

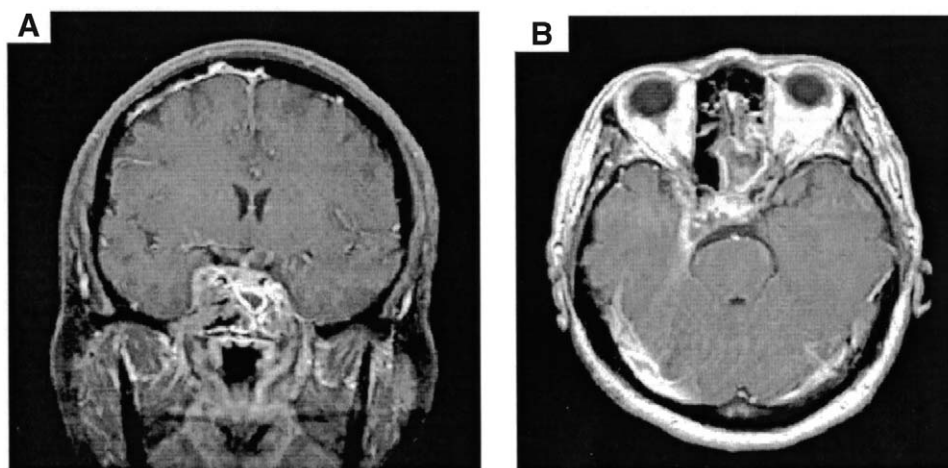


FIG 1. A, Coronal postcontrast T1-weighted image of the brain shows fluid and abnormal mucosal enhancement in the sphenoid sinus and right cavernous sinus thrombosis. B, Axial postcontrast T1-weighted image shows thrombosis of the right cavernous sinus.

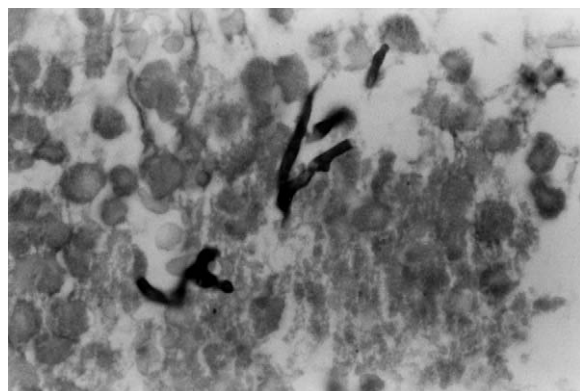


FIG 2. Photomicrograph shows branching irregular hyphae. Gomori methenamine silver (under oil immersion).

good outcome from combined surgical and anti-inflammatory therapy. Clinicians need to be aware of the expanding spectrum of AAS as we learn more about this condition.

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Soluble decoy receptor 3: Increased levels in atopic patients

To the Editor:

This is the first report to describe the serum decoy receptor 3 (DcR3) levels in atopic patients. DcR3 is a soluble molecule that lacks a transmembrane domain and was initially found by Pitti et al.¹ DcR3, also known as TR6 or M68, is a member of the TNF receptor superfamily and is also a receptor for Fas ligand and LIGHT.¹⁻³ Its expression was supposed to contribute to the ability of some tumors to escape immune-cytotoxic attack. In addition, DcR3 expression can be detected in some virus-associated lymphoma (Epstein-Barr virus or HTLV-1) as well as in

