

◎総説

Effect of aging on onset mechanism of bronchial asthma

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Abstract : Skin tests, serum total IgE levels, specific IgE antibodies against each allergen, bronchial reactions provoked by allergens and histamine release from basophils are well known as parameters of immediate allergic reactions. The incidence of positive immediate skin reaction to allergens such as house dust, ragweed, *Aspergillus*, *Alternaria*, *Cladosporium* and *Broncasma* decreased with aging. On the other hand, the incidence of positive skin reaction to *Candida albicans* was higher in cases between the age of 41 and 50 and cases over the age of 61 compared to that in the other groups classified by age. Serum IgE levels was highest in cases aged between 0 and 30. The levels of serum IgE decreased with aging. The incidence of positive RAST scores (more than 2+) and positive bronchial reaction to house dust were highest in cases between 0 and 30, and decreased with aging. However, the positive ratio of these tests against *C. albicans* were highest in cases between 41 and 50. The degree of histamine release from basophils of asthmatics induced by anti-IgE was consistently high without any correlation to aging when their serum IgE levels were more than 501 IU/ml. In the cases with serum IgE levels of less than 300 IU/ml, basophil reactivity to anti-IgE decreased with aging. Basophil reactivity to house dust was generally dependent on the levels of specific IgE antibodies against the allergen. Although basophil reactivity to *C. albicans* was also high in cases with positive RAST scores, some cases with a RAST score of 0+ or 1+ showed high or moderate basophil reactivity. Moderate or high reactivity of basophils was frequently observed in cases between 41 and 50 and cases over age 61.

Key words : Skin test, IgE, Provocation test, Basophil reactivity, Aging

Introduction

The IgE-mediated immediate allergic reaction is well known as one of onset mechanisms of bronchial asthma^{1,2)}. This allergic reaction leads to bronchospasm, mucosal

edema and mucus hypersecretion in asthmatics³⁾. Skin tests, serum total IgE levels, specific IgE antibodies against each allergen, bronchial reactions provoked by allergens and histamine release from basophils are usually adopted as examinations of immediate aller-

gic reactions^{4,5}. It is still unclear how these parameters are affected by aging. We examined the effect of aging on these parameters, such as skin tests, serum total IgE levels, specific IgE antibodies, bronchial provocation tests and histamine release from basophils.

Skin reactions

Seven kinds of allergens were tested in order to investigate the influence of aging on skin reactions. Skin test positivity of each age group was shown in Table 1. The incidence of positive immediate skin reaction to allergens such as house dust, ragweed, Aspergillus, Alternaria, Cladosporium and Broncasma decreased with aging. The skin test positivity against house dust was highest in subjects between 0 and 30(82.6%), decreasing with aging, and was lowest in subjects over age 61 (43.4%). On the other hand, the ratio of positive skin reaction to Candida albicans was high in patients between 41 and 50 and over age 61, while it is relatively low in patients between 0 and 30 (Table 1).

Table 1. Skin reactivity to various allergens in asthmatics with aging

Age	N	Allergens						
		HD	Rag	Can	As	Al	Clad	Bro
0-30	115	95 (82.6)	36 (31.3)	69 (60.0)	38 (33.0)	31 (27.0)	22 (19.1)	36 (31.3)
31-40	71	47 (66.2)	15 (21.1)	49 (69.0)	27 (38.0)	23 (32.4)	15 (21.1)	25 (35.2)
41-50	54	25 (46.3)	12 (22.2)	41 (75.9)	14 (25.9)	6 (11.1)	7 (13.0)	12 (22.2)
51-60	37	17 (45.9)	5 (13.5)	23 (62.2)	5 (13.5)	1 (2.7)	2 (5.4)	5 (13.5)
61-	23	10 (43.4)	2 (8.7)	17 (73.9)	1 (4.3)	0 (0%)	0 (0%)	3 (13.0)

HD:House dust, Rag:Ragweed, Can:Candida, As:Aspergillus, Al:Alternaria, Clad:Cladosporium Bro:Broncasma.

Serum IgE levels

In comparison with average serum IgE level of each age group, it was highest in cases between 0 and 30 (715 IU/ml), and decreased

with aging. Therefore the serum IgE level of cases between 0 and 30 was significantly higher than that of cases between 51 and 60 (322 IU/ml)(p<0.01). On the contrary, the IgE level of group over age 61(451 IU/ml) seemed to be higher than that of group between 51 and 60 (Fig. 1).

