

Immunodeficiency and other clinical immunology

Serum total and specific IgE levels in children infected with human immunodeficiency virus

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Background: Human immunodeficiency virus (HIV) infection is associated with polyclonal B-cell activation, and elevated IgE levels are found in infected adults. Chronic nasal symptoms, sinusitis, and otitis media are particularly common in children infected with HIV. The possible allergic cause of nasal symptoms in children infected with HIV has not been explored.

Objective: The study was designed to evaluate the relationship between HIV infection and IgE levels in a group of children infected with HIV.

Methods: Total serum IgE was measured by enzyme immunoassay and compared with values for age-matched normal subjects. Specific IgE was determined by RAST test to *Dermatophagoides pteronyssinus*, *American cockroach*, *Bahia grass*, *short ragweed*, *cat*, and *oak*. Lymphocyte subpopulations were determined by standard flow cytometry.

Results: Fifty-seven total IgE and 342 specific IgE levels were determined from 29 infected children (19 girls and 10 boys; ages, 7 to 150 months; mean age, 49 months). Initial IgE levels of 29 subjects ranged from 1.4 to 787.6 IU/ml (mean = 123.4 ± 34.4 IU/ml). Nine of 29 (31%) subjects had initial IgE levels greater than two standard deviations higher than age-matched normal subjects. No patients had detectable specific IgE to any of the six aeroallergens. There was no correlation, as determined by linear regression analysis, between IgE levels and absolute CD4 number or CD4:CD8.

Conclusion: Elevated total but not specific IgE is common in children infected with HIV and does not correlate with absolute CD4 lymphocyte count, suggesting that the elevated IgE level reflects a somewhat independent polyclonal activation of B lymphocytes. (*J ALLERGY CLIN IMMUNOL* 1996;97:692-7.)

Key words: IgE, pediatric HIV

The incidence and prevalence of human immunodeficiency virus (HIV) infection in children has increased since the first cases were described in the

Abbreviation used

HIV: Human immunodeficiency virus

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early 1980s.¹⁻⁴ Sinusitis and upper respiratory tract infections frequently occur in children infected with HIV.⁵ Allergic rhinitis, asthma, and atopic dermatitis have been associated with HIV infection in adults, and atopic disease may occur with increased frequency in adult patients with progressive HIV illness.⁶⁻¹⁰ HIV infection causes polyclonal activation of B cells, resulting in increased serum levels of IgG, IgA and sometimes IgM.¹¹⁻¹⁴ Increased serum IgE occurs in adults and is inversely correlated with CD4⁺ absolute lymphocyte

TABLE I. Demographic data ($n = 29$)

Age (mo)	Ethnic group						
	Female	Male	African-American	Caucasian	Hispanic	Haitian	Biracial
7 to 150 (mean = 49 ± 6.8)	19 (65.5%)	10 (34.5%)	16 (55.1%)	6 (20.6%)	3 (10.3%)	2 (6.8%)	2 (6.8%)

numbers less than $200/\text{mm}^3$; however, studies in HIV-infected children that evaluate serum IgE are not available.¹⁵ Elevated total serum IgE may not be a good indicator of allergy in children infected with HIV because the polyclonal immunologic dysregulation may not be accompanied by increased specific IgE production. Sinusitis and upper respiratory tract infections are frequently related to allergic rhinitis in otherwise healthy children; however, the correlation between atopy and sinusitis in children infected with HIV has not been studied.¹⁶

METHODS

Study population

The study population consisted of 29 children infected with HIV, 7 to 150 months of age (mean age, 49 ± 6.8 months). Nineteen children were female and 10 were male. Sixteen children were African-American, six were Caucasian, three were Hispanic, two were Haitian and two were biracial (Table I). The subjects were treated by members of the Division of Allergy and Clinical Immunology, University of South Florida, College of Medicine, All Children's Hospital, Tampa and St. Petersburg, Florida during the past 5 years. All children enrolled in the study were infected with HIV as determined by HIV ELISA and Western blot in those older than 2 years or by two direct tests for HIV (polymerase chain reaction for HIV genetic sequences and/or HIV culture) if they were younger than 2 years old. Follow-up was long enough to unequivocally establish infection. Informed consent was obtained from all patients or their parents or guardians before HIV testing, and the study was approved by the Institutional Review Board of the University of South Florida.

