



CLINICAL

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TREATMENT OF ALLERGIC MANIFESTATIONS WITH TRANSFER FACTOR (TF)

SUMMARY

Experiments on animals and preliminary data on humans have shown that Transfer Factor (TF), the protein responsible for cell mediator reactivity against specific antigens, induces Cytokine profiles with Th1 Lymphocyte-activation characteristics. This, therefore, demonstrates that the use of allergen-specific TF therapy in patients with abnormal Th2 stimulation, typical of allergic conditions, has a "suppressor" action on these Th2s, which is physiologically induced by Th1 stimulation. In order to confirm these findings, we prepared and standardised a homeopathic drug known as "TF22 suppressor", containing specific Lymphocyte extracts to act against the proteins of the more common pollens and house dust.

This report is a clinical evaluation of a pilot study on 47 patients suffering from Allergic Rhinitis, Infantile Asthma and Cutaneous Eczema. The results suggest the use of TF22 in all these pathologies.

KEY WORDS

TRANSFER FACTOR, ATOPY, Th1/Th2 LYMPHOCYTES, POLLENS, HOUSE DUST

ALLERGIC DISORDERS: PROFILE OF LYMPHOKINES

Atopy is a disease characterised by a genetic disorder that manifests itself, via the increased capacity of the B Lymphocytes, in the production of IgE antibodies against some ubiquitous antigens (allergens) that can trigger an immune response after inhalation, ingestion or penetration of the skin. CD4+ Lymphocytes play a very important part in causing the production of IgE by the B Lymphocytes as this only occurs if Interleukin-4 (IL-4), produced by the T-helper 2 cell, is secreted [the latter can be inhibited by Interferon-gamma (IFN-gamma) produced by the T-helper 1 cell (1, 2)].

Specific IgEs are pathogenetically involved in diseases associated with atopy and, in particular allergic asthma, as well as all types of Rhinitis and allergic

dermatitis. One hypothesis that could explain the excessive production of allergen-specific IgEs would be a regulation defect at T Lymphocyte level (3). This hypothesis is corroborated by the analysis of the production of Lymphokines by T Lymphocytes that are reactive to the allergens.

Although the T clones specifically for bacterial antigens that originate from the peripheral blood of atopic donors display a predominant number of T-helper 1 phenotypes (Th1), the vast majority of allergen-specific T clones (CD4+) originating from the same donors prove to be Th2 Phenotype with a high capacity for producing IL-4 and very little or absolutely no capacity for producing IFN-gamma (4-7). It is still not clear why the allergens in atopic subjects "expand" the CD4+ Th2 clones. Some authors hypothesise that this could be due to the physico-chemical structure of the allergens. Compounds full of polyph-

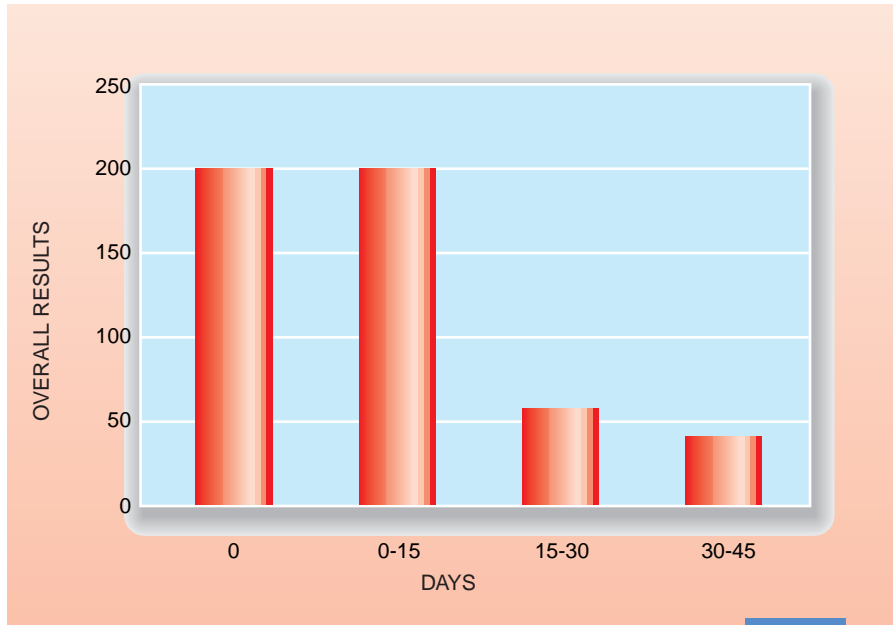


Figure. 1

nols tend to activate Th2 cells (8). Helminths, that usually activate Th2s, release numerous proteolytic enzymes (some allergens are proteases).

