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Heterogeneity of Serum IgE Levels in Atopic Dermatitis

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To determine whether serum IgE levels in patients with atopic dermatitis (AD) have a relationship to familial background of atopic respiratory disease (ARD), serum IgE levels were measured in 50 AD patients who had personal history of ARD, 37 AD patients who did not have personal history of ARD but had family history of ARD, and 52 "pure" AD patients who had neither personal nor family history of ARD. The "pure" AD patients showed significantly lower serum IgE levels than AD patients who had personal or family history of ARD. It is suggested that AD patients may be classified into at least two subgroups: 1) those with ARD predisposition who have an enhanced IgE producing potential, and 2) those without ARD predisposition who have a low or not-enhanced ability for IgE production. (Received January 20, 1986.)

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Since the first publication of Juhlin et al. (1) that serum IgE levels are elevated in the majority of patients with atopic dermatitis (AD), many investigators (2–10) have reported that severity of skin disease and presence of coexistent respiratory atopic disease (ARD) are the important clinical factors which stimulate IgE producton in AD. At the present time, however, there is still considerable obscurity as to what roles these two factors exactly play in elevating serum IgE levels in AD (11, 12). All previous studies have confirmed that although serum IgE levels roughly correlate with the severity of AD, some patients with severe AD have normal serum IgE values. Similarly, despite the fact that patients with AD and coexistent ARD show statistically higher levels of serum IgE than those with AD alone, some patients with AD and very high serum IgE levels do not have ARD.

The main purpose of the present study was to clarify these points and to see whether presence of familial background of ARD implies a relationship to serum IgE levels in AD.

MATERIAL AND METHODS

A total of 139 patients with AD, 70 mild cases and 69 severe cases, were included in this study. They ranged in age from 13 to 46 years: 98 were 13–24 years of age, and 41 were 25–46 years of age. The diagnosis was made on the basis of the morphologic appearance and distribution of skin lesions, the clinical course, and the family history of AD or ARD. We previously reported that the incidence of family history of atopic diseases is markedly lowered when the family members are four or less (13). In the present study, therefore, only those patients with AD who had family members of five or more were examined. They were classified into three subgroups: 1) those who had personal history of ARD (50 cases), 2) those who did not have personal history of ARD but had family history of ARD (37 cases), and 3) those who had neither personal history nor family history of ARD (52 cases). The incidence of family history of AD in these subgroups was 48% (24/50), 49% (18/37), and 44% (23/52), respectively.

The degree of dermatitis was determined on the following criteria: *Mild*: localization of active skin lesions to two or three anatomical areas (face, neck, upper limbs, upper trunk, lower trunk, or lower limbs) for at least a year prior to the present study. *Severe*: generalized skin lesions, or involvement of

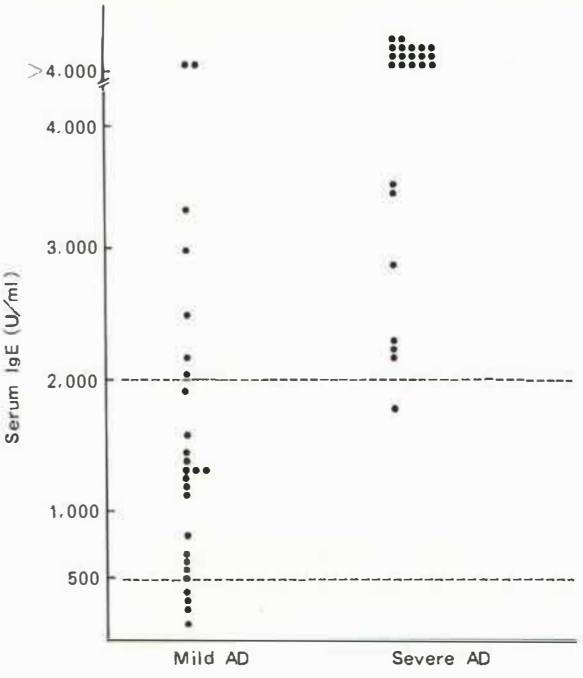

Fig. 1. Serum IgE levels in patients with atopic dermatitis who had personal history of atopic respiratory disease.

70% or more of the total body surface, for at least 6 months prior to the examination. All patients had been treated with topical corticosteroids and occasional antihistamines for at least a year prior to this study.

Serum IgE concentrations were quantitated by means of the radio-immunosorbent assay (Pharmacia, Uppsala), and expressed in U/ml of serum. While the upper confidence limit (mean +2 SD) of serum IgE values in normal Japanese adults is not yet definitely established, Mikawa et al. (14) report that the upper limit of normal values is 500 U/ml. In the present study, then, serum IgE values greater than 500 U/ml were assigned to be abnormal.

RESULTS

In the group of patients with AD who had personal history of ARD, serum IgE levels were elevated in nearly all cases of mild AD and all cases of severe AD (Fig. 1). Most cases of severe AD in this group, however, had very high serum IgE values (i.e., greater than 2000 U/ml). When serum IgE levels greater than 2000 U/ml were then compared, severe AD cases showed significantly higher incidence of such very high serum IgE levels than mild cases ($p<0.01$).

In the group of "pure" AD patients who had neither personal nor family history of ARD, elevated serum IgE levels were found in 6 of 28 (21%) mild cases, and 15 of 24 (63%) severe case (Fig. 2). This difference was significant ($p<0.01$). However, the degrees of serum IgE elevation in severe cases of this group usually were moderate (i.e., lower than 2000 U/ml). Thus, as can be seen from Figs. 1 and 2, there was a striking difference of serum IgE levels between patients with severe AD who had personal history of ARD and severe cases of "pure" AD who had neither personal history nor family history of ARD.

