ALLERGOLOGY

The Role of Lectins in Allergic Reactivity

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The aim of this study was to assess the skin reactivity to phytohemagglutinin (PHA) in healthy volunteers and in patients suffering from infectious-allergic bronchial asthma (IABA) before and after specific hyposensitization (SH). An attempt was also undertaken to elucidate the relationship between the extent of skin sensitivity to PHA and several parameters of immunity, as well as to explain certain components of the mechanism of lectins action in allergic processes.

MATERIALS AND METHODS

We examined 20 healthy volunteers and 106 patients with different types of uncomplicated IABA of medium severity. The patients were in remission and had no accompanying diseases at the time of examination. The patients were divided into four groups, according to the results of clinical allergological observations: 1) 35 patients with bronchial asthma of the neisseria-allergic type (NABA); 2) 21 patients with the staphylococcal-allergic type (SABA); 3) 35 patients with the neisseria-staphylococcal variant (N-SABA); and 4) 15 patients (5 from each group) who, unlike the other patients in the corresponding groups, had no previous history of SH therapy. The age of the patients was in the range of 24 to 50 years, and 67-80% were women. The median period from the onset of disease was about 6 years. The control group consisted of essentially healthy individuals of both sexes aged 20-50 years. The intracutaneous test with PHA was performed as described [1]. PHA (Difco, USA) was used in a concentration of 10 μg per 0.1 ml. Skin reactions were evaluated 24-48 hours after challenge. Intracutaneous tests with bacterial allergens, *Neisseria perflava* (NP) and *Staphylococcus aureus* (SA), were performed using one skin dose (50 million microbial bodies in 0.05 ml allergen). SH therapy was carried out according to a previously described scheme [4]. The main course consisted of 48 subcutaneous injections at 3-5-day intervals, followed by maintenance injections once every 7-10 days. The treatment lasted for 2 years. During this period, the mean total dose of allergen was equal to 410×10^6 microbial bodies. Serum immunoglobulin of the A, M, and G classes were measured by the method of radial immunodiffusion in gel [10]. The T- and B-lymphocyte content in the peripheral blood of patients was estimated using the rosette-forming cell (RFC) test. The phagocytic activity of neutrophils was determined in the latex assay [4].

RESULTS

The observation of patients with different types of IABA and of healthy individuals revealed the reduction or even total absence of the intracutaneous PHA

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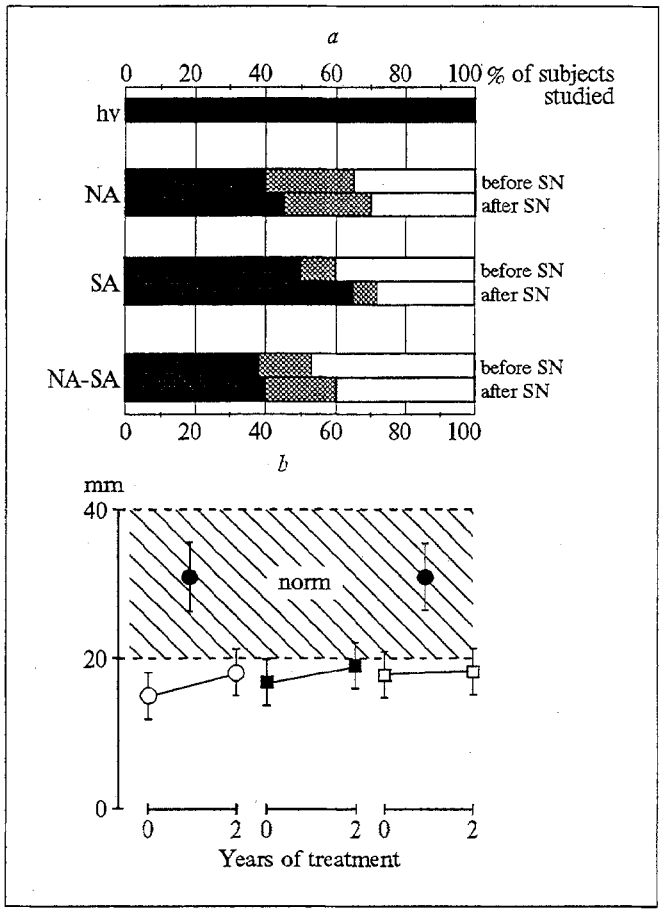