THE PATTERN OF LYMPHOKINES IN ALLERGIC ASTHMA

Many studies show that Th2 cells and the Lymphokine they produce are involved in the physiopathology of allergic disorders mediated by IgEs. Higher percentages of T clones producing IL-4 and lower percentages of T clones producing IFN-gamma were obtained from the peripheral blood of patients suffering from severe atopic diseases in comparison with the control patients (3, 9).

In addition, the stimulation using mitogens of the lymphocytes of conjunctival infiltrates in patients suffering from allergic conjunctivitis displays a notable prevalence of Th2 cells (10). By using the hybridisation techniques in situ, the RNA messenger for Th2 Lymphokines rather than Th1 Lymphokines, was found in the cutaneous biopsies of atopic subjects (11), in bronchial biopsies or in the bronchial lavages of asthmatic subjects (12, 13) and after allergenic stimulation in allergen-induced Rhinitis (14).

LYMPHOKINE PATTERN IN ATOPIC DERMATITIS

The role of CD4+s and their Lymphokines in the pathogenesis of Atopic Dermatitis is still rather controversial. However, more than 80% of these patients have a high strength of serous IgEs with

specificity for numerous environmental allergens that cause immediate allergic skin reactions. Nevertheless, the relationship between Atopic Dermatitis and allergenic pathogenesis still remains unclear, even though high proportions of Th2 clones were found in the cutaneous lesions of patients (15). Th2 Lymphocyte clones can also be isolated on intact skin after its intradermal exposure to allergens, suggesting that percutaneous sensitisation to allergens can play an important part in the induction of lesions in patients with Atopic Dermatitis (16, 17).

TRANSFER FACTOR ACTIONS ON T-HELPER POPULATIONS

It is well-known that TF causes cyclic AMP in T Lymphocytes to be increased by 3 to 8 times and that this can lead to a functional increase in T-suppressor Lymphocytes (18), thus carrying out an immunoregulatory action where a hyperergic response is underway. It has also been noted in HIV-positive patients being treated with Zidovudine (ZVD) and TF, that the Lymphokine pattern with the usual prevalence of the activation of Th2 clones that one sees in AIDS

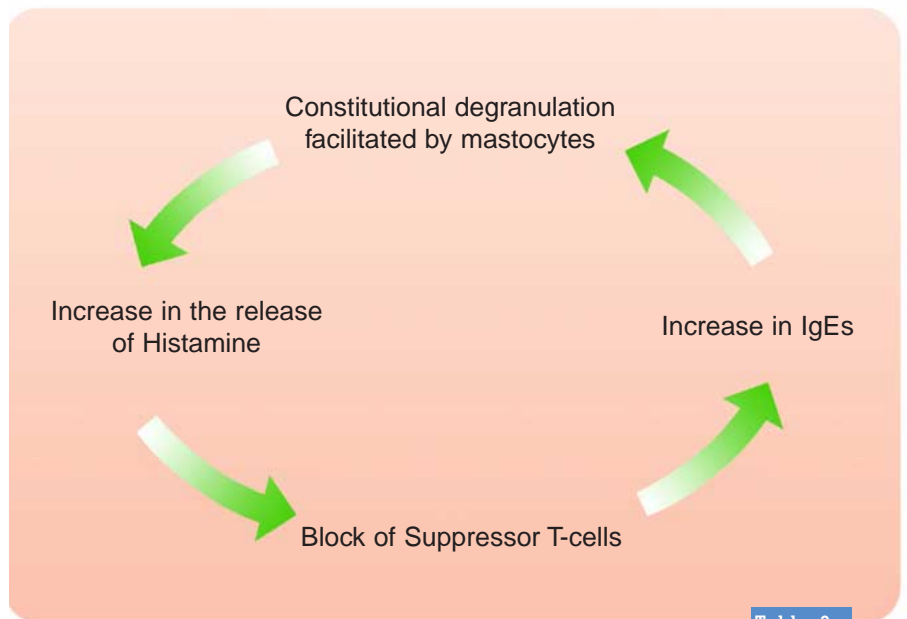


Table. 2

Auto-reverberating vicious circle in atopic patients.