Medical records were reviewed for previous evidence of sinus disease. Acute and chronic sinusitis were defined according to the criteria proposed by Wald.¹⁷ Acute sinusitis was defined as persistent symptoms of nasal discharge, congestion, or fever lasting more than 10 but fewer than 30 days with radiographic evidence of sinus opacity or air fluid level. Chronic sinusitis was defined by symptoms lasting more than 30 days with positive radiograph results and evidence of mucosal thickening or opacification.

From frozen stored sera, total IgE and specific IgE levels were measured by RAST. Six patients had one specimen tested, 19 had two specimens tested on differ-

TABLE II. Prevalence of elevated total serum IgE in HIV-infected children

Age range (mo)	Normal serum IgE values by age group: Mean $\pm$ 2 SD (IU/ml)	Percentage of specimen with elevated IgE by age group
0 to 11	0 to 57	1/5 (20.0%)
12 to 23	0 to 83	4/13 (30.7%)
24 to 35	0 to 86	0/8 (0.0%)
36 to 59	0 to 228	2/7 (28.5%)
60 to 83	0 to 126	7/13 (53.8%)
84 to 119	0 to 211	3/8 (37.5%)
120 to 179	0 to 615	0/8 (0.0%)

ent dates, three had three specimens tested, and one had four specimens tested. Total IgE was determined by Kallestad Total IgE microplate (Sanofi Diagnostic Pasteur, Chaska, Minn.). Pediatric values for normal levels of IgE were obtained from Sanofi Diagnostics Pasteur, which assayed serum samples from 219 pediatric patients (<22 years old) with no known history of allergies.¹⁸ Elevated total serum IgE was defined as greater than two standard deviations from the normal values for age.

Specific antibodies to six common aeroallergens (Bahia grass, American cockroach, *Dermatophagoides pteronyssinus*, cat, oak, short ragweed) were tested by RAST (Sanofi Diagnostic Pasteur). A modified RAST classification was used with class 0 defined as an absence of specific IgE, class I as equivocal, and classes 2 through 6 as increased levels of specific IgE.¹⁹

T-cell lymphocyte subpopulations were determined by direct immunofluorescence with the EPICS automated flow cytometer (Coulter Diagnostics, Hialeah, Fla.) after standard Ficoll-Hypaque (Pharmacia, Uppsala, Sweden) separation.²⁰

Statistical analysis

Total serum IgE was compared with absolute CD4 numbers and CD4:CD8 ratio by linear regression. R values were calculated by Pearson's correlation coefficient.

RESULTS

Of the 57 total IgE levels obtained from 29 patients, 17 (29.8%) were greater than two standard deviations from the age-matched control

TABLE III. Initial total serum IgE levels, CD4 number, CD4:CD8, and presence or absence of sinusitis in HIV-infected children

Patient	Age (mo)	Absolute CD4 (cells/mm ³)	CD4/CD8	IgE (IU/ml)	Sinusitis
DJ	31	1242	0.37	17.5	Chronic
AD	25	1427	1.45	20.2	No
RS	28	20	0.02	5.6	Unknown
JD	13	637	0.17	2.8	Acute
BM1	10	469	0.49	75.9	No
BM2	10	1496	0.9	50.0	Acute
RC	18	2536	1.06	93.7	Acute
JC	62	512	0.5	244.9	Acute
SW	54	1167	0.44	314.5	No
SA	81	146	0.08	141.4	No
RG	89	480	0.62	133.2	Acute
MB	43	346	0.24	212.3	Chronic
CS	19	66	0.05	339.5	Acute
KM	25	8	0.07	8.3	Chronic
MD	10	1329	0.84	2.7	Chronic
DO	14	527	0.32	3.2	Chronic
SD	28	265	0.07	4.2	Chronic
SS	7	234	0.22	6.8	Chronic
JM	14	1887	0.85	23.3	Chronic
AN	51	317	0.08	3.7	Chronic
LG	56	1932	2	5.2	Chronic
JL	69	713	0.74	12.7	Chronic
AS	64	562	0.6	311.9	Acute
AH	96	3	0.03	1.4	Unknown
LS	87	184	0.38	5.5	Chronic
NC	71	790	1.26	787.6	Chronic
RH	79	123	0.14	5.2	Chronic
ER	119	15	0.02	504.9	Acute
PJ	150	564	0.82	241.1	Chronic

