内因性喘息例では, いずれの抗ヒトIgE濃度でも有意のヒスタミン遊離はみられなかった. ハウスダスト抗原の添加濃度別検討では, ハウスダストが抗原である気管支喘息症例において dose-dependent なヒスタミン遊離が観察されたが, 使用された抗原濃度の範囲では Max. % release をひきおこす至適濃度は明らかでなかった.