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Studies on the release of histamine from basophils

5. Clinical evaluation

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Introduction

Histamine release from basophils of hypersensitive individuals has been studied by using washed leucocytes (LICHTENSTEIN, L. M., et al. 1971, 1973, NORMAN, P.S., et al., 1973). These results have shown that basophils release a significant amount of histamine after stimulation with antigen and anti-IgE (LICHTENSTEIN, L. M., et al., 1970), and that the histamine release from human basophils is a valuable tool for in vitro studies of IgE-mediated, immediate hypersensitivity (RADERMECKER, M. F., et al., 1980).

During the last three years, histamine release from basophils has been extensively studied at Department of Medicine, Okayama University Medical School, Misasa Medical Branch, to clarify the pathogenesis of bronchial asthma (TANIZAKI, Y., et al., 1983b, 1983c, 1984b, 1984d, 1984f). In the following section, we summarize the results obtained for three years.

Determination of Histamine

Histamine release from basophils has been mainly examined by using washed leucocytes. Our experiments of histamine release have been carried out by using whole blood (TANIZAKI, Y., et al, 1983f, 1984a, 1984c). There are some diffe rences between a washed leucocytes method and a whole blood method. Firstly, the incubation time of basophils with antigen and anti-IgE required to reach the maximum percent histamine release is shorter (15 min) in the whole blood method than the time (60 min) in the washed leucocytes method (TAMIZAKI, Y., et al., 1984a). Secondly, histamine release from whole blood is affected by several factors, such as total serum IgE, specific IgE antibodies and the reactivity of basophils (TANIZAKI, Y., et al. 1984e). The effect of serum factors on histamine release is more remarkable in anti-IgE-induced release than in antigen-induced release. The dose-response curves of histamine release clearly shows that the curves produced by anti-IgE are different from those by antigen. In antigen-induced histamine release, basophils release more histamine with a high concentration of antigen than with a low antigen concentration. The dose-response slope from the low to the high concentration of antigen becomes higher in accordance with higher RAST scores. On the other hand, basophils from cases with a high concentration of serum IgE require much more anti-IgE to cause maximum histamine release, because of the interaction of IgE molecules contained in their serum. In cases with a low serum IgE level (less than 300 IU/ml), a large amount of histamine was released by a low concentration of anti-IgE compared to a high concentration of anti-IgE. Thirdly, the whole blood method is easier to perform and reflects the true in vivo immediate allergic reaction better than the washed leucocytes method.

In the determination of histamine released

from leucocytes of allergic individuals, a sensitive fluorometric method has been utilized. The method is time-consuming and must be performed by a highly trained technician to get a reliable result. SIRAGANIAN, R.P., et al. (1974, 1975) has developed an automated fluorometric histamine analysis system. The method made it possible to measure histamine release more easily. Through the use of the method 30 samples per hour can be analyzed. Our histamine release experiments have been carried out by the automated fluorometric histamine analysis system. Our long-term studies on histamine release shows that the automated fluorometric histamine analysis is an easy method for the determination of extent of histamine release and that the method could be used for clinical studies of allergy (TANIZAKI, Y., et al., 1983f, 1984a).

Clinical Indications

Recent studies have clarified that phospholipid methylation caused by antigen and anti-IgE enhances membrane permeability of the target cells, inducing an increase of Ca^{2+} influx into the cells, which is accompanied by histamine release (FOREMAN, J.C., et al., 1977, HIRATA, F., et al., 1979, ISHIZAKA, T., et al., 1979, RANADIVE, N.S., et al, 1980). Our previous studies also showed that antigen causes an increase in Ca^{2+} uptake by sensitized mast cells and that inhibition of Ca^{2+} influx leads to the inhibition of histamine release (TANIZAKI, Y., et al., 1983a, 1983d, 1983e). The mechanism of histamine release through IgE receptors on the target cells seems to be similar, although MARONE, G., et al. (1981) reported that there are some differences between anti-IgE-and antigen-induced histamine release. It is important for clinical application of histamine release experiments to measure anti-IgE- and antigen-induced release from basophils of allergic individuals.

