Body Composition in Prepubertal Children With Human Immunodeficiency Virus Type 1 Infection

Stephen M. Arpadi, MD, MS; Mary N. B. Horlick, MD; Jack Wang, MS; Patricia Cuff, RD, MPH; Marukh Bamji, MD; Donald P. Kotler, MD

Objective: To characterize the body composition of human immunodeficiency virus (HIV)-infected children, especially those with growth failure (GF), using laboratory-based methods.

Design: A cross-sectional study of body composition measurements.

Setting: Urban, hospital-based body composition laboratory.

Participants: Thirty-four prepubertal children with HIV infection, aged 4 to 11 years, recruited from a pediatric HIV clinic. Eighteen HIV-infected children with GF, 16 HIV-infected children with normal rates of growth, and 52 healthy children were studied.

Main Outcome Measurements: Anthropometrics, body cell mass (BCM) by total body potassium counting, body fat percent, fat mass, and fat-free mass (FFM) by dual-energy x-ray absorptiometry were determined.

Results: Both groups of boys with HIV infection had significantly lower FFM/height ratios compared with healthy boys. The mean BCM/height ratio was also lower in HIV-infected boys with GF compared with healthy boys. Measures of fat of the HIV-infected boys with GF did not differ from healthy controls, but a statistical trend suggesting decreased body fat percent and fat mass/height ratio was observed in HIV-infected boys without GF (P = .06 and .07, respectively). Mean height-for-age, weight-for-age, and weight-for-height percentiles were significantly decreased in HIV-infected boys regardless of growth status as compared with healthy boys. The mean FFM/height and BCM/height ratios were decreased in HIV-infected girls with GF compared with healthy girls. Body fat percentage and fat mass/height ratio did not differ among the 3 groups of girls. The mean weight-for-height percentiles were not different among the 3 groups of girls. The HIV-infected girls with GF had significantly lower mean height-for-age and weight-for-age percentiles than HIV-infected girls without GF and healthy girls. The mean height-for-age percentiles of the HIV-infected girls with GF did not differ from the healthy girls.

Conclusions: Boys and girls with HIV-associated GF had diminished FFM and BCM. The decrease in FFM and BCM was in striking contrast to the fat compartment, which was normal. Decreased FFM was also detected in boys with HIV infection and normal growth but not in girls with HIV infection and normal growth, suggesting that HIV infection may affect boys differently than girls. The preferential decrease in FFM and BCM over fat observed in these children is similar to findings reported in adults with acquired immunodeficiency syndrome wasting.


Editor's Note: More bad news about HIV infections—they bypass the fat and go straight to the good stuff.

Catherine D. DeAngelis, MD

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DISTURBANCES in growth, including growth failure (GF) and wasting, are common complications of childhood human immunodeficiency virus (HIV) infection and contribute to morbidity and mortality. 1 Children with HIV infection and poor growth have as much as a 5-fold increase in the risk of death. 2

Studies of children with HIV infection reveal early compromise of both height and weight gain. 3-5 Various patterns such as stunting, decreased weight-for-height, and weight loss have been reported. Few studies in children with HIV infection have included evaluations of body composition. 6,7 These studies, which may not be relevant to older, perinatally infected children who now comprise the majority of cases, used anthropometric measurements such as weight, height, skin-fold thickness, and arm circumference in younger perinatally infected children or older children who acquired HIV through contaminated blood products. Assessment of body composition in children with chronic diseases is valuable for understanding the pattern of growth and development. Measurement of fat mass (FM) reflects the adequacy of energy stores while fat-free mass (FFM) reflects pro-