Fig. 1. Skin response to PHA in IABA patients before and after specific hyposensitization (*n*: number of observations). *a*) hv: healthy volunteers; $n=20$; NA: neisseria–allergic type of IABA ($n=35$); SA: staphylococcal–allergic type of IABA ($n=21$); NA–SA: neisseria–staphylococcal type of IABA ($n=35$); cross-hatched part: normal PHA skin reaction; dotted part: decreased reaction; open part: no reaction. *b*) open circles: NA–type IABA ($n=35$); dark squares: SA–type IABA ($n=21$); open squares: NA–SA–type IABA ($n=35$); dark circles: normal PHA skin reaction (healthy volunteers, $n=20$).

reaction in the patients when compared with the healthy volunteers. Figure 1 presents the results of allergometric measurement of the PHA skin reaction conducted 48 hours after PHA intracutaneous injection.

It can be seen that in the N-SABA group with no history of SH treatment the PHA skin reaction was negative in 45.7%, weak in 14.3%, and normal in 40.0% of patients (Fig. 1, *a*). The skin infiltrates were on average 14.0±3.1 mm in diameter. In the SABA group the skin PHA reaction was negative in 33.3% of patients, weak in 14.3%, and normal in 52.4%. The mean diameter of the skin papula induced by intracutaneous PHA injection was 17.4±3.9 mm. In the N-SABA group the skin PHA reaction was negative in 42.9% of patients, weak in 20.0%, and normal in 37.1%. The mean diameter of the skin infiltrate was 13.2±2.1 mm.

The skin reaction to PHA was positive 24-48 hours after challenge in all individuals of the control group. Here the mean diameter of the infiltrate was 30.1±3.2 mm.

Following SH therapy, a trend toward normalization of the skin reaction to PHA was revealed (Fig. 1, *b*). We then attempted to analyze the relationship between a weak skin PHA reaction in patients and such parameters as: a) the peripheral blood T- and B-cell content; b) the phagocytic activity of blood neutrophils; c) the degree of expression of skin sensitization to the bacterial allergens; and d) the concentration of serum, IgA, IgG, and IgM.

Table 1 shows the relationship between the skin reaction to PHA and the level of T and B lymphocytes in the venous blood of IABA patients (N-SABA). It can be seen that in the patients with a low content of T and B lymphocytes (groups A_T and A_B, respectively) a negative skin test is observed most frequently (55% and 77 %). These patients also exhibited the lowest frequency of positive reactions (45% and 23%) when compared with patients of the other groups. The mean diameter of papulae was 8.8±2.3 mm in the A_T group ans 4.5±1.8 mm in the A_B group. In parallel with the increase of the percent of T and B lymphocytes, a rise in the frequency and intensity of positive tests was observed, while the frequency of negative reactions decreased (Table 1).

Thus, in the patients a low T-lymphocyte content tended to correlate with a drop of skin PHA reactivity ($tA_TC_T=1.78$; $tA_TB_T=0.46$, and $tB_TC_T=1.43$; the differences are insignificant). However, patients with a low B-lymphocyte number in the peripheral blood significantly differed from the normal volunteers in the dimensions of infiltrates ($tA_BB_B=2.69$, $p<0.05$; $tA_BC_B=3.25$, $p<0.01$). Hence, IABA patients with a low T- and B-lymphocyte level in the peripheral blood exhibited a reduced skin PHA reaction. Moreover, the reactivity depended not only on the T-lymphocyte, but also on the B-lymphocyte level.