patients (19), tends to be inverted and one instead sees an increase in Th1-derived Lymphokines in the peripheral blood of the patients treated (20).

In experimental systems, TF also induces Cytokine profiles that are characteristic of the activation of Th1 Lymphocytes. The splenic cells in mice treated with TF, specifically induce the production of IFN-gamma in response to antigens, whereas the production of IL-4 or IL-10 is negligible (21). We, therefore, fully understand how the admission of TF specifically for particular allergens in patients who have an abnormal stimulation of T-helper 2 cells (admission induces the activation of T-helper 1s), can have an inhibiting action on the Th2s, decreasing the activity and reducing the production of Lymphokines (22). This is the mechanism that we can hypothesise on the basis of the results obtained from Jarisch (1981) who, while treating 10 paediatric patients suffering from severe Atopic Dermatitis, noticed a significant reduction in serous IgEs in 8 patients and a significant clinical improvement in 6 when compared with a control group of 10 patients (23). It is well-known that specific-IgE production by the B Lymphocytes is induced by a typical stimulation of IL-4 (produced in excess by Th2 clones occurring in excess in atopy) and the latter can be inhibited by Interferon-gamma (IFN-gamma) produced by the Th1 cells (1, 2).

Standard TF is obtained from Lymphocytes of the peripheral blood. Some parts of TF, isolated using chromatography, or the dialyzates obtained from some lymphocyte populations, have immune response suppressor properties (24-27, 1-4).

That said, one fully understands how some TFs with a notable suppressor characteristic can be used to effectively treat the various allergic manifestations in which the action of Th2 clones is prevalent (28). We therefore went on to prepare two Suppressor TFs: one for pollen and the other for house dust (29).

These TFs have been used in a single product (TF22) to treat 47 patients included in a pilot study: 20 cases suffering from Allergic Rhinitis, 20 from infantile Asthma and 7 from Cutaneous Eczema.

SURVEY OF TREATMENT WITH TF AGAINST POLLEN AND HOUSE DUST

ALLERGIC RHINITIS

In order to test the effectiveness of TF22, we selected 20 patients suffering from seasonal Allergic Rhinitis. After 15 days of observation without administering

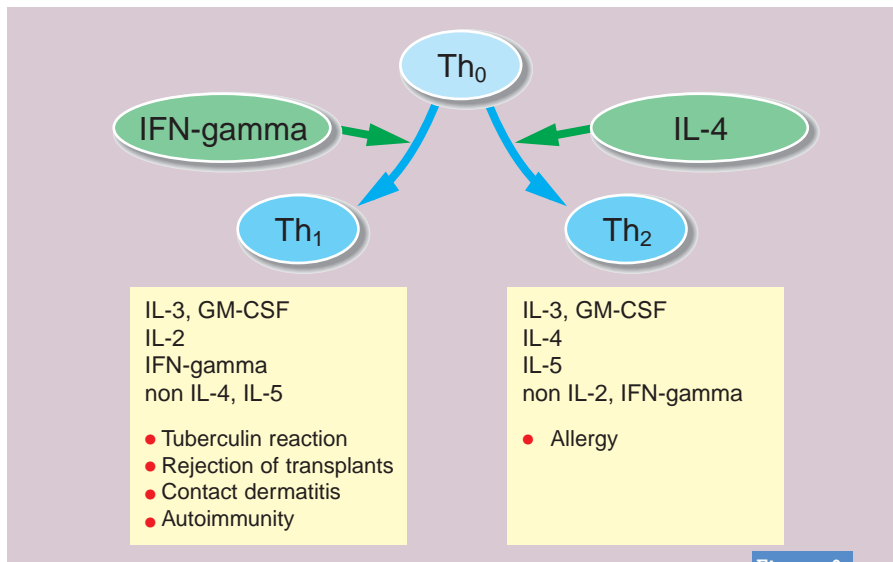


Figure. 3

Differentiation of T-helper Lymphocytes (Th0) in Th1 and Th2 cells.