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SUBJECTS AND METHODS

Thirty-four prepubertal children with HIV infection, aged 4 to 11 years, were recruited from the St Luke’s–Roosevelt Hospital Center Pediatric HIV/AIDS program in New York City from January 1994 through November 1996. Eighteen HIV-infected children with GF and 16 HIV-infected children with normal rates of growth were enrolled. Growth failure was defined as a 12-month height velocity of the fifth percentile or lower for age using standard reference norms. One child acquired HIV as a result of transfusion of contaminated blood during the neonatal period. All others were HIV-infected as a result of perinatal transmission. Fifty-two healthy children of similar age and ethnicity, volunteers in an ongoing study of body composition in normal children, were used as controls. Healthy volunteers were recruited by notices in local newspapers, at schools, in after-school activity centers, and from children receiving routine health maintenance in a hospital-based clinic. A medical history obtained from a parent or guardian and a physical examination performed at the time of body composition evaluation confirmed normal health status. Informed consent was obtained from the parent or guardian for each child prior to participation; assent was also obtained whenever possible. The study was approved by the study site institutional review board.

Human immunodeficiency virus infection was diagnosed and disease stage was classified using Centers for Disease Control and Prevention criteria. Pubertal classification was performed according to Marshall and Tanner. Height-for-age, weight-for-age, and weight-for-height percentiles were calculated using Epilinfo software. Information concerning prior illnesses or other HIV-related conditions, treatments, and medications and results of lymphocyte phenotype analyses were obtained from medical records. No children treated with megestrol acetate or corticosteroids were enrolled. None of the subjects had clinically apparent renal or cardiac disease or known or suspected active intercurrent illnesses at the time of evaluation of body composition. Eighty-five percent of HIV-infected subjects were receiving antiretroviral medications.

Weight was measured with children wearing light clothing to the nearest 0.1 kg using a beam balance. Height was measured without shoes to the nearest 0.5 cm using a fixed wall-mounted stadiometer.

All body composition measurements were performed at the Body Composition Unit during a study visit at St Luke’s–Roosevelt Hospital Center. Fat mass, body fat percent (BF%), and FFM were determined by dual-energy x-ray absorptiometry (Lunar DPX model, Lunar Radiation, Madison, Wis). Body cell mass was ascertained by the measurement of total body potassium in a 4-π whole-body liquid scintillation counter as previously described. Arm muscle area was calculated using triceps skinfold thickness and midarm muscle circumference determined by a single researcher (J.W.) using a standardized technique. Fat-free mass, FM, and BCM were normalized for height to allow comparisons between groups.

Descriptive statistics of the demographic variables were calculated. Means and SDs of the continuous variables were calculated by HIV infection status, growth category (ie, GF and normal growth), and sex. There were 3 groups each for boys and girls as follows: HIV-infected with GF, HIV-infected without GF, and healthy. Frequency distributions of the discrete variables were calculated in the same fashion.

The dependent variables were initially analyzed using 2-factor analysis of covariance (ANCOVA) for unbalanced designs, including HIV-infected with GF, HIV-infected without GF, healthy, and sex.

Because there were significant interactions between the HIV/GF status and sex, these data were reanalyzed using a single-factor ANCOVA for boys and girls. Age was used as the covariate and age-adjusted means of the dependent variables are reported for each group by sex. All statistical calculations were performed using the SAS statistical software package for personal computers (SAS Institute, Cary, NC). The level of significance was .05 for all statistical tests.

The purpose of this study was to characterize the body composition of children with HIV infection using laboratory methods. In particular, we compared the body composition of HIV-infected children with and without GF to add to our understanding of its causes.

RESULTS

The characteristics of boys and girls in the study are presented separately in Table 1. Consistent with our classification criteria, the mean growth rate (centimeters per year) and growth velocity percentile were lower in the HIV-infected children with GF. The mean height-for-age percentiles were lower among the boys and girls in the HIV-infected group with GF compared with the HIV-infected without GF and healthy groups.

