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Prevalence of asthma in children and young adults with HIV infection

To the Editor:

Asthma is generally believed to be no more prevalent in individuals with HIV infection than in healthy children and adults. The potential for decreased CD4⁺ T-lymphocyte numbers and function in patients with HIV infection would seem to support this assumption. In animal models of asthma, the loss of CD4⁺ T lymphocytes protects against the development of this disease.¹ Similarly, in adults with HIV infection, self-report of asthma has been associated with higher CD4⁺ T cell counts.²

Studies of the pulmonary complications of HIV infection in the pre-highly active antiretroviral therapy (HAART) era did not demonstrate a higher than expected prevalence of airway obstruction, hyperresponsiveness, or bronchospastic symptoms in adults without AIDS-related pulmonary complications.³ Reviews of airway obstruction and bronchospasm in patients with AIDS have reported contradictory findings. More recently, Poirer et al⁴ have reported that men with HIV infection have increased wheezing, bronchial hyperresponsiveness, and higher serum IgE levels compared to uninfected controls. There have been no other large studies of asthma in adults with HIV since the introduction of HAART. There are no published studies examining the prevalence of asthma in children with HIV infection.

During regular clinical and study visits at the Texas Children's Hospital (TCH) Allergy and Immunology Clinic, many children and young adults with HIV infection on combination antiretroviral treatments were noted to have a diagnosis of asthma. Because CD4⁺ T lymphocytes play a key role in the pathogenesis of asthma, and these same cells are the principal targets of HIV infection, our general hypothesis is that children and young adults with HIV infection on antiretroviral treatment regimens are at increased risk for developing asthma due to immune preservation or immune reconstitution. The objective of this study was to determine the prevalence of asthma in children with HIV on combination antiretroviral therapy.

We performed a cross-sectional chart review of the 83 HIV-infected patients actively followed in 2005 in the

TCH Allergy and Immunology Clinic. The electronic medical record for all TCH encounters was reviewed for asthma International Classification of Diseases, 9th revision (ICD-9) codes and current asthma and HIV medications. Demographic variables including reported race/ethnicity and gender were abstracted. The median household income in each patient's zip code was used as a marker of socioeconomic status. The most recent laboratory assessments of degree of immunosuppression (CD4⁺ and CD8⁺ T-cell counts and percentages) and extent of viral replication (HIV RNA) were also abstracted. We also reviewed the charts of all patients who began treatment for asthma while under our care to determine their ages and antiretroviral regimens at the time they were initially prescribed asthma medications. All CD4⁺ T-cell data from the 2-year period before these patients were prescribed asthma medications were collected from a laboratory database.

The prevalences of asthma diagnostic codes, rescue bronchodilator medications, and daily controller medications were determined for our 83 patients with HIV infection (ages 1 to 24 years). As nearly all of our patients with HIV at TCH are on Medicaid, we also determined the number of children on Medicaid with a principal or secondary diagnosis of asthma who use TCH as their care center. The χ^2 , Fisher exact, and *t* tests were used to test for significant differences between groups for race/ethnicity, gender, socioeconomic status, viral load, and CD4⁺ and CD8⁺ T-cell counts and percentages. Confidence intervals (95%) were calculated for the prevalence estimates. For the subset that began treatment for asthma after coming under our care, linear mixed models with spatial power correlation structures were used to evaluate patterns of CD4⁺ T cells during the 2-year period before the initiation of asthma medications. Approval of the Baylor College of Medicine Institutional Review Board was obtained for this study.

There were no significant differences among the demographic variables between the asthmatic and nonasthmatic patients with HIV (Table I). Twenty-eight of 83 (34%; 95% CI, 24-45%) patients with HIV (ages 0.9 to 24.9 years) had an ICD-9 code for asthma. Thirty-five of 83 (42%; 95% CI, 31-54%) patients were on short-acting inhaled bronchodilators, and 16 (19%; 95% CI, 11-29%) were on daily preventative medications for asthma (inhaled corticosteroids with or without long-acting bronchodilators and/or leukotriene antagonists). Of 50,254 pediatric patients with Medicaid using TCH as their care center, 2970 (5.9%; 95% CI, 5.7-6.1%) had a principal or secondary diagnosis of asthma.

