

Variations in T Cell Subsets During Hyposensitization of Grass-Sensitive Patients with Formaldehyde Modified Extracts

Allergoids

F. ANFOSSO, G. ALCARAZ, D. VERVLOET and J. CHARPIN

INSERM U.174, Marseille, France

In atopic patients with clinical symptoms of hay fever, changes in T_{γ} and T_{μ} cells were evaluated during desensitization. A significant increase in T_{μ} and overall in T_{γ} cells was noted. These results suggested that T cell defect could be restored by desensitization treatment.

Key words: desensitization; grass pollen; T lymphocyte.

Accepted for publication 25 June 1982

T_{γ} and T_{μ} cells have been demonstrated to exert suppressor or helper functions in humans (4). Atopic patients have lower numbers of T lymphocytes than normal (7) and their relative percentages of T_{γ} and T_{μ} cells still appear controversial (1, 2). Desensitization of atopic patients seems to restore a defect in the suppressive function of T cells (6). Recent therapeutic developments are based on the use of modified extracts of allergens. This is the case with allergoids whose binding to IgE antibodies is altered (3). This paper reports the modification in total T cells, T_{γ} and T_{μ} cells in two groups of five patients desensitized with alum-precipitated or allergoid-treated grass pollen extracts. Results supported previous findings of reduced T_{γ} cells in atopy and indicated that desensitization increased their number.

MATERIAL AND METHODS

Patients

Ten patients with positive skin tests to grasses and grass-specific IgE as assayed by RAST,

were selected in the Pneumology Department (Hôpital Sainte Marguerite Marseille, France). The patients had not previously been desensitized. Five received injections of alum-precipitated grass extracts and the other five were treated with allergoids (Allergopharma) for 1 year. They were randomly distributed.

Total T cells, T_{γ} and T_{μ} cell determination

T_{γ} and T_{μ} cells were counted before, during and after the treatment. Subsets of peripheral blood T lymphocytes were determined as described by Moretta et al. (4). Peripheral blood lymphocytes (PBL) were isolated by Ficoll-hypaque centrifugation. T cells were recovered by E rosettes. T_{γ} and T_{μ} were isolated by rosetting with ox red blood cells coated with anti-bovine erythrocyte IgG or IgM antibodies. Each T lymphocyte surrounded by more than three red cells was considered as bearing Fc receptors for IgG or IgM. PBL from seven healthy adult non-atopic patients served as controls.

Table 1
T cell subsets in the two groups of patients

Patients	Total dose received (PNU)	Before treatment			After treatment		
		T _{total} *	T _μ **	T _γ **	T _{total}	T _μ	T _γ
<i>Group A</i>							
HOF	11,150	68	43	2.6	65	44	5.2
FED	14,150	71	41	5.7	75	53	6.2
MAN	12,150	60	55	3.6	70	58	4.2
MAT	13,710	55	62	2.4	55	63	3.5
POG	19,650	53	67	1.9	55	72	5.6
Mean ± SEM		61.4 ± 3.8	53.6 ± 5.6	3.2 ± 5.1	64 ± 4.0	58 ± 6.3	4.9 ± 0.6
<i>Group B</i>							
HAD	4,050	63	56	2.6	72	78	4.9
GIM	44,200	55	69	1.8	65	81	4.1
MAU	120,750	52	44	3.7	58	46	7.2
REZ	117,700	59	57	2.0	68	66	2.9
CAL	10,700	67	61	4.4	77	70	10.1
Mean ± SEM		59.2 ± 3.2	57.4 ± 6.0	2.9 ± 0.5	68 ± 4.5	68.2 ± 9.9	5.8 ± 1.3
Controls*** (n = 7)		67 ± 4.0	53.3 ± 2.5	7.4 ± 0.8			

* Percentages of total blood leucocytes.
 ** Percentages of total T cell.
 *** Normal donors.

Allergens

An ammonium bicarbonate-extracted and alum-precipitated mixture of six grass pollen extracts and the allergoid-treated extracts were purchased from Allergopharma. The allergenic activity determined by RAST inhibition of the allergoid extract was reduced 1,000 fold as indicated by the manufacturers. The two extracts were quantified in Protein Nitrogen Unit (PNU).

Statistical data

Comparison of control and patient groups, and values before and after treatment, were made by Student's t-test. Percentages of the T cell subsets were determined by computed linear regression analysis. The F values indicated if a linear relationship existed for each patient, between two stages of the treatment.