No significant differences were observed between the boys and girls in corresponding growth pattern groups with respect to disease stage, degree of immune suppression as measured by CD4 cell count and CD4%, or the...
A different pattern was observed among the girls. These results are presented in Table 2 and the bottom part of the Figure. The HIV-infected girls with GF had significantly lower mean height-for-age and weight-for-age percentiles than HIV-infected girls without GF and healthy girls. In contrast to the boys, the mean height-for-age percentile of the HIV-infected girls without GF did not differ from the healthy controls and the mean weight-for-height percentiles were not different among the 3 groups of girls. The mean FFM and BCM/height ratio was lower in HIV-infected girls with GF compared with HIV-infected girls without GF and healthy girls. Arm muscle area was smaller in HIV-infected girls with GF. In addition, there was a statistical trend suggesting smaller arm muscle area in HIV-infected girls without GF compared with healthy controls ($P = .06$). Body fat percentage and FM/height ratios did not differ among the 3 groups.

To evaluate the effect of the inclusion of children with weight loss in the study results, a second analysis was performed with removal of 2 boys with weight loss of 10% of body weight or more. No significant changes in the intergroup differences in FM and FFM patterns were observed (results not shown).

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**Table 1. Characteristics of Human Immunodeficiency Virus (HIV)–Infected Children With Growth Failure (GF), HIV-Infected Children With Normal Growth, and Healthy Children**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Boys HIV+/GF</th>
<th>Boys HIV+/No GF</th>
<th>Boys Healthy</th>
<th>Girls HIV+/GF</th>
<th>Girls HIV+/No GF</th>
<th>Girls Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>6.8 (2.4)</td>
<td>5.5 (1.8)</td>
<td>8.4 (2.9)</td>
<td>6.8 (2.2)</td>
<td>6.2 (2.2)</td>
<td>7.9 (1.7)</td>
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<tr>
<td>Weight, kg</td>
<td>21.6 (8.4)</td>
<td>18.8 (4.4)</td>
<td>36.0 (11.8)</td>
<td>21.1 (4.1)</td>
<td>29.3 (14.5)</td>
<td>29.6 (6.5)</td>
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<tr>
<td>Height, cm</td>
<td>114.3 (13.4)</td>
<td>110.8 (13.3)</td>
<td>136.5 (16.8)</td>
<td>113.8 (14.3)</td>
<td>121.1 (15.8)</td>
<td>131.2 (9.5)</td>
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<tr>
<td>Growth rate, cm/y</td>
<td>2.4 (1.7)</td>
<td>6.0 (1.0)</td>
<td>. . .</td>
<td>3.0 (1.2)</td>
<td>6.9 (1.2)</td>
<td>. . .</td>
</tr>
<tr>
<td>Growth velocity percentile, %</td>
<td>1.4 (0.9)</td>
<td>30.7 (24.8)</td>
<td>. . .</td>
<td>1.3 (0.7)</td>
<td>56.4 (35.0)</td>
<td>. . .</td>
</tr>
<tr>
<td>Height-for-age percentile, %</td>
<td>14.1 (11.2)</td>
<td>29.4 (31.1)</td>
<td>68.6 (26.2)</td>
<td>13.3 (19.3)</td>
<td>56.2 (27.8)</td>
<td>61.2 (24.3)</td>
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<tr>
<td>Weight-for-age percentile, %</td>
<td>19.9 (29.5)</td>
<td>25.8 (20.2)</td>
<td>69.6 (27.8)</td>
<td>33.9 (29.7)</td>
<td>74.6 (19.8)</td>
<td>62.6 (24.3)</td>
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<tr>
<td>Weight-for-height percentile, %</td>
<td>41.2 (36.8)</td>
<td>37.2 (16.1)</td>
<td>80.6 (27.2)</td>
<td>82.7 (21.7)</td>
<td>78.0 (20.0)</td>
<td>73.2 (28.3)</td>
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<tr>
<td>CD4 cell count, No./dL</td>
<td>109.4 (149.9)</td>
<td>633.0 (500.6)</td>
<td>. . .</td>
<td>216.0 (243.9)</td>
<td>596.7 (382.1)</td>
<td>. . .</td>
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<td>CD4%</td>
<td>6.8 (10.0)</td>
<td>23.6 (14.4)</td>
<td>. . .</td>
<td>11.1 (10.9)</td>
<td>22.0 (7.2)</td>
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<td>Ethnicity, No. (%)</td>
<td>Black</td>
<td>2 (22.2)</td>
<td>6 (75)</td>
<td>12 (55)</td>
<td>2 (22)</td>
<td>4 (50)</td>
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<tr>
<td></td>
<td>Hispanic</td>
<td>7 (77.8)</td>
<td>2 (25)</td>
<td>10 (45)</td>
<td>7 (78)</td>
<td>4 (50)</td>
</tr>
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<td>CDC class, No. (%)†</td>
<td>A2</td>
<td>1 (11.1)</td>
<td>0 (0)</td>
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<td>0 (0)</td>
<td>1 (12.5)</td>
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<tr>
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<td>A3</td>
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<td>1 (12.5)</td>
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<td>B2</td>
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<td>3 (37.5)</td>
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<td>1 (11.1)</td>
<td>3 (37.5)</td>
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<td>2 (22.2)</td>
<td>3 (37.5)</td>
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<td>3 (33.3)</td>
<td>2 (25)</td>
</tr>
<tr>
<td></td>
<td>C1</td>
<td>. . .</td>
<td>. . .</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
<td>. . .</td>
</tr>
<tr>
<td></td>
<td>C3</td>
<td>3 (33.3)</td>
<td>0 (0)</td>
<td>. . .</td>
<td>2 (22.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No. of antiretroviral drugs prescribed</td>
<td>0</td>
<td>2 (22.2)</td>
<td>3 (37.5)</td>
<td>. . .</td>
<td>3 (33.3)</td>
<td>2 (25)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>5 (55.6)</td>
<td>3 (37.5)</td>
<td>. . .</td>
<td>4 (44.4)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2 (22.2)</td>
<td>2 (25)</td>
<td>. . .</td>
<td>2 (22.2)</td>
<td>5 (62.5)</td>
</tr>
</tbody>
</table>