A decrease in the blood neutrophil phagocytic activity (37% and less) was observed in 13 out of 83 (15.7%) IABA patients. In the patients of this group the mean diameter of the infiltrate following intracutaneous PHA injection was 19.1±3.7 mm, thus approximating the normal skin reaction. At the same time, in the patients with high phagocytic activity of neutrophils (70-92%) the infiltrates were of mean diameter 10.0±2.5 mm, which was significantly lower than in the patients with a low phagocytic activity if neutrophils ($t=2.1$, $p<0.05$). thus, the weaker the phagocytic activity of neutrophils of IABA patients, the more intensive the skin PHA reaction, in some cases even reaching the normal level.

The relationship between the patients' skin PHA reaction and the degree of sensitization to the SA and NP bacterial allergens was also followed up.

TABLE 1. Skin Reaction to PHA in IABA Patients as a Function of Peripheral Blood T– and B–Lymphocyte Levels, %

Cell content, %	Number of patients	Diameter of skin reaction to PHA, mm				*M*±*m*	Group
		normal (20-40)	weak (1-19)	negative (0)	total number of positive tests		
T lymphocytes							
34–69	28	22	23	55	45	8.8±2.3	A_T
70–80	28	29	27	44	56	10.3±2.2	B_T
81–92	27	30	40	30	70	16.3±3.3	C_T
B lymphocytes							
1–9	28	18	5	77	23	4.5±1.8	A_B
10–15	28	30	33	37	63	12.5±1.8	B_B
16–27	27	36	44	20	89	16.6±3.2	C_B

Table 2 shows the skin PHA reactivity in relation to the intensity of patients' sensitization to SA and NP.

It is seen that patients with negative skin reactions to bacterial allergens have a lowered skin PHA reaction. The mean infiltrate diameter in this case was 9.2-9.1 mm in the A and A_1 groups, while the percentage of positive skin PHA reaction was 19% and 20%, respectively. In parallel with the rise of skin sensitivity to SA and NP (B, C, D and B_1, C_1, and D_1 groups) the skin sensitivity to PHA also increased. This trend was especially obvious regarding the sensitization of patients to SA. For instance, when the diameter of the infiltrate following intracutaneous allergen injection was 30 mm or more (see the D group), the diameter of the skin papula appearing in response to PHA was on average 22.5±4.1 mm, and the percentage of patients exhibiting a normal reaction to PHA (60%) was more than three times higher than in the A group. In N-SABA patients with a similar diameter of the skin response to NP (30 mm or more) the mean diameter of the papula resulting from intracutaneous PHA injection increased to 17.9±3.3 mm (the same index in patients with a negative skin NP reaction was 9.1±2.7 mm). The frequency of a normal skin PHA reaction increased from 20% in the A_1 group to 53% in the D_1 group (Table 2).

It was also shown that the average levels of serum immunoglobulins of the A, M, and G classes in the N-SABA and SABA patients in remission revealed no significant differences and were within the range of normal variations. Nor were reliable changes observed in patient skin reactivity to PHA in relation to the Ig level variations, with the exception of IgA. The patients with a serum IgA level below 150 mg% (the normal variability being within 42-370 mg%) exhibited the least frequent occurrence of positive skin PHA reactions, and the mean papula diameter was about 9.1±3.6 mm. An increase in the serum IgA level (to 260 mg% and more) was accompanied by a rise in the percentage of positive PHA reactions as well as in the mean diameter of papulae (to 15.1±3.1 mm). However, the groups with relatively low and high serum IgA contents did not differ significantly ($p>0.05$). Nevertheless, there was a tendency for a reduced skin PHA reactivity to be associated with a relatively low concentration of serum IgA in the IABA patients.