value (Table II). Nine of 29 patients (31%) had initial total serum IgE levels greater than two standard deviations higher than the normal age group values (Table III). Initial total serum IgE ($n = 29$) ranged from 1.4 to 787.6 IU/ml (mean IgE = 123.4 ± 34.4 IU/ml). Absolute CD4 numbers at or within 1 week of the time of initial IgE determination ranged from 3 to 2536/mm³ (mean, 689 ± 123). CD4:CD8 ratio ranged from 0.02 to 2 (mean = 0.51 ± 0.09). Six subjects had only one specimen tested; 23 had more than one specimen tested (Table I). Subsequent IgE determinations in 19 patients who had two specimens tested revealed increased IgE levels in eight. The second specimen was collected 2 to 10 months after the first (mean = 5.53 ± 3.02 months). Of the 19 patients with two IgE determinations, three had high initial total serum IgE, which remained high on subsequent determination. Two had normal initial total serum

IgE levels, which became high on subsequent determination. Three patients had high initial IgE, which decreased with subsequent determination but remained greater than two standard deviations above the age-matched control group. Eleven patients with initial normal IgE levels continued to have normal values with subsequent determinations.

The three patients with high initial IgE values that subsequently increased had a decreased absolute CD4 count in the second determination. Three patients had three specimens. The second specimen was obtained 1, 4, and 6 months after the first specimen; and the third specimen was obtained 3, 3, and 9 months after the second. IgE progressively increased in all three on subsequent measurements. One patient with four specimens had serial levels that increased and decreased. Fourteen of 19 patients (73.6%) from whom two specimens were obtained had a decrease in CD4 count on second determination. Nine of these patients (64.2%) had increased IgE levels in the second specimen.

Fifteen of 29 patients (51.7%) had chronic sinusitis. Eight of 29 patients (27.6%) had acute sinusitis. Four of 29 patients (13.8%) had no episodes of documented sinusitis. Two patients (6.8%) had insufficient information regarding sinusitis.

None of 342 specific IgE levels for six common aeroallergens obtained from these 57 sera were positive; all were class 0. No correlation was found between initial total serum IgE ($n = 29$) and CD4 count ($r = -0.10949$). Also, no correlation was found between initial total serum IgE levels ($n = 29$) and absolute CD4:CD8 ratio ($r = 0.09687$). No correlation was found between total serum IgE ($n = 57$) and CD4 count ($r = 0.053221$) or between total serum IgE ($n = 57$) and CD4:CD8 ratio ($r = 0.175942$).

DISCUSSION

Total serum IgE is frequently elevated in children infected with HIV. Thirty percent of the IgE measurements were greater than two standard deviations above age-matched control values. However, specific IgE antibodies to common aeroallergens, including *D. pteronyssinus*, American cockroach, cat, Bahia grass, short ragweed, and oak could not be identified.

Total serum IgE was previously found to be increased in adults infected with HIV. Wright et al.¹⁵ demonstrated that the mean total serum IgE in adults infected with HIV with CD4 number less

than or equal to $200/\text{mm}^3$ was significantly greater than mean IgE levels of uninfected control groups and infected subjects with more than 200 CD4^+ lymphocytes/ mm^3 . The increase in IgE did not reflect increased prevalence of atopic disease.¹⁵ Lucey et al.,¹⁰ studying 622 patients with HIV infection, demonstrated that IgE increased in those subjects who experienced marked depletion of CD4^+ lymphocytes. Israel-Biet et al.⁹ demonstrated that increased IgE was associated with significant CD4^+ T-cell depletion and was correlated with a poor prognosis in adults.