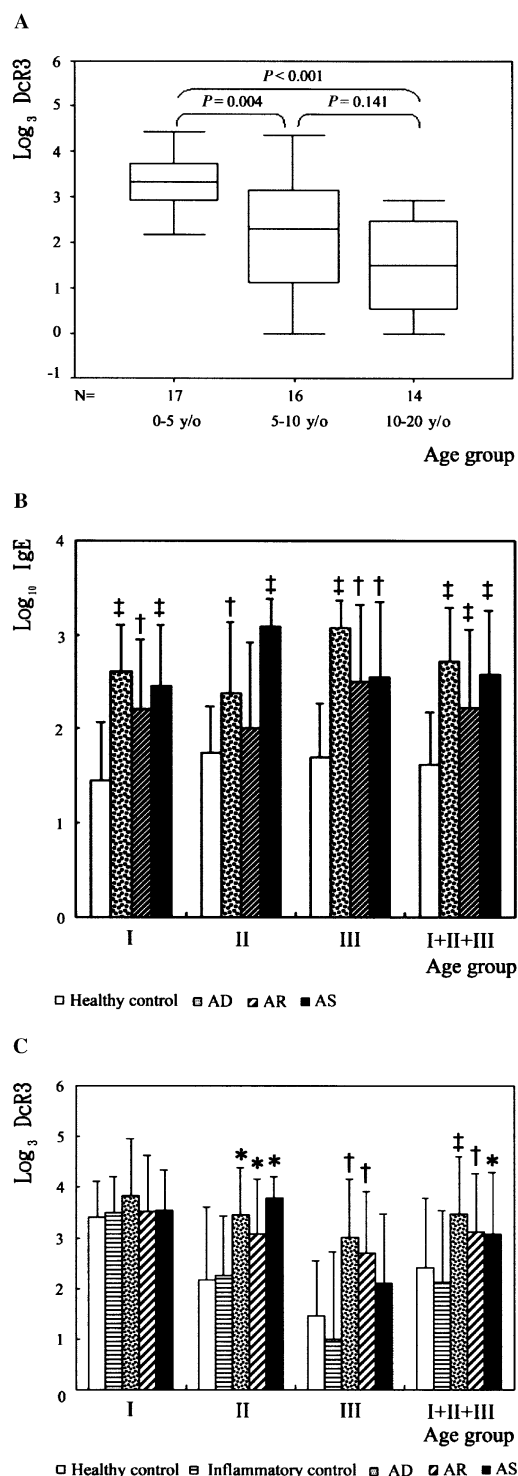


FIG 1. Serum total IgE and soluble DcR3 levels in controls and in atopic patients. **A**, Comparison of serum DcR3 in healthy controls by 3 different age groups. **B**, Comparison of serum total IgE in healthy controls and allergic patients. **C**, Comparison of serum DcR3 levels in healthy controls, inflammatory controls, and allergic patients. AS, Asthma. * $P<.05$. † $P<.01$. ‡ $P<.001$.

malignant melanoma, malignant glioma, silicosis, and systemic lupus erythematosus.⁴⁻⁶ The possible mechanism is that DcR3 can neutralize the cytotoxic effects of Fas and FasL interaction and can escape surveillance by the patient's own immune system.⁷

Most of the studies about DcR3 have focused mainly on its effect on binding with FasL. A recent study, however, showed that DcR3 might modulate the maturation and differentiation of dendritic cells and, subsequently, the T_H2 response.⁸ Although the etiologies are complex and multifactorial, allergic diseases are believed to be caused by T_H2 -like immunity to allergens in affected tissues. With these data taken together, it is hypothesized that DcR3 may play a role in the pathogenesis of allergic diseases.

Nevertheless, little is known about the relationship between DcR3 and children's age, sex, serum total IgE level, and allergic diseases. Therefore, sera were collected from 101 patients having 1 or more allergic disease, including 53 patients with atopic dermatitis (AD; age, 1.0-18.8 years; mean, 7.9 ± 5.4 years), 82 patients with allergic rhinitis (AR; age, 1.0-17.5 years; mean, 7.8 ± 4.4 years), with asthma (age, 2.5-18.0 years; mean, 8.3 ± 5.2 years). Sera were collected from 47 healthy Taiwanese children (age, 1.3-19.5 years; mean, 8.5 ± 5.7 years); these children served as healthy control subjects during the study. Another 12 patients with juvenile rheumatoid arthritis (age, 4.8-19.3 years; mean, 8.9 ± 4.8 years) served as nonatopic inflammatory control subjects. The diagnosis of atopic disease was based on the medical history, physical examination, and objective measures. All samples were stored at -20°C until tested. Human DcR3 was measured by using the ELISA kit (Anawrahta Biotech Co, Taipei, Taiwan), and the sensitivity was 1 ng/mL. Standard curve was set up by 1:3 serial dilution. Serum IgE was assayed by AlaSTAT microplate (Diagnostic Products Corp, Los Angeles, Calif), and the detection limit was 1.0 IU/mL. Because the DcR3 and IgE levels were not normally distributed, data were log-transformed to obtain a Gaussian distribution, and the results were expressed as geometric means $\pm$ SDs. The unpaired Student *t* test was used for comparisons between clinical groups. Correlation coefficients and statistical significance were determined by using Pearson analysis, and a *P* value $<.05$ was considered statistically significant.

