Growth and body composition in children infected with the human immunodeficiency virus–1

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ABSTRACT Anthropometric data were collected on 89 children born to human immunodeficiency virus (HIV)-infected women (37 who seroreverted and 52 who were HIV-infected). The main outcomes included birth weight, gestational age, weight, height, arm muscle circumference (AMC), and triceps skinfold thickness (TSF). Gestational age and birth weight were not different between the two groups. The earliest anthropometric evaluation on seroreverted children (age 19 mo) when compared with HIV-infected children (age 21 mo) revealed that weight and weight-for-height percentiles were significantly different (51% vs 33% and 66% vs 48%, respectively). Height and TSF percentiles were not different, although AMC percentiles were lower in infected children (64% vs 43%). In follow-up evaluations, the weight differences between infected and control children did not change. We conclude that HIV does not affect birth weight, but postnatal events result in altered weight gain in HIV-infected children. Lean body mass is lower than in an HIV-negative comparison group at early stages of HIV infection. Am J Clin Nutr 1993;57:588–92.

KEY WORDS Body composition, growth, HIV, children, acquired immunodeficiency

Introduction

Growth failure and weight loss are prominent findings in human immunodeficiency virus (HIV)–infected children (1, 2), although the pathophysiology is not well-defined. In utero congenital, non-HIV viral infection may impair both pre- and postnatal growth but the effects of HIV on growth in children have not been established. Primary gastrointestinal malabsorption (1, 3, 4), excessive energy expenditure (5), or poor oral intake are putative mechanisms that may induce or promote growth failure or weight loss in both adults and children with HIV. Carbohydrate malabsorption has been documented in HIV-infected children (1, 4), yet the correlation with weight loss or gastrointestinal symptoms is controversial (1, 4).

Nutritional status has an impact on morbidity and mortality in many disease processes (6). Functional abnormalities of B and T cell lymphocytes and macrophages have been associated with malnutrition (7), and opportunistic infections such as Pneumocystis carinii pneumonia were first described in otherwise well, but significantly malnourished children in developing countries (8). Gray (9) and Jain and Chandra (10) found striking similarities in immune-system dysfunction between patients with acquired immune deficiency syndrome (AIDS) and those with protein-energy malnutrition. Malnutrition has been proposed to act as a co-factor of immune dysfunction by influencing both susceptibility to HIV infection and progression of disease (11–13). Because many HIV-infected children are malnourished, an improvement in their nutritional status may significantly decrease their morbidity. Thus, determining the etiology and temporal course of malnutrition in children with HIV infection will be important for early intervention and development of refeeding regimens.

HIV-infected children are frequently born to mothers with incomes below the poverty level. Low maternal socioeconomic status and poor prenatal care have been correlated with low gestational weights and prematurity in otherwise well children (14). Thus, comparison of growth and weight gain of HIV-infected children with traditional American growth standards may not be appropriate for assessing the effect of HIV on nutritional status. Children born to HIV-infected mothers who serorevert and are presumed to be uninfected represent an ideal comparison group in whom to estimate growth indexes, because there is an intrinsic adjustment for socioeconomic background. In this study we compared birth weights, gestational ages, and subsequent growth indexes of children born to HIV-infected women, who seroreverted to negative HIV serology, with HIV-infected children. Through these comparisons we hoped to define the extent of weight loss and changes in body composition in HIV-infected children.

Methods

Subjects

Patients from the Children’s Hospital HIV clinic were followed between 1986 and 1991. Data from clinic visits, as well as hospital admissions relating to HIV, were collected as part of a Natural

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History of HIV Infection protocol and entered into a comprehensive gastroenterological HIV database with a focus on nutrition. All available anthropometric data were incorporated into this database. Patients were referred to the HIV Clinic because of clinical signs compatible with HIV infection, for follow-up evaluation from a recent hospitalization relating to HIV infection, or because the child was at risk for HIV infection because of maternal HIV infection or high-risk social habits.