In the group of patients with AD who did not have personal history of ARD but had family history of ARD, severe cases showed significantly higher incidence of elevated serum IgE levels than mild ones ($p<0.01$) (Fig. 3). An interesting finding was that very high serum IgE values were observed in many severe cases of this group.

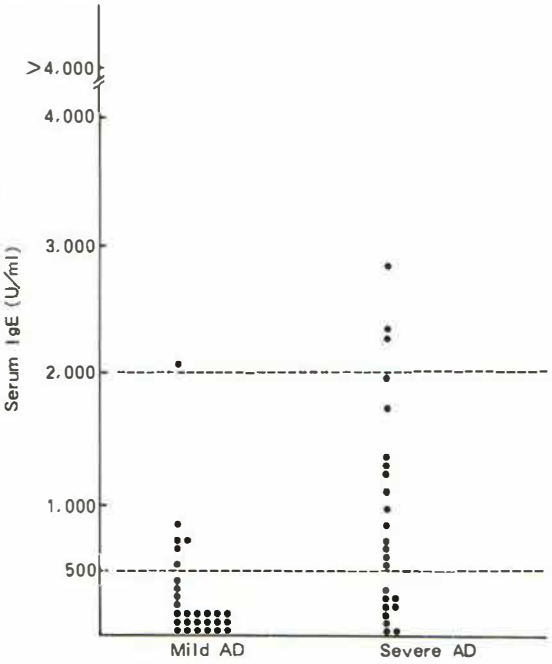

Fig. 2. Distribution of serum IgE values in patients with only atopic dermatitis who did not have family history of atopic respiratory disease.

Hanifin & Rajka (15) have stated that serum IgE level greater than 2000 U/ml is an important feature for the diagnosis of AD. When the three subgroups of AD in the present study were analysed, however, serum IgE values greater than 2000 U/ml were observed almost exclusively in AD patients who had personal or family history of ARD (Figs. 1, 2

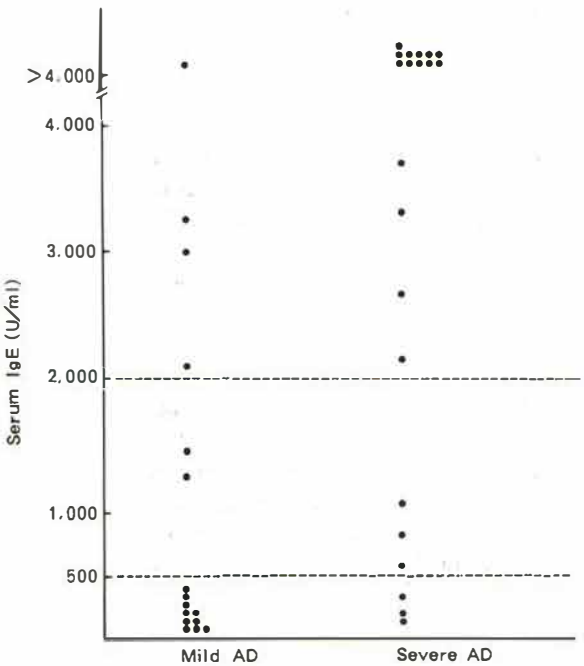

Fig. 3. Serum IgE levels in patients with only atopic dermatitis who had family history of atopic respiratory disease.

and 3). Such very high serum IgE levels were seen only rarely in the group of "pure" AD patients.

DISCUSSION

The present study demonstrates that presence of ARD family history is an important factor which stimulates serum IgE elevation in patients with AD.

In the past, serum IgE levels were compared simply between AD patients who had personal history of ARD and those who did not have personal ARD history (1–10). All the previous studies found very high serum IgE values in a considerable number of AD patients who had no personal ARD history. Many dermatologists (2, 3, 16) then held the view that presence of coexistent ARD does not directly elevate serum IgE levels of AD patients. But the present study shows that the majority of patients with solely AD and very high serum IgE levels has a family history of ARD. Therefore, the occurrence of very high serum IgE values in some patients with solely AD in previous studies might be due to a material including both patients with and without ARD family history.

The analysis of serum IgE values in severe AD patients revealed that the pattern of serum IgE elevation in this dermatosis is not homogeneous. Very high serum IgE values were consistently observed in severe AD patients who had personal history of ARD, while normal or only moderately elevated serum IgE values were seen in most cases of severe AD, who had neither personal history nor family history of ARD. It is then likely that AD *per se* brings about a moderate elevation of serum IgE levels, and that the AD-induced serum IgE elevation is greatly amplified in AD patients who have personal history of ARD.

An important finding in the present study was that very high serum IgE values were frequently observed in severe cases of AD, who did not have personal ARD history, but had familial ARD history. This suggests that the AD-induced serum IgE elevation is also amplified in AD patients who have subclinical ARD or predisposition to ARD.

The present study could not give a complete assent to the statement of Hanifin & Rajka (15) that serum IgE level greater than 2000 U/ml adds considerable support to the diagnosis of AD. Such very high serum IgE levels occurred almost exclusively in AD patients who had personal history or family history of ARD. A normal or only moderately elevated serum IgE value was common in patients with "pure" AD who had neither personal nor family history of ARD. It is well known that there is a subgroup of AD patients who do not have familial background of ARD (13, 16). In the present study, "pure" AD patients occupied 36% of total AD patients examined.

In summary, on the basis of serum IgE producing potential, patients with AD may be classified into at least two subgroups: 1) those with ARD predisposition who have an enhanced ability for biosynthesis of IgE, and 2) those without ARD predisposition who do not have an enhanced potential for IgE production.

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