The serum DcR3 of healthy controls ranged from 1 to 288 ng/mL with the geometric mean $\pm$ SD of 2.99 ± 1.23 . We measured the association between $\text{Log}_3 \text{ DcR3}$, $\text{Log}_{10} \text{ IgE}$, age, and sex. Significant negative correlation was noted between $\text{Log}_3 \text{ DcR3}$ and age ($r = -0.547$, $P < .001$). The comparison of serum DcR3 levels in healthy controls of 3 different age groups is summarized in Fig 1, A. The data suggested that DcR3 levels in younger children (group I) were higher than those of groups II and III. DcR3 was higher in group II than in group III, but the difference was not statistically significant ($P = .141$).

On the basis of our data, all patients with AD, asthma, and AR as a whole or in the 3 age groups showed a significantly higher $\text{Log}_{10} \text{ IgE}$ than in controls, except

AR in group II (Fig 1, B). In addition, Log₃ DcR3 was significantly higher in patients with AD, AR, and asthma than in healthy controls, with the significant difference existing in patients with AD, AR, and asthma in group II, and in patients with AD and AR in group III, after age group matching (Fig 1, C). No significant difference of Log₃ DcR3 was found between healthy and nonatopic inflammatory controls. Therefore, the elevation of DcR3 in atopic patients is not dependent on inflammation. Juvenile rheumatoid arthritis has been suggested to be T_H1-mediated, which may be different from T_H2-mediated allergic diseases in the mechanisms of inflammation. Neither healthy controls nor patients with AD, AR, and asthma showed a significant correlation for Log₃ DcR3 and Log₁₀ IgE. The findings also implied that the change is not dependent on IgE.

The pathogenesis of this phenomenon may be far more complex, and there are 2 possible hypotheses. First, DcR3 may act as an effector molecule to skew T-cell response to the T_H2 phenotype.⁸ Hsu et al⁸ reported that DcR3 profoundly modulated dendritic cell differentiation and maturation from CD14⁺ monocytes, including the up-regulation of CD86 and the downregulation of CD40, CD80, CD1a, and HLA-DR. The dendritic cells then migrate to the regional lymph nodes, where they act as antigen-presenting cells for both B cells and T cells. In the presence of IL-4 and IL-13, the B cell undergoes class switching to produce IgE and initiates the T_H2 response. Thus, T_H2 response may play an important role in increasing DcR3 levels in allergic patients.

Second, dysregulated apoptosis in AD and asthma were also reported.⁹ T cells infiltrating the skin of patients with AD expressed both Fas and FasL. Yet they did not show any signs of apoptosis. In addition, the upregulation of several prosurvival cytokines and significant differences in the expression of apoptosis-related genes were found in the peripheral blood of atopic individuals with or without asthma by cDNA array.¹⁰ We do not know whether these findings also imply that DcR3 may play a role in the dysregulated apoptosis by FasL binding.

We conclude that serum DcR3 declines with age significantly, and the change is not dependent on IgE. DcR3 is also obviously higher in patients with some allergic diseases than in the healthy and the nonatopic inflammatory controls. Knowledge of the molecular basis for dysregulated apoptosis or T_H2 skewing is pivotal in understanding the pathogenesis of DcR3 involvement in allergic diseases. This may lead to a more focused therapeutic application in the future.

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Cysteinyl leukotrienes and collagen type I synthesis in asthma

To the Editor:

Airway inflammation in asthma can be evaluated by noninvasive sputum analyses, including the counting of eosinophils and the measurement of soluble factors such as eosinophil cationic protein, cytokines, and cysteinyl leukotrienes (CysLTs). CysLTs have been implicated in the pathogenesis of asthma.¹⁻³ CysLTs are believed to take part in acute airway narrowing by induction of bronchoconstriction, disturbance of ciliary movement, mucous secretion, and plasma leakage. In addition to their acute effects on airways, CysLTs have been reported to attract eosinophils,⁴ proliferate airway smooth muscle,⁵ and increase collagen production from fibroblasts,^{6,7} suggesting that CysLTs might be also involved in chronic inflammation and airway remodeling. In fact, it has been shown that the blockade of CysLT₁ receptor suppresses subepithelial fibrosis in a mouse asthma model.⁸

Procollagen type I C-terminal peptide (PICP) is also increased in the sputum of asthma subjects.⁹ PICP is