*For HIV-infected boys with GF, n = 9; for HIV-infected boys without GF, n = 8; and for healthy boys, n = 22. For HIV-infected girls with GF, n = 9; for HIV-infected girls without GF, n = 8; and for healthy girls, n = 30. All data are given as mean (SD) unless otherwise indicated. Ellipses indicate not applicable.
†CDC indicates Centers for Disease Control and Prevention. For clinical categories, A indicates mildly symptomatic; B, moderately symptomatic; and C, severely symptomatic. For immunologic categories, 1 indicates no evidence of suppression; 2, evidence of moderate suppression; and 3, severe suppression.13
In our sample, boys and girls with HIV-associated GF had diminished FFM. Our data indicate that the lower FFM is largely due to reductions in BCM, the major constituent of the FFM. The decrease in FFM is in striking contrast to the fat compartment, which was normal in children with HIV-associated GF. Decreases in FFM were also detectable in boys with HIV infection and normal growth, suggesting that alterations in FFM are measurable even in the absence of GF.

The decrease in FFM in children with HIV-associated GF was demonstrated by arm muscle area calculated from anthropometric data as well as by dual-energy x-ray absorptiometry. These findings are similar to previous observations by anthropometrists reported in younger children. Miller et al. reported decreased muscle mass measured by midarm circumference, with preservation of fat mass by age 2 years in children with perinatally acquired HIV. In contrast, a study of older hemophiliac boys with transfusion-acquired HIV and significantly impaired linear growth found no alteration in lean body mass by skinfold methods. 7

The pattern of preferential decrease in FFM over fat observed in boys and girls with HIV-associated GF has been described in the cachexia of cancer as well as in adults with early HIV infection and with AIDS wasting. 20,21 and is distinct from the body composition alterations observed in starvation and in children with nutritionally based stunting. 22,23