HIV infection was defined as positive HIV serology by enzyme-linked immunosorbad assay (ELISA) and Western Blot analysis after 15 mo of age, positive HIV culture, and/or clinical signs (15) compatible with the diagnosis of HIV infection (in those children age < 15 mo). Children who acquired HIV through blood products were excluded from the study population. The comparison population were those children born to HIV-infected mothers who had no clinical evidence of HIV infection and had negative HIV serology (by ELISA and Western Blot analysis) after 15 mo of age. Children who had positive serologic markers for HIV, who had negative HIV cultures, and who were < 15 mo of age at the time of statistical analysis were not included in this study because their HIV status was indeterminate (CDC class P-0).

Data from HIV-infected children who were receiving nucleoside antiretroviral medications [zidovudine or 2',3'-dideoxycytidine (ddC)] or supplemental feedings (nasogastric tube, gastrostomy tube, or parenteral nutrition) were excluded from the analysis to appreciate the effect of HIV on growth in these children before an intervention that may be expected to increase weight. Children were included in the analysis if they were receiving formula providing increased energy. None of the children in the comparison population were receiving supplemental feedings through gastrostomy tube, nasogastric tube, or total parenteral nutrition.

Absolute CD4 T-lymphocyte counts were collected within 6 mo of the follow-up anthropometric evaluation on each patient, when available. In patients without absolute CD4 T-lymphocyte counts within 6 mo of the anthropometric evaluation, the first available record of absolute CD4 T-lymphocyte count after anthropometric evaluation was recorded as well as the time lapse between them. The number of children with AIDS, as defined by the criteria of the Centers for Disease Control, was recorded at the time of their first anthropometric evaluation (8).

The study was approved by the Children's Hospital Institutional Review Board.

Anthropometric data collection

Medical records of both HIV-infected and -noninfected children were reviewed retrospectively for birth weights and gestational ages. These data were obtained from a reliable source (biologic parent, relative, foster parent, or hospital birth record). Birth weights were expressed as percentiles and Z scores appropriate for gestational age and sex. Gestation was expressed in weeks from date of conception, Dubowitz score at birth, or when both were available. Dubowitz score. Although birth weight data were available for children without follow-up anthropometric data, only birth weights and gestational ages from children with at least one follow-up visit with anthropometric data were used in the analysis.

For follow-up data, recumbent length for children < 2 y of age, standing height for children > 2 y of age, and weights were recorded by using recommended techniques (16). Length or height and weight were plotted on the National Center for Health Statistics percentiles (17) to obtain age- and sex-adjusted measurements. Skinfold-thickness measurements were used because they are reproducible and correlate with other more sophisticated measures of body composition (18). Triceps-skinfold thickness (TSF) and midarm circumference (MAC) were measured with standard techniques and used to derive arm-muscle circumference (AMC) (19). Age-adjusted percentiles for AMC and TSF were derived from the Ten-State Nutrition Survey for infants and children (20). Two trained nutritionists (SE and VM) performed anthropometric evaluations on the same subject and obtained similar results, thus confirming the reproducibility of their measurements.

Statistical analysis

Data were analyzed from children who had a birth weight and at least one follow-up visit recorded in the database after birth. Birth weights were compared by using a Wilcoxon rank-sum test, whereas the percentages in each group who were born at full-term gestation were compared by using Fisher’s exact test (21).

Because events leading to the administration of nucleoside antiretroviral medications or supplemental feedings may precede the actual day they were administered, we used follow-up data collected ≥ 2 mo before these interventions for analysis. We used the first available follow-up visit in the database to compare the age, weight percentile, weight Z score, height percentile, height Z score, weight-for-height percentile, weight-for-height Z score, AMC percentile, and TSF percentile between HIV-infected children and seroreverters through use of a Wilcoxon rank-sum test. All the growth indexes were age- and sex-adjusted by using national norms, as described previously, before statistical analysis. A repeated-measures, linear-regression model was used to analyze all 71 follow-up measurements from the 37 seroreverted children and all 172 follow-up measurements from the 52 HIV-infected children. The model allowed us to estimate the rate of change in Z score or percentiles over time for anthropometric indexes. The regressions included different intercepts for each child and took into account correlation between successive measurements on the same child. The regression allowed estimation of a common slope, representing the monthly rate of change. Absolute CD4 T-lymphocyte counts were expressed as mean ± SD. All reported P values are two sided.