1. Basophil Reactivity to Anti-IgE

Basophil reactivity to anti-IgE can be observed by measuring histamine release from the cells. Anti-IgE-induced histamine release has been reported to correlate to a certain extent with serum IgE levels (LICHTENSTEIN, L. M., et al., 1970). ASSEM, E.S.K., et al. (1981), however, showed that there was no positive correlation between the release of histamine with anti-IgE and serum IgE levels, because allergic patients' serum IgE level was very variable, but their leucocytes showed a concistently high response to anti-IgE. In our experiments, patients with a high level of serum IgE consistently showed a significant amount of histamine release when their basophils were incubated with anti-IgE. While, basophil histamine release was low in some cases and significantly high in other cases with a low serum IgE level. That is, histamine release from basophils induced by anti-IgE is variable in cases with a low serum IgE level (TANIZAKI, Y., et al., 1984d).

2. Basophil Reactivtty to Antigen

Our previous studies showed that basophils participate in an attack of asthma and change morphologically after in vitro stimulation with anti-IgE and antigen (KIMURA, I., et al., 1973, 1974, 1975a, 1975b, 1981a, 1981b, 1983, In press). When basophils are incubated with antigen, histamine release and morphological changes are both observed. The morphological changes of basophils (reactive basophils) induced by antigen have a close correlation with the skin end-point titrations of antigen, RAST score and bronchial challenge tests. It is, therefore, important for detection of antigen to observe morphological changes of basophils and histamine release after addition of antigen.

1) Histamine release by house dust extract

House dust extract induces histamine release from basophils of asthmatic patients sensitive to house dust. The release of histamine induced by house dust correlates with the level of specific IgE antibodies expressed as a RAST score. The amount of histamine release induced by house dust paralleled the amount of the release caused by anti-IgE in the cases with a RAST score of 2+ or higher (TANIZAKI, Y., et al., 1984g). Skin sensitivity to house dust correlates with basophil

reactivity to the antigen. Skin sensitivity to house dust was lower in the cases with basophils low reactive to the antigen, and skin sensitivity was higher with higher reactivity of basophils. These results show that observation of histamine release from basophils is useful for detection of specific antigen and that basophil reactivity to antigen might reflect the degree of in vivo IgE-mediated allergic reaction.

2) Histamine release by Candida albicans extract

Candida albicans also induces histamine release from basophils of asthmatic patients sensitive to the antigen (TANIZAKI, Y., et al, 1984f, In press). Histamine release induced by C. albicans correlates with serum levels of specific IgE antibodies, and the amount of histamine release increases as the RAST score is higher. The release of histamine induced by C. albicans seems to be similar to the release by house dust. There is, however, several differences between house dust- and C. albicans-induced histamine release. House dust-induced release of histamine correlates with the release induced by anti-IgE in cases with a positive RAST score, but the release induced by C. albicans does not correlate with anti-IgE-induced release. House dust extract never causes histamine release in cases with a negative RAST score, while C. albicans-induced histamine release can be observed even in cases with a negative RAST score. These results shows that non-IgE-mediated reaction participates in C. albicans-induced release of histamine.

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好塩基球からのヒスタミン遊離に関する研究.
5. 臨床的評価

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過去3年間にわたり，気管支喘息患者末梢血好塩基球からのヒスタミン遊離について，ヒスタミン自動分析装置を用いて全血法により検討を加えてきた．

1. 抗ヒト IgE によるヒスタミン遊離は，症例間で著しい差がみられた．この際血清 IgE 値が高値を示す症例では全般的に高度なヒスタシン遊離がみられたが，血清 IgE 値が正常かまたはむしろ低値を示す症例のヒスタミン遊離は，かなり高度なものから全くみられないものまでさまざまであった．

2. ハウスダストやカンジダなどの抗原物質によるヒスタミン遊離は，特異的 IgE 抗体依存性であり，抗体価が上昇するにつれヒスタミン遊離は高度となる傾向がみられた．しかし，ハウスダストとカンジダによるヒスタミン遊離には若干の差がみられた．すなわち，ハウスダストと抗ヒト IgE によるヒスタミン遊離の間には密接な関連がみられたが，カンジダと抗ヒト IgE の間には全く関連がみられなかった．またカンジダによるヒスタミン遊離においては，IgE系反応以外の反応が関与する可能性が一部示唆された．