Elevated total serum IgE occurs in patients with several primary immunodeficiency diseases, including Wiskott-Aldrich syndrome, DiGeorge syndrome, Nezelof syndrome, and primary hyper-IgE syndromes.²¹⁻²⁷ Allergy is not a consistent finding in patients with these diseases, which are characterized by abnormalities in thymus-dependent immune function. IgE is also elevated in patients with IgA deficiency; however, the frequency of allergic diatheses is increased in this population.²⁸ Clinical conditions resembling primary hyper-IgE syndrome have been described in adults infected with HIV.²⁹ Elevated total serum IgE levels also occur in patients with a variety of nonallergic diseases, including parasitic infections, viral infections, atopic dermatitis, and neoplastic disease such as Hodgkin's lymphoma and IgE myeloma.³⁰ This study did not include an exhaustive search for parasites in subjects; however, no such conditions were diagnosed, with the exception of giardiasis in one child, a pathogen that is not associated with high IgE levels.

Children with HIV infection have frequent viral infections that may alter total serum IgE levels. In this regard, cytomegalovirus, Epstein-Barr virus, and respiratory syncytial virus may all be associated with increased IgE levels.³⁰ Another report showed no consistent pattern of IgE levels in patients with acute viral upper and lower respiratory tract infections. Children with measles have lower IgE levels during convalescence.³¹ The mechanism by which viral infection may alter IgE production is not known.

HIV may suppress the function of $\text{T}_{\text{H}1}$ -type CD4^+ lymphocytes while sparing $\text{T}_{\text{H}2}$ -type lymphocytes, resulting in increased IL-4 and IL-5 and decreased IL-2 and interferon- γ production; this cytokine profile favors IgE synthesis. Interferon- γ suppresses IgE synthesis by normal B cells, and subjects infected with HIV have impaired production of this lymphokine in response to antigen stimulation.³² This study suggests that IgE produc-

tion is a result of polyclonal activation because no specific IgE was detected. In contrast to studies in adults, no correlation was found between CD4 and IgE levels or between CD4:CD8 ratios and IgE levels. This lack of correlation may be related to concurrent viral illness and its effects on IgE production. Alternatively, this study may not have included a sufficient number of patients or follow-up long enough to demonstrate such an association. In this regard, two patients with high initial total IgE levels, which became higher in subsequent measurements, and two patients with normal IgE, which became greater than two standard deviations from normal values, subsequently experienced a progressive decrease in the absolute CD4 count.

Specific IgE antibodies to viral and yeast antigens were previously detected in adults infected with HIV. Sample et al.³³ suggested a correlation among total IgE, specific RASTs to environmental antigens, and clinical atopy in patients infected with HIV and a history of invasive or life-threatening opportunistic infections. In other studies inconsistent associations between elevated IgE and the occurrence of atopic diseases in patients infected with HIV have been described.^{33,34} Specific IgE to common aeroallergens was not detected in this study. The majority of atopic subjects in the Tampa Bay area are sensitized to *D. pteronyssinus*³⁵; however, none of the children infected with HIV had specific IgE to *D. pteronyssinus* allergen. Specific IgE antibodies may be difficult to detect in infants because of very low IgE concentrations. The study population had a mean age of 49 months with a standard deviation of 6.8 months at the time the first specimen was obtained. Thus we expected to find evidence of specific IgE to the common aeroallergens tested in at least some of our patients, but did not. The lack of specific IgE detection does not rule out its presence. Skin prick testing is a more specific method, but it was not performed in this study. There may be IgE specific to antigens for which we did not test, such as fungal or viral protein, or IgE may be produced to HIV proteins. Alternatively, polyclonal B-cell activation in subjects infected with HIV occurs frequently in patients who do not produce a specific antibody after immunization. Perhaps specific IgE is produced to multiple antigens in such small amounts that it cannot be detected. It seems likely that the children who were selected for the study were children who by genetic disposition do not produce IgE to environmental allergens.

Small et al.³⁶ found an increased incidence of

sinusitis in adults infected with HIV and the severity of the sinusitis was correlated with disease progression. They found a correlation between IgE levels and severity of sinusitis. This study demonstrates a very high frequency of sinusitis in children infected with HIV; however, the presence of sinusitis could not be correlated with high IgE levels. The occurrence of sinusitis in children infected with HIV is probably not related to allergy. Also, high IgE levels do not correlate with the presence of atopic diseases in children infected with HIV. There may be a correlation between severity of sinus disease and progression of HIV disease, but sufficient follow-up to prove such a correlation was not carried out. The correlation between high IgE levels and sinusitis may be indirect in the adult study population, and progression of HIV disease results in both higher IgE levels and a tendency to develop and express sinusitis.