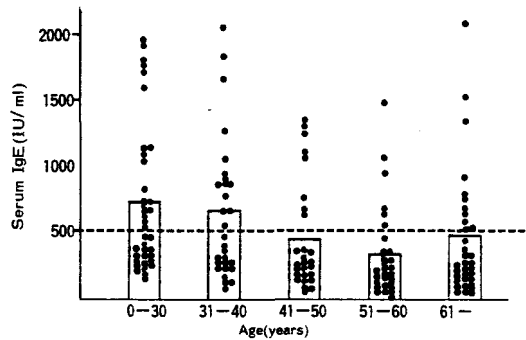


Fig 1. Serum IgE levels of asthmatics with aging

Specific IgE antibodies

The patients between 0 and 30 showed the highest positive ratio of specific IgE antibodies against house dust (77.8%). The aging caused the decrease of positive RAST score ratio as follows : cases aged 31-40 (64.3%), 41-50 (31.2%), 51-60 (20.0%). There were significant differences between two groups such as 0-30 and 51-60 groups, 31-40 and 51-60 groups (p<0.001, p<0.01). Whereas the positive ratio of specific IgE antibodies against C. albicans was highest in cases between 41 and 50 (38.5%), lowest in cases between 51 and 60 (12.5%). Although positive RAST scores against both antigens were more frequent in cases over age 60 than in those between 51 and 60, there was statistically no significant difference between the two groups (Fig. 2).

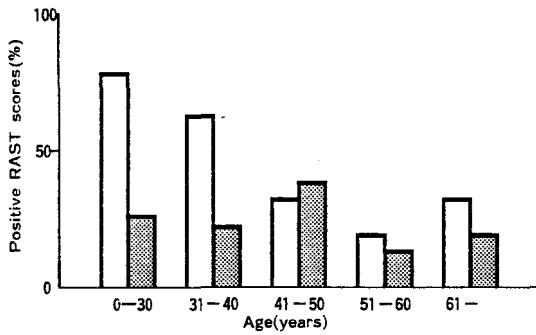


Fig. 2. Specific IgE antibodies against allergens in asthmatics with aging (house dust ; □ , C. albicans ; ▨)

Bronchial provocation test

The incidence of positive bronchial reaction to house dust was highest in subjects between 0 and 30 (53.3%), and decreased with aging as follows : cases aged 31-40 (43.3%), 41-50 (22.2%), 51-60 (12.5%), 60+ (0%). On the other hand, the positive rate of bronchial provocation test by C. albicans was highest in subjects between 41 and 50 (42.8%), and it was higher in cases over age 61 (33.3%) than in those between 51 and 60 (20.2%) with no significant difference (Fig. 3).

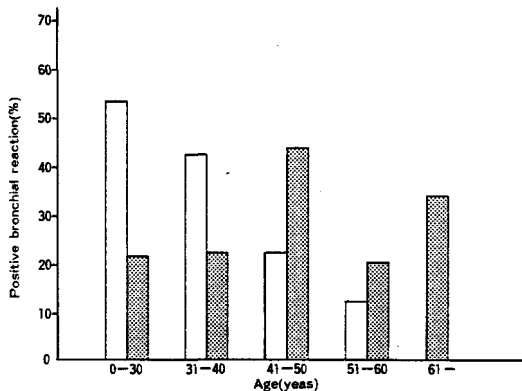


Fig. 3. Bronchial provocation test by allergens in asthmatics with aging (house dust ; □ , C. albicans ; ▨)

Histamine release from basophils induced by anti-IgE

The degree of histamine release from basophils of asthmatics induced by anti-IgE was consistently high without any correlation to aging when their serum IgE levels were more than 501 IU/ml. When their serum IgE levels were less than 300 IU/ml, basophil reactivity to anti-IgE decreased with aging (Table 2). It was extremely high in patients with high serum IgE levels whose age at onset were less than 40, and generally low in patients over the age of 31 at onset when their serum IgE levels were less than 300 IU/ml (Table 3). Comparing with age at onset over and under age 40, mean % histamine release in asthmatics under age 40 at onset was 30.5%, which was remarkably higher than that in asthmatics over age 41 at onset (18.6%) (Fig. 4).

Table 2. Histamine release from basophils of asthmatics induced by anti-IgE in relation to serum IgE levels and aging

Age (years) / Serum IgE (IU/ml)	0-30	31-40	41-50	51-60	61+
1001 - ↑	●●●●●●●●		●●●●●	●	
501 - 1000	●	●●●●			●
301 - 500	●●●●	●●	○●○	●	●●●○
201 - 300	●●●●	●●○	●○	●○○○	●○
0 - 200	○	○	○○○	●○○○○	●○○○○

%Histamine release: ○: 0-19%, ●: 20-29%, ●: 30-

Table 3. Histamine release from basophils of asthmatics induced by anti-IgE in relation to serum IgE levels and age at onset

Age at onset (years) \ Serum IgE (IU/ml)	0-30	31-40	41-50	51-60	61-
1001- ↑	●●●●●●●●	●●●●	●		
501-1000	●●●●●●				
301- 500	●●●●●●●●	○ ○	⊗ ○	● ○	●
201- 300	●●●●●●●●	○ ○	○ ○ ○	●	○
0- 200	⊗ ○	○	● ○ ○ ○ ○	● ⊗ ○ ○ ○	○ ○