Results

Fifty-two HIV-infected and 37 HIV seroreverted children had birth weights, gestational ages, and longitudinal follow-up information available for analysis. Comparisons of birth weights and gestational ages (Table 1) show no significant differences between HIV-infected and seroreverted infants. Additional birth weights and gestational ages were available from a larger cohort of 140 children (65 seroreverters) for whom longitudinal follow-up was not available. This larger cohort was consistent with the smaller sample of children in that there were no differences in gestational age \( P = 0.83 \) (Fisher exact test) and birth weights \( P = 0.61 \), Wilcoxon rank-sum test.

Thirteen of the 52 HIV-infected children had only a single follow-up measurement after birth; 9 had two, 16 had three, 3 had four, and 11 had five or more. Similarly, 24 of the 37 HIV seroreverted children had only a single follow-up measurement...
after birth; 7 had two to three; and 6 children had between four and six.

The first available follow-up visit in the database for 37 seroverted children was at a mean of 19 mo after birth (range 2–79 mo). Data from children who had seroverted after 15 mo were used exclusively to ensure that the child was HIV negative. The first available follow-up visit in the database for 52 HIV-infected children was at a mean of 21 mo after birth (range 1–103 mo, with 75% of the children evaluated by 26.5 mo). The mean age at the first follow-up visit was not significantly different between the two groups (P = 0.53). All HIV-infected children met the Centers for Disease Control criteria for P-2 symptomatic HIV infection and 6 children had AIDS at the time of the first anthropometric evaluation. Diarrhea and vomiting were found more frequently in HIV-infected children although this trend was not significantly different (P = 0.23 vomiting, P = 0.11 diarrhea). The mean absolute CD4 T-lymphocyte count of HIV-infected children within 6 mo of the first anthropometric evaluation was 1134 ± 863 cells/mm³ (x ± SD). An additional 12 children had absolute CD4 T-lymphocyte counts obtained at a mean of 28 mo after anthropometric evaluation. The mean absolute CD4 T-lymphocyte count was 1000 ± 668 cells/mm³.

Three children had no absolute CD4 T-lymphocyte counts available.

Although there was no difference in weights between the seroverted and HIV-infected groups at birth, weights were significantly different at their first anthropometric evaluation. The mean weight of the HIV-infected children started at the 45th percentile (SD = 33) for age and sex but decreased to the 33rd percentile (SD = 31), whereas noninfected children improved from the 40th percentile (SD = 36) to the 51st percentile (SD = 30). A regression model using all available follow-up data revealed that the weight Z scores remained stable for both HIV-infected and -noninfected children at least until 2 mo before nutritional intervention or zidovudine therapy.

In addition to the linear-regression model described in the methods section, follow-up data were analyzed by two alternative methods. Fifty-two of 89 children had two or more anthropometric evaluations. The change between the first and last visits was determined and averaged over the number of months of follow-up. Alternatively, all available anthropometric evaluations, regardless of birth weight availability, were incorporated into a linear-regression model to determine weight change over time. Both of these methods of analysis confirmed that both samples of children had no significant change in weight Z scores during the follow-up evaluations.

Comparisons of weight, height, weight-for-height, TSF, and AMC both at the initial visit and over time are displayed in Table 2.

### Table 2. At the initial visit, weight, weight-for-height and AMC were statistically different between HIV-infected and -noninfected children. Heights and TSF were not different between the two groups of children. A linear-regression model predicted an accelerated decline in fat stores, as measured by TSF in HIV-infected children, whereas noninfected children appeared to have accelerated growth in muscle stores, as measured by AMC, over time. Weights, heights and weight-for-height did not change substantially over time.

### Discussion

In this study we evaluated growth and body composition of HIV-infected children and compared the results with those of a control population from similar socioeconomic backgrounds. The children selected in this study were relatively healthy on the basis that they had not received prior therapy with antiretroviral medications or supplemental feedings and had absolute CD4 T-lymphocyte counts > 1000 cells/mm³. We found that both HIV-infected and seroverted children had similar birth weight percentiles and gestational ages, but by 19–21 mo of age their weight percentiles diverge significantly, with preservation of height. Lean body mass, although within the normal range, was significantly different from the HIV-negative, comparison children.