Total serum IgE concentrations are higher in allergic adults and children compared with nonallergic control subjects; however, there is limited value in use of IgE as a screening test for atopic diseases.³⁰ Total serum IgE does not have value to screen children infected with HIV for atopic diseases because there is no evidence for specificity of the IgE response. None of 57 sera from 29 infected children had specific antibodies to the six most common aeroallergens in the Tampa Bay area. This study demonstrates a high frequency of increased IgE in the serum of children infected with HIV. This IgE appears not to reveal specific immune responses and is most likely attributable to polyclonal activation and altered cytokine production associated with HIV infection and/or its effect on the immune system. A correlation between IgE and CD4, previously demonstrated in adult studies, was not present in the children studied.

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REFERENCES

- Oleske J, Minnefor A, Cooper A Jr, et al. Immune deficiency syndrome in children. *JAMA* 1983;249:2345-9.
- Rubenstein A, Sicklick M, Gupta A, et al. Acquired immunodeficiency with reversed T4/T8 ratios in infants born to promiscuous and drug addicted mothers. *JAMA* 1983;249:2350-6.
- Scott GB, Buck F, Leterman J, Bloom F, Parks WP. Acquired immunodeficiency syndrome in infants. *N Engl J Med* 1984;310:76-81.
- Chu SY, Buehler JW, Berkelman RL. Impact of the human immunodeficiency virus epidemic on mortality in women of reproductive age, United States. *JAMA* 1990;264:225-9.
- Brigino EN, Nelson RP, Koutsonikolis A, et al. Prevalence of sinusitis in HIV-infected children [Abstract]. *J ALLERGY CLIN IMMUNOL* 1994;93:237.
- Straka BF, Whitaker DL, Morrison SH, Oleske IM, Grant-Kels JM. Cutaneous manifestations of the acquired immunodeficiency syndrome in children. *J Am Acad Dermatol* 1988;18:1089-102.
- O'Donnell CR, Bader MB, Zibrak JD, Jensen WA, Rose RM. Abnormal airway function in individuals with the acquired immunodeficiency syndrome. *Chest* 1988;94:945-8.
- Lim DT, Enright T, Shetty R, Park L. Asthma recurrent sinopulmonary disease and HIV infection (Clinical Conference). *Ann Allergy* 1988;61:175-6, 224-6.
- Israel-Biet D, Labrousse F, Tourani JM, Sors H, Andrieu JM, Even P. Elevation of IgE in HIV-infected subjects: a marker of poor prognosis. *J ALLERGY CLIN IMMUNOL* 1992;89:68-75.
- Lucey DR, Zajac RA, Melcher GP, Butzin CA, Boswell RN. Serum IgE levels in 622 persons with human immunodeficiency virus infection: IgE elevation with marked depletion of CD4+ T-cells. *AIDS Res Hum Retroviruses* 1990;6:427-8.
- Mizuma H, Litwin S, Zolla-Pazner S. B-cell activation in HIV infection: relationship of spontaneous immunoglobulin secretion to various immunological parameters. *Clin Exp Immunol* 1988;71:410-6.
- Lane HC, Masur H, Edgar LC, Whalen G, Rook AH, Fauci AS. Abnormalities of B-cell activation and immunoregulation in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1983;309:453-8.
- Schnittman SM, Lane HC, Higgins SE, Folks T, Fauci AS. Direct polyclonal activation of human B lymphocytes by the acquired immune deficiency syndrome virus. *Science* 1986;233:1084-6.
- Fling JA, Fischer JR, Boswell RN, Reid MJ. The relationship of serum IgA concentration to human immunodeficiency virus (HIV) infection: a cross-sectional study of HIV-seropositive individuals detected by screening in the USAF. *J ALLERGY CLIN IMMUNOL* 1988;82:965-70.
- Wright DN, Nelson RP, Ledford DK, Fernandez-Caldas E, Trudeau WI, Lockett RF. Serum IgE and human immunodeficiency virus (HIV) infection. *J ALLERGY CLIN IMMUNOL* 1990;85:445-52.
- Slavin RG. Nasal polyps and sinusitis. In: Middleton EJ, Reed CE, Ellis EF, et al., eds. *Allergy: principles and practice*. 4th ed. St. Louis: Mosby, 1993:1457-70.
- Wald ER. Sinusitis in children. *N Engl J Med* 1992;326:319-23.
- Sanofi Diagnostic Pasteur, Inc. KallestadTM total IgE microplate: expected values. Chaska, Minnesota: Sanofi Diagnostic Pasteur, Inc., 1991:9.
- Sanofi Diagnostic Pasteur, Inc. KallestadTM AllercoatTM RAST isotope reagent: results. Chaska, Minnesota: Sanofi Diagnostic Pasteur, Inc., 1992:11.
- Boyum A. Isolation of mononuclear cells and granulocytes from human blood. *Scand J Clin Lab Invest* 1968;21:51-76.
- Peterson RDA, Page AR, Good RA. Wheal and erythema allergy in patients with agammaglobulinemia. *J Allergy* 1962;33:406-11.
- Polmar SH, Waldmann TA, Terry WD. IgE in immunodeficiency. *Am J Pathol* 1972;69:499-512.