There were no significant differences in viral loads (HIV RNA), CD4⁺ T-cell counts, or percentages between the patients with and without asthma markers, but there was a consistent trend toward lower CD8⁺ T-cell counts and percentages in the asthma group (Table I). Moreover, only 6 of the 83 patients included in the study met immunologic criteria for AIDS by CD4⁺ T percentage (<15%), and only 1 of the 6 had asthma. Of the 83 patients studied, 62 (75%) were on HAART therapy

TABLE I. Prevalence of asthma diagnoses, rescue bronchodilator and daily controller medication use, and clinical characteristics of an HIV-infected study population at Texas Children's Hospital

	Asthma diagnosis		Rescue bronchodilators		Controller medications	
	Yes	No	Yes	No	Yes	No
N (%)	28 (34)	55 (66)	35 (42)	48 (58)	16 (19)	67 (81)
Demographic characteristics						
Mean age, y $\pm$ SD (range)	13.0 $\pm$ 5.6 (2.9-24.9)	13.7 $\pm$ 6.7 (0.9-23.2)	13.3 $\pm$ 5.9 (2.4-24.9)	13.5 $\pm$ 6.7 (0.9-23.2)	13.4 $\pm$ 4.7 (2.9-24.9)	13.4 $\pm$ 5.4 (0.9-23.2)
Gender, n						
Female	17	37	20	34	11	43
Male	11	18	15	14	5	24
Race/ethnicity, n						
Black	17	31	24	24	11	37
Hispanic	7	10	7	10	2	15
White	4	5	4	5	3	6
Undetermined/other	0	9	0	9	0	9
Mean median household incomes in ZIP code	36,212 $\pm$ 12,325	36,168 $\pm$ 14,002	36,638 $\pm$ 12,201	35,847 $\pm$ 14,314	37,990 $\pm$ 14,229	35,731 $\pm$ 13,239
Disease progression markers						
Mean CD4 ⁺ T cells/ μ L (normal range 538-1569)	745 $\pm$ 379	768 $\pm$ 500	739 $\pm$ 447	776 $\pm$ 474	718 $\pm$ 393	770 $\pm$ 477
Mean % CD4 ⁺ T cells (normal range 23-50)	31 $\pm$ 10	28 $\pm$ 10	30 $\pm$ 10	29 $\pm$ 10	30 $\pm$ 11	29 $\pm$ 9
% CD4 ⁺ less than 15%, n	1	5	2	4	1	5
Mean CD8 ⁺ T cells/ μ L (normal range 371-936)	807 $\pm$ 346*	984 $\pm$ 486*	835 $\pm$ 411	989 $\pm$ 469	835 $\pm$ 342	945 $\pm$ 471
Mean % CD8 ⁺ T cells (normal range 15-35)	34 $\pm$ 10†	40 $\pm$ 12†	35 $\pm$ 10‡	40 $\pm$ 13‡	36 $\pm$ 10	38 $\pm$ 12
CD4/CD8 ratio (normal range 0.72-2.40)	0.98 $\pm$ 0.50	0.84 $\pm$ 0.50	0.92 $\pm$ 0.48	0.87 $\pm$ 0.52	0.87 $\pm$ 0.45	0.89 $\pm$ 0.52
Mean viral load, copies/mL	10,100 $\pm$ 26,800	34,000 $\pm$ 110,000	14,400 $\pm$ 42,300	34,400 $\pm$ 114,000	7,240 $\pm$ 11,000	30,500 $\pm$ 101,000
HAART, n (%)	20 (74)	42 (75)	26 (74)	36 (75)	10 (62)	52 (78)
Combination of $\geq$ 2 anti-retrovirals, n (%)	25 (93)	50 (89)	32 (91)	43 (90)	14 (88)	61 (91)

Normal ranges reported for 10- to 18-year-olds from the Texas Children's Hospital Immunology Research Laboratory (n = 196).

**P* = .090.

†*P* = .056.

‡*P* = .099.

[3 or more drugs from at least 2 of the 3 antiretroviral drug classes: (1) nucleoside reverse transcriptase inhibitors; (2) nonnucleoside reverse transcriptase inhibitors; and (3) protease inhibitors]. Seventy-five patients (90%) were on a combination of at least 2 antiretroviral drugs, and the usage of these drugs did not differ between the groups with or without asthma.