There are a limited number of studies that have evaluated birth weights, gestational ages, and subsequent growth of HIV-infected children. A study of Haitian children found that birth weights of infants born to HIV-positive mothers were similar, regardless of their HIV status later in life, but differed from those of infants born to HIV-negative mothers (13). The findings in our study of American children are similar to those in Haiti, although we cannot comment on the difference in birth weights.
between infants born to HIV-infected women and those born to noninfected women.

In follow-up, the weight percentiles of our cohort of HIV-infected and seroreverted children diverge. Because we do not have early growth data, we cannot accurately determine when this divergence occurs and what course the divergence takes. In the referenced study from Haiti, significant changes in weight occurred as early as 3 mo of age (13). The weight change in our HIV-infected group may be due to several factors. Although the HIV-infected group of children did not have significantly more gastrointestinal signs, there was a trend toward more vomiting and diarrhea in the HIV-infected cohort. We and others have shown that HIV-infected children and adults are at risk for developing malabsorptive syndromes (1, 4), although in our study there was no association between malnutrition, gastrointestinal signs, and carbohydrate malabsorption (1). Despite the findings in our previous study, we cannot exclude the possibility that increased losses through vomiting, diarrhea, and gastrointestinal malabsorption may be partially responsible for the divergence in weights between the HIV-infected children and seroreverters because many of these children were not screened for malabsorption.

The follow-up data after the first anthropometric evaluation suggest that growth is stable before the time when antiretroviral therapy is required. The stable period may extend over months to years in some children. Recent literature concerning weight loss and metabolic rates in adults with HIV infection suggest that adults also experience stable periods with interceding periods of wasting that are often associated with the onset of an opportunistic infection (22, 23). We as yet cannot comment on growth indexes of children who have an opportunistic infection or who require antiretroviral therapy.

Suboptimal oral intake may be another mechanism for poor growth in children with HIV infection; however, we have preliminary data (24) showing that nutrient intake is both similar and adequate for growth in HIV-infected and -noninfected children. Thus, abnormal oral intake does not appear to account for the difference in weights in this smaller subset of children. This finding would suggest that energy utilization and needs may be altered. Larger data sets are currently being collected to validate this preliminary study.

Anthropometry is a noninvasive method for determining muscle and fat mass in both children and adults. The composition of weight loss in HIV-infected adults has been studied by Kotler et al (25). Lean body mass was determined by using measures of total-body potassium, total body water, extracellular water volumes, and body fat. HIV-infected patients were significantly underweight and their total-body potassium content was lower than that of control subjects, suggesting depletion of lean body mass. There was preferential loss of lean body mass compared with fat, suggesting cachexia rather than protein-energy malnutrition. Our findings in children are similar to the findings of Kotler et al in adults. HIV-infected children have less muscle mass (AMC) than do children who have seroreverted. This finding would suggest that factors associated with a decline in velocity of weight gain in HIV-infected children also may promote preferential muscle wasting over depletion of fat stores.

Defining the temporal course of the onset of malnutrition in HIV disease is important because malnutrition may influence morbidity and mortality by altered organ function, impaired tolerance to therapy, increased duration of hospitalizations, and decreased quality of life (26, 27; B Broderick, J Nesset, unpublished observations, 1989). In adult AIDS patients, depletion of body cell mass but not body-fat content, correlated with the timing of death (26, 28). Thus, timing of death from wasting in AIDS was related to depletion of body cell mass to a critical level rather than to a specific disease process. Malnutrition is a frequent concomitant of prolonged hospitalizations and there may be better quality of life with better nutritional status (K Weaver, L Mingoia, S Eastey, MS Hickey, unpublished observations, 1990).

Nutritional assessment and advice are more widely available and are less invasive than other therapeutic interventions that are commonly performed on HIV-infected children. Early intervention, with appropriate energy supplementation, could result in decreased morbidity and prolonged life in HIV-infected children. Larger studies to determine energy requirements and to further delineate growth and body-composition abnormalities in HIV-infected children are needed.

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References