RESULTS

Although IgE antibody changes were identical in both the alum-precipitated and allergoid-treated groups during desensitization (data not shown), we looked for differences at the cellular level.

Total T cells

The total numbers of PBL in the patients were similar to those of normal subjects (5830 ± 1248/mm³) before treatment, but their percentages of total T cells were significantly lower (0.02 < P < 0.05). Although in both treated groups the mean percentage increased after treatment, this variation was only significant in the allergoid-treated group B (Table 1).

T_γ cells

Patients had lower T_γ percentages than controls ($P < 0.01$). In the allergoid-treated group B all the T_γ cells increased $0.02 < P < 0.05$. In the alum-precipitated patients (group A) T_γ levels changed quite independently (Table 1).

T_μ cells

T_μ percentages were identical in atopic and non-atopic patients before treatment. After desensitization a significant rise was only noted in the allergoid-treated group in spite of large individual variations (Table 1). The F values were always significant (data not shown) indicating an analogous effect of the treatment on all patients $0.02 < P < 0.05$.

DISCUSSION

Our results confirmed preceding reports describing abnormally low levels of T cells in atopic patients (1, 7). Total T cells and a T cell subset bearing receptors for IgG were decreased. A positive correlation was found between absolute numbers of T_γ and total T cells in our patients, (data not shown) which was not found in normal subjects. T_γ cells appeared to act as non-specific, or as specific suppressor cells (4, 6). It would be of interest to ascertain whether the quantitative defect in T_γ cells, which could be correlated with a decreased suppressive function, would be restored after desensitization. We noted that in patients receiving allergoid-treated grass pollen extracts the total T cell, T_γ and T_μ levels increased whatever the dose of allergens. They all showed similar changes within their T cell subsets, whereas, in the other groups, the levels were modified quite independently. These results did not confirm those of Canonica et al., but the explanation could be that either a same T cell subset expresses both Fc_μ and Fc_γ receptors or that activated T_γ cells can sequentially express Fc_μ receptors (5).

Clinical results indicated that improvement was not correlated with IgE Ab, blocking Ab levels (data not shown), and cellular changes.

Although these results showed that desensitization may modify the immune response at the cellular level, many more experiments are needed to demonstrate the efficiency of allergoid versus the usual allergenic extracts.

ACKNOWLEDGEMENTS

We are grateful to Dr A. Friggi for his help in statistical studies, and to Mrs. A. Renaux for typing this manuscript.

REFERENCES

1. Canonica, G. W., Mingari, M. C., Melioli, G., Colombatti, M. & Moretta, L.: Imbalances of T cell subpopulations in patients with atopic diseases and effect of specific immunotherapy. *J. Immunol.* **123**, 2669–2672, 1979.
2. Gupta, S., Fikrig, S. & Good, R. A.: Subpopulations of human T lymphocytes. XIII. T cell subpopulations (T_M and T_G) in children with bronchial asthma. *Int. Arch. Allergy Appl. Immunol.* **61**, 293–298, 1980.
3. Marsh, D. G.: Preparation and properties of allergoids derived from native pollen allergens by mild formalin treatment. *Int. Arch. Allergy Appl. Immunol.* **41**, 199–215, 1971.
4. Moretta, L., Webb, S. R., Grosso, C. E., Lydyard, P. M. & Cooper, M. D.: Functional analysis of two human T cell subpopulations: help and suppression of B cell responses by T cells bearing receptors for IgM or IgG. *J. Exp. Med.* **146**, 184–200, 1977.
5. Pichler, W. J., Lum, L. & Broder, S.: Fc-receptors on human T lymphocytes. I. Transition of T_γ to T_μ cells. *J. Immunol.* **121**, 1540–1548, 1978.
6. Rocklin, R. E., Breard, J., Gupta, S., Good, R. A. & Melmon, K. L.: Characterization of the human blood lymphocytes that produce a histamine-induced suppressor factor (HSF). *Cell Immunol.* **51**, 226–237, 1980.
7. Strannegard, O. & Strannegard, I. L.: T lymphocyte numbers and function in human IgE-mediated allergy. *Immunol. Rev.* **41**, 149–170, 1978.

Address:

Francine Anfosso
I.N.S.E.R.M. Unité 174
10, Avenue Viton
13009 Marseille
France

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.