A subset of patients with HIV who were started on asthma medications after beginning or transferring care to TCH (n = 25) had an insignificant decline of 1.8% in CD4⁺ T-cell percentages during the 2-year period before starting asthma medications (*P* = .58), a pattern similar to that reported in a cross-sectional study of 807 children not exposed to HIV from birth through 18 years of age.⁵ Six of the 25 patients gave evidence of immune reconstitution ($\geq$ 5% increase in CD4⁺ T-cell percentage) on combination therapy of at least 2 antiretroviral drugs in the 2 years prior to beginning treatment for asthma. The mean age and CD4⁺ T-cell percentage when these 25 patients started taking medications for asthma were 7.5 $\pm$ 6.4 years

(median 3.8 years) and 25 $\pm$ 12%, respectively. The mean time between starting combination antiretroviral therapy and starting asthma medications was 1.8 $\pm$ 3.3 years (median 1.0 years). Eighteen of these patients were on combination antiretroviral therapy at the time they were started on asthma medications.

Studies of pulmonary disease in children with HIV from the pre-HAART era did not find an increased prevalence of asthma (M. Kattan, personal communication, 2006). Several adult studies have had similar findings. This analysis of our cross-section of minority-predominant, inner-city patients indicates that the prevalence of asthma in children and young adults with HIV may exceed the prevalence of 6% reported by the Centers for Disease Control and Prevention for children in the United States.⁶ The prevalence of physician-diagnosed asthma in inner-city youth (predominately African American and Hispanic children) ranges from 11% to 17%.⁷ The prevalence of asthma among all children 0 to 17 years in the 13-county region including the Houston metropolitan

area (the same geographic catchment area as the TCH Allergy and Immunology Clinic) is 5.0%, with a rate of 6.3% reported for all of Texas.⁸ Compared to these studies, we observed a several-fold higher prevalence of asthma in our patients with HIV. This higher prevalence of asthma diagnoses and asthma medication use may suggest that children and young adults with HIV infection on the improved antiretroviral drug regimens currently available are at increased risk for developing asthma due to immune preservation or reconstitution.

There was evidence that antiretroviral medications preserved CD4⁺ T-cell numbers prior to the development of asthma, because most pediatric patients perinatally infected with HIV in the United States, including our cohort, are treated from birth. As this group of patients with HIV overall has relatively well-controlled disease, with only 6 meeting immunologic criteria for AIDS, it may not be the ideal population in which to correlate CD4⁺ T-lymphocyte levels with asthma, although a few showed immune reconstitution prior to requiring asthma medications. There was a suggestion of a treatment effect in the subjects with asthma in that they had lower CD8⁺ T-cell counts and percentages. A prospective study of individuals with HIV (study in progress) is needed to determine whether or not there is a link between immune preservation or reconstitution due to improved HIV therapy and the development of asthma.

Our study speaks to the activation of CD4⁺ T lymphocytes confronting infectious agents (HIV in this case) with release of inflammatory cytokines as a possible explanation of the increased prevalence of asthma in the general population.⁹ These findings indicate a need for additional research to determine whether or not the immune preservation or restoration observed with treatment of HIV infection promotes airway inflammation and hyperreactivity that may necessitate initiation of or changes in asthma medications. More careful screening for asthma in children and young adults with HIV may also be appropriate, as more aggressive asthma management may decrease the need for potentially immunosuppressive asthma medications in an immunocompromised population already at risk.

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Successful treatment of delayed pressure urticaria with anti-TNF- α

To the Editor:

A 42-year-old white male presented for treatment of psoriasis that had begun 17 years ago and was overwhelming him. The patient's skin was affected with severe erythrodermia; the Psoriasis Area and Severity Index (PASI) was 18.3. On inquiry, the patient reported that he also had delayed pressure urticaria (DPU) for 14 years. If pressure was applied anywhere to the skin, the patient would experience swelling, burning, itching, and wheals 4 to 6 hours later at the pressure site. The symptoms would spontaneously resolve completely 10 to 14 hours later. The patient did not have arthritis, and he did not experience spontaneous wheals without a pressure stimulus. The general physical assessment showed that the patient was otherwise in good general health and was coping well. There was no known DPU in the family history; his father had had psoriasis. The results of laboratory tests were normal (tryptase 8.83 $\mu\text{g/L}$ [$<17 \mu\text{g/L}$], angiotensin converting enzyme 24.0 [range 15-80 U/L], erythrocyte sedimentation rate 12/25).

DPU is a distinct entity, the time course of which differentiates it from other conditions. The time course of this patient's symptoms made it clear that he had DPU. After the first year of suffering symptoms, the patient was