

Eosinophilia in early-stage human immunodeficiency virus infection

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It has been recognized that pathophysiologic events related to human allergic diseases, such as IgE and eosinophil production, are controlled by T lymphocytes. The present epidemics of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), with its wide range of immune disturbances and selective involvement of T helper/inducer cells, could give us additional clues about the normal regulatory functions of T lymphocytes.

An increase in asthma, allergy, and drug reactions has been reported in patients with acquired immunodeficiency syndrome, and elevated serum total and specific IgE levels have also been observed in these patients.¹ Increased HIV antigen-mediated and anti-IgE-mediated histamine release have been found in these patients, and T cells from HIV-positive subjects are able to release in vitro IgE-binding factors capable of regulating IgE production. Recently, Paganelli et al.² reported an increase of eosinophil cationic protein in the serum of HIV-infected individuals, and they suggested that there is in vivo eosinophil activation and degranulation in these patients.

Seventy-seven HIV-1-infected individuals (69 men and 8 women) aged 18 to 54 years (average age, 32 ± 9.2 years) have been followed up for 3 to 42 months (average, 12 ± 9 months); and serum total and mite-specific IgE, eosinophil counts, T-cell subpopulations, and stool examination were investigated every 3 months. Results of stool analysis were positive in nine patients: *Giardia lamblia* was present in six; *Ascaris lumbricoides* in one; *Entamoeba histolytica* in one; and *Cryptosporidium* species in one.

Atopy, as determined by a personal or family

Abbreviations used

HIV: Human immunodeficiency virus
IL: Interleukin

history of asthma, rhinitis, eczema, or food allergy plus positive immediate hypersensitivity (prick) skin test results to inhalant allergens, was present in 23 patients (29.8%). Increased total serum IgE levels (>200 kilounits per liter [KU/L]) were present in 19 patients (32.7%), 10 atopic (66.6%) and 9 nonatopic patients (20.5%) ($p = \text{NS}$). Significantly higher levels of IgE were present in stage 2 when compared with stage 1 levels. IgE was also elevated in stages 3 and 4, but these differences were not statistically significant (Fig. 1). We speculate that a progressive CD4+ T-cell depletion could be responsible for the IgE increase. IgE levels were 322.8 ± 70.7 KU/L in atopic patients and 183.8 ± 32.1 KU/L in nonatopic patients ($p = \text{NS}$).

High blood eosinophil counts (>500 cells/mm³) were present in 20 patients (28.2%) including six atopic (33.3%) and 14 nonatopic patients (26.4%) ($p = \text{NS}$). There was a significant increase of eosinophils in stage 2 when compared with stage 1, and eosinophil levels decreased to values below those from stage 1 in patients in stages 3 and 4 (Fig. 1). Eosinophil counts were 253.7 ± 42.9 cells/mm³ in atopic patients and 271.8 ± 27.0 cells/mm³ in nonatopic patients ($p = \text{NS}$).

There were statistically significant correlations between eosinophil counts and both total and specific IgE, but no significant correlations were present between CD4+ or CD8+ T-lymphocyte counts and IgE or eosinophil levels. In a previous study of Hodgkin's lymphoma, another disease associated with decreased cellular immunity, we observed a good correlation among eosinophilia, serum IgE, and skin reactivity.³

In the mouse, and possibly in human beings, IgE production is controlled by T cells of two

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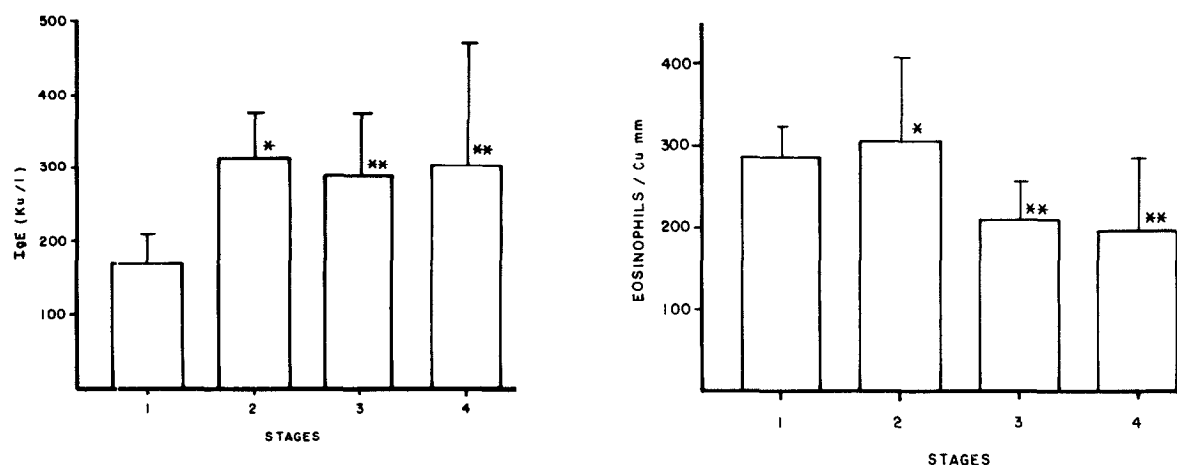


FIG. 1. IgE and eosinophil levels according to clinical stage. Results are expressed as mean values $\pm$ SEM (* $p < 0.05$; ** $p = NS$). For clinical staging, the World Health Organization staging system for HIV infection and disease was used.⁵

subtypes: T_{H1} cells producing interferon- γ , interleukin-2 (IL-2), and lymphotoxin and T_{H2} cells, which synthesize IL-4, IL-5, and IL-6. It has been suggested that imbalances between interferon- γ and IL-4 production may result in disordered IgE secretion, with interferon- γ inhibiting and IL-4 stimulating IgE production. Murray et al.⁴ reported decreased interferon- γ production in patients with acquired immunodeficiency syndrome.⁴

In the present study we could not demonstrate significant correlations between CD4+ cell counts and total or specific IgE levels. There may be some alternative hypotheses to explain this lack of correlation. (1) IL-4 may be produced by cell sources other than T lymphocytes, such as mast cells and macrophages. (2) Autonomous ("spontaneous") IL-4-independent IgE may be produced by B cells. (3) Long-lasting increases of IgE production, similar to those observed in the increased IgE levels associated with helminthic infestations, may occur even after effective treatment. The mechanism for the latter has not been clearly established.

Eosinophilia is regulated by a number of cytokines, of which IL-5 is the most prominent. We observed increased eosinophil counts in both atopic and nonatopic HIV-infected individuals. Patients in stage 2 (early symptomatic infection) had significantly higher eosinophil levels than patients who were free of symptoms (stage 1), but levels progressively decreased in stages 3 and 4

(Fig. 1). Thus eosinophil counts appeared to be more sensitive than IgE levels as indicators of clinical deterioration, because IgE levels did not progressively decrease during stages 3 and 4 in our patients.

Eosinophil and IgE levels are elevated simultaneously in a number of other clinical conditions such as allergic diseases, intestinal parasitic infections, hyper-immunoglobulin E syndrome, and others. However, it is not yet known whether this excessive formation is controlled by different mechanisms in different disease states.

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