TABLE 2. Skin Reaction to PHA as a Function of Severity of Sensitization to *St. aureus* and *N. perflava*

Result of intracutaneous allergen test (diameter), mm	Number of patients	Results of intracutaneous PHA test		Group	Statistical values
		M±*m*, mm	Percent of patients with normal PHA test		
Staphylococcus aureus					
0	31	9.2±2.1	19	A	–
1–19	13	8.6±2.2	15	B	$tAD=3.1$, $p<0.01$
20–29	13	9.5±3.2	38	C	$tBD=2.57$, $p<0.02$
30 and more	20	22.5±4.1	60	D	$tCD=2.16$, $p<0.05$
Neisseria perflava					
0	15	9.1±2.7	20	A_1	
1–19	9	10.7±3.4	11	B_1	tA_1D_1 ns
20–29	20	7.9±2.5	20	C_1	tB_1D_1 ns
30 and more	28	17.9±3.3	53	D_1	tC_1D_1, $p<0.05$

Note: ns: nonsignificant.

Our results and the reported data of other workers make it plausible to assume that lectins and lectin receptors (oligosaccharide carbohydrates of membrane glycoproteins and/or glycolipids) participate in the generation of allergic reactivity [12]. It was shown, for instance, that the formation of a lectin-receptor complex on the lymphocyte membrane can block the antigen-binding receptors of lymphocytes [5]. The lectin-induced reduction in the functional activity of antigen-binding receptors on lymphocytes indirectly reflects the participation of lectins in immune processes. This corresponds well to the data showing the inhibition of immune receptor activity following the action of some choline preparations [2], antibodies to choline receptors [3], and certain toxin antigens [6]. Lectins may also directly act upon human basophils and mast cells of germ-free rats, inducing histamine release. This phenomenon occurs under the influence of PHA and ConA. The release of allergy transmitters (including C_3) in the course of development of hypersensitivity to bacterial allergens also necessarily requires the participation of lectins, specifically ConA [9,11]. The interaction of two kinds of receptors, lectin and immune [5], is consistent with the concept expounded by A. D. Ado regarding the interaction between the antigen-binding and transmitter receptors of lymphocytes.

From the standpoint of this concept, the decrease in skin PHA reactivity of IABA patients associated with hypersensitivity to bacterial allergens may be explained by a feedback effect of immune receptors on the lectin receptors of immunocompetent cells, i.e., a change in the functional state of antigen-binding receptors on the lymphocytes in allergic states may specifically change the functional activity of lectin receptors, leading to a decreased capacity of the latter to interact with the corresponding lectins.

At the same time, it is well established that the development of delayed hypersensitivity of the skin is to a considerable extent mediated by the dermal immunocytes. A decline in their ability to interact with lectins can result in reduced lymphokine production, leading to a derangement of dermal cell-transmitter interaction. One of the consequences of such derangement is a diminished sensitivity of the skin to lectins, specifically PHA. Evidently, SH therapy, along with other effects, promotes the recovery of the functional activity of the lectin receptors and the restoration of skin PHA reactivity.

Analysis of the relationships between several immunological parameters and the skin PHA reaction revealed that a decrease of skin sensitivity to this lectin is connected with a reduced level of not only T lymphocytes, but also B lymphocytes in the peripheral blood of IABA patients. The extent of patients' sensitization to the bacterial allergens also influenced the skin sensitivity to PHA, i.e., the intensity of the skin reaction to bacterial allergens correlated positively with the skin PHA reactivity. Negative or weakly positive reactions to bacterial allergens were associated with a weak skin PHA reaction or no reaction at all. Probably, at a certain stage of development of delayed hypersensitivity the dermal immunocytes prove to be not "ready" to release lymphokines and to form papulae in response to the action of bacterial allergens and/or lectins.

The disclosed tendency toward a decrease of the skin PHA reaction associated with a relatively low serum concentration of IgA, but not other immunoglobulins in IABA patients may be explained by the preferential harboring of this particular immunoglobulin in the mucosal organs and by the peculiarities of its structure and functions.

The inverse relationship between the skin PHA reaction and phagocytic activity of IABA patients' blood neutrophils may reflect the differences in the specific change of the reactivity of polymorphonuclear and mononuclear cells in the course of the establishment of allergic reactivity. In addition, a high phagocytic activity of the blood neutrophils can reduce the concentration of bacterial allergens and lectins in the skin.

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