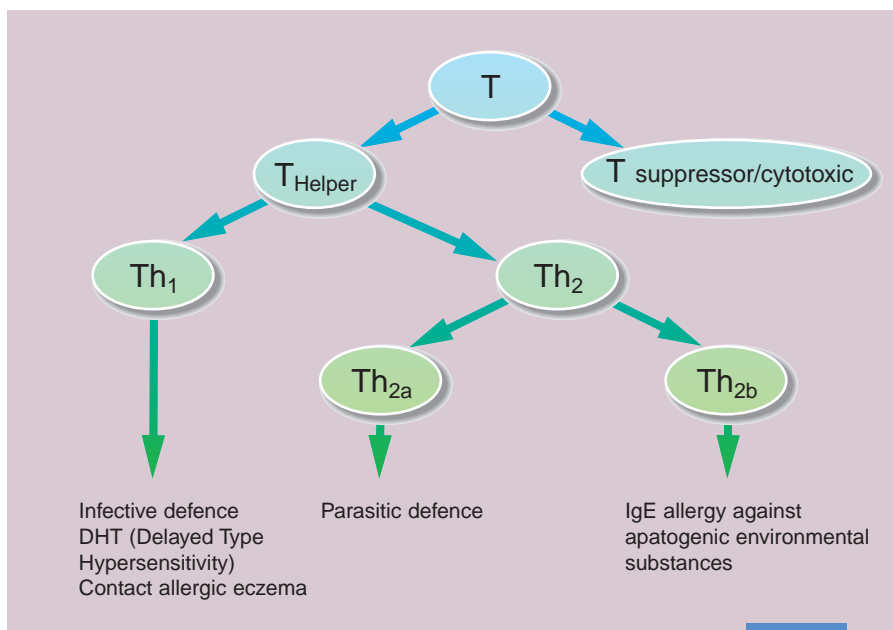


Table. 4

Differentiation of the T-helper subpopulation in allergies, infective defence and parasitic defence.

TF22 but just topical medicines, we introduced TF22 treatment using a dose of 2 capsules per day. The symptomology was assessed before and during treatment (frequency of sneezing, rhinorrhoea, lachrymation) rating the symptoms on a scale of 1 to 4.

Figure 1 illustrates how administering TF22 induces a rapid and lasting reduction in symptomology with statistical significance (between the groups $p < 0.01$).

In 5 patients, the treatment was initiated during a phase of proclaimed symptomological development.

TF22 enabled us to control the disorders relating to Allergic Rhinitis in this case as well.

The following year, 8 of the 20 patients in our survey received preventive treatment immediately before the allergy season and did not present any hyperergic manifestations, confirming what was observed by other authors (27).

We should point out that these patients had been presenting with seasonal Allergic Rhinitis for many years.

INTERDIGITAL CUTANEOUS ECZEMA

Seven patients suffering from recurring interdigital Eczema were treated with TF22. Only a slight improvement was observed in 2 patients whilst in the remaining 5, we saw a complete remission of the symptomology, which lasted for 3 months after treatment finished.

ASTHMA

20 children, aged between 8 and 12, who were allergic to seasonal pollen, were treated with TF22. Their clinical conditions had already clearly improved after 2 weeks. The number of episodes on a monthly basis is 80%. The quantity of aid drugs required for these patients (Cortisones, Beta stimulants,

Teophillin) was reduced by 70%. The treatments were continued without collateral effects or contraindications throughout the period of exposure to pollens.

CONCLUSIONS

Although the number of patients treated was still limited and did not allow us to give conclusive evaluations of the effectiveness of TF in allergic manifestations, the theoretical supposition of its use, the absence of collateral effects and our current clinical results, which were also observed by other authors, appear to suggest its use in treating atopic manifestations, particularly asthma, eczema and Rhinitis. ■

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