% Histamine release: ○:0-19%, ⊗:20-29%, ●:30% -

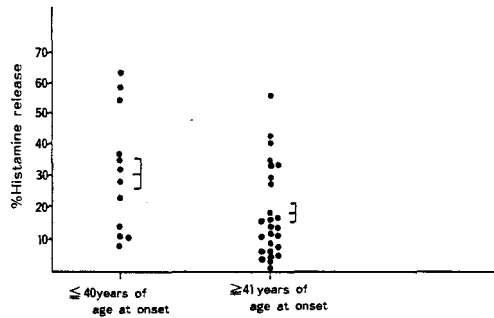


Fig. 4. Histamine release from basophils induced by anti-IgE in asthmatics older than 40 years in relation to age at onset

Histamine release from basophils induced by house dust and *C. albicans*

Basophil reactivity against house dust was generally dependent on the levels of specific IgE antibody against the allergen. The majority of cases with positive RAST scores (more than 2+) showed moderate or high basophil reactivity. However, some cases over age 61 with positive RAST scores showed low reactivity, suggesting that basophil reactivity to house dust decreased with aging.(Table 4). Although histamine release of basophils against *C. albicans* was also high in asthmatics with positive RAST scores, some cases

with a RAST score of 0+ or 1+ represented high or moderate basophil reactivity. It was distinctive that moderate or high reactivity of basophils was frequently observed in patients between 41 and 50 and ones over age 61 (Table 5).

Table 4. Histamine release from basophils of asthmatics by house dust extract in relation to specific IgE antibodies and aging

Age (years) \ RAST score	0-30	31-40	41-50	51-60	61-
3+ ~ ↑	●●●●●●●●	●●●●	●●	●●	●●○
2+	●●●●●●	●●●●	●●	●	●○
1+		○	○	○	○
0+	⊗ ○ ○	○ ○	○ ○ ○ ○ ○	○ ○ ○ ○	○ ○ ○ ○ ○

% Histamine release: ○:0-19%, ⊗:20-29%, ●:30% -

Table 5. Histamine release from basophils of asthmatics by *Candida albicans* in relation to specific antibodies and aging

Age (years) \ RAST score	0-30	31-40	41-50	51-60	61-
3+ ~ ↑	●		○		
2+	○	⊗ ○ ○	● ⊗ ○	⊗ ○	● ● ⊗ ○
1+	○	○ ○	○		○
0+	○ ○ ○	○ ○ ○	● ●	○ ○ ○ ○ ○	● ● ⊗ ○ ○

% Histamine release: ○:0-19%, ⊗:20-29%, ●:30% -

Discussion

Both IgE-mediated allergic reaction and basophil reactivity are closely related to the onset mechanism of bronchial asthma. However, it is still unclear how those are affected by aging. In our present studies, we inve-

stigated the effect of aging to IgE-mediated allergic reaction and basophil reactivity in asthmatics⁶⁻⁸⁾. Serum IgE levels were highest in cases between 0 and 30, and decreased with aging. The positive rate of skin test, IgE RAST and provocation test against house dust decreased with aging, while that against *C. albicans* was highest in cases between 41 and 50. The reactivity of basophils from asthmatics against anti-IgE was affected by both age and serum IgE levels. Basophil reactivity to house dust was generally dependent on the levels of specific IgE antibodies. On the other hand, histamine release from basophils induced by *C. albicans* was high or moderate in asthmatics between 41 and 50 and over age 61. Therefore, it is suggested that IgE-mediated allergic reaction and basophil reactivity against *C. albicans* are different from those against other allergens.

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気管支喘息の発症における加齢の影響について

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気管支喘息の発症機序の一つとして, IgE抗体にmediateされる即時型アレルギー反応や好塩基球の反応性の関与が明らかにされている。本論文では, 即時型アレルギー反応や抗ヒトIgEや特異抗原に対する好塩基球の反応性が加齢によりどのような影響を受けるかについて検討を加えた。

ハウスダスト, プタクサ, アスペルギルス, アルテルナリア, クラドスポリウム, ブロンカスマなどによる皮内反応の陽性率は, 加齢とともに低下する傾向を示した。一方カンジダによる皮内反応の陽性率は, 41~50歳および61歳以上の年齢層で高度であった。血清IgE値は加齢とともに低

下する傾向がみられた。ハウスダスト特異的IgE抗体, 吸入誘発試験の陽性率は, 加齢とともに低下する傾向を示した。一方カンジダでは特異的IgE抗体, 吸入誘発試験いずれも41~50歳および61歳以上の年齢層で比較的高い陽性率が観察された。抗ヒトIgEに対する好塩基球の反応性は, 血清IgEが高値(501IU/ml以上)の場合は年齢と関係なくIgE依存性であったが, 血清IgE値の低い症例(301IU/ml以下)では年齢が高い群でその反応性が低い症例の比率が大きかった。ハウスダストに対する好塩基球の反応性は, 抗ヒトIgE同様年齢が高い群ほど反応性が低い症例の比率が大きかった。カンジダに対する好塩基球の反応性は, 41~50歳および61歳以上の年齢層の症例でより高度であった。

キーワード: 皮内反応, IgE, 吸入誘発試験, 好塩基球の反応性, 加齢