23. Waldmann TA, Polmar SH, Balestra ST, Jost MC, Bruce RM, Terry WD. Immunoglobulin E in immunologic deficiency diseases. II. Serum IgE concentration of patients with acquired hypogammaglobulinemia, myotonic dystrophy, intestinal lymphangiectasia and Wiskott-Aldrich syndrome. *J Immunol* 1972;109:304-10.
24. Buckley RH, Fiscus SA. Serum IgD and IgE concentrations in immunodeficiency diseases. *J Clin Invest* 1975; 55:157-65.
25. Buckley RH, Sampson HA. The hyperimmunoglobulinemia E syndrome. In Franklin EC, ed. *Clinical immunology update*. Elsevier North-Holland, 1981;147-68.
26. Goldfarb AA, Fudenberg H. Hypogammaglobulinemia and its relationship to the allergic diathesis. *NY State J Med* 1961;61:2721-31.
27. Buckley RH. Immunologic deficiency and allergic disease. In: Middleton E Jr, Reed CE, Ellis EF, et al., eds. *Allergy: principles and practice*. 4th ed. St. Louis: Mosby, 1993; 1059-76.
28. Buckley RH. Clinical and immunologic features of selective IgA deficiency. In: Bergsma D, Good RA, Finstad J, et al, eds. *Immunodeficiency in man and animals*. Sunderland, Massachusetts: Sinauer Associates, 1975:134-42.
29. Paganelli R, Scala E, Mezzaroma J, et al. Hyper-IgE syndrome induced by in HIV infection. *Immunodeficiency* 1993;4:149-52.
30. Ownby DR. Clinical significance of IgE. In: Middleton E, Reed CE, Ellis EF, et al., eds. *Allergy: principles and practice*. 4th ed. St. Louis: Mosby, 1993:1059-76.
31. Griffin DE, Cooper SJ, Hirsch RL, et al. Changes in plasma IgE levels during complicated and uncomplicated measles virus infections. *J ALLERGY CLIN IMMUNOL* 1985;76:206.
32. Sample S, Chernoff DN, Lanahan GA, et al. Elevated serum concentrations of IgE antibodies to environmental antigens in HIV-seropositive male homosexuals. *J ALLERGY CLIN IMMUNOL* 1990;86:876-80.
33. Maggi E, Mazzetti M, Ravina A, et al. Increased production of IgE protein and IgE antibodies specific for fungal antigens in patients with the acquired immunodeficiency syndrome. *Ric Clin Lab* 1989;19:45-9.
34. Ring J, Froschl M, Brunner R, Braun-Falco O. LAV/HTLV-III infection and atopy: serum IgE and specific IgE antibodies to environmental allergens. *Acta Derm Venerol (Stockh)* 1986;66:530-2.
35. Fernandez-Caldas E, Fox RW, Bucholtz GA, Trudeau WL, Ledford DK, Lockey RF. House dust mite allergy in Florida. Mite survey in households of mite-sensitive individuals in Tampa, Florida. *Allergy Proc* 1990;11:263-7.
36. Small CB, Kaufman A, Armenaka M, Rosenstreich DL. Sinusitis and atopy in human immunodeficiency virus infection. *J Infect Dis* 1993;167:283-90.