The causes of GF in HIV infection are not well understood but are likely multifactorial. While endocrine abnormalities are occasionally encountered, including cases of classic growth hormone deficiency, 24 overall endocrine function is usually intact. 25,26 Gastrointestinal tract dysfunction, including infection and malabsorption, has also been reported, but no clear relationship to GF has been documented.27,28 Our data suggest that for some children with HIV infection, metabolic abnormalities leading to preferential adipogenesis over anabolism and growth may be involved. Disturbances in the growth hormone–insulinlike growth factor axis that have been described in HIV infection could play a role in the growth and body composition abnormalities we observed.29 Physical activity and exercise might also influence body composition and should be evaluated in future studies. The effect of antiretroviral medications on body composition also warrants investigation in this population, especially in light of recent reports of abnormal fat distribution in HIV-infected adults receiving protease inhibitors. 30

Studies of AIDS-related weight loss and wasting in adults indicate that both decreased dietary intake and altered metabolism are factors. Abnormalities in metabolism, including increased basal energy requirements and altered metabolic efficiency, have been reported in some adults with HIV infection and AIDS wasting. 31,32 In adults these abnormalities seem to be less significant to actual weight loss than episodic decreases in dietary intake associated with secondary illnesses. 33 There are no published studies measuring metabolic rates of children infected with HIV. Studies of dietary intake indicate that decreased nutrient intake is not encountered in children with HIV infection. The dietary intake among children with symptomatic HIV infection is reported to be equal to or greater than that in noninfected children. 32 Also, increasing the nutritional

### Table 2. Mean Age-Adjusted Body Composition Measurements in Human Immunodeficiency Virus (HIV)–Infected Children With Growth Failure (GF), HIV-Infected Children With Normal Growth, and Healthy Children

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1, HIV+/GF</th>
<th>Group 2, HIV+/No GF</th>
<th>Group 3, Healthy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>Girls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height-for-age percentile, %</td>
<td>16.4</td>
<td>12.6</td>
<td>14.4</td>
<td>.001</td>
</tr>
<tr>
<td>Weight-for-age percentile, %</td>
<td>20.1</td>
<td>16.2</td>
<td>21.2</td>
<td>.005</td>
</tr>
<tr>
<td>Weight-for-height percentile, %</td>
<td>13.7</td>
<td>16.2</td>
<td>14.9</td>
<td>.003</td>
</tr>
<tr>
<td>Arm muscle area, mm²</td>
<td>1.86</td>
<td>1.97</td>
<td>1.83</td>
<td>.001</td>
</tr>
<tr>
<td>Body fat %</td>
<td>15.8</td>
<td>12.6</td>
<td>18.2</td>
<td>.005</td>
</tr>
<tr>
<td>FM/height ratio, g/cm</td>
<td>45.4</td>
<td>21.8</td>
<td>63.6</td>
<td>.005</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>17.8</td>
<td>21.2</td>
<td>25.6</td>
<td>.001</td>
</tr>
<tr>
<td>FFM/height ratio, g/cm</td>
<td>145.3</td>
<td>165.6</td>
<td>194.1</td>
<td>.001</td>
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<tr>
<td>BCM, g</td>
<td>3862</td>
<td>10,232</td>
<td>11,669</td>
<td>.002</td>
</tr>
<tr>
<td>BCM/height ratio, g/cm</td>
<td>73.8</td>
<td>79.6</td>
<td>85.6</td>
<td>.001</td>
</tr>
</tbody>
</table>

**Notes:**
- FM indicates fat mass; FFM, fat-free mass; and BCM, body cell mass. See footnote to Table 1 for sample sizes of groups.

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An unexpected finding in our study was the striking difference in anthropometric and body composition patterns between boys and girls with HIV infection. Boys with HIV infection without GF had significantly lower weight-for-height and FFM/height ratios than the other boys, while the HIV-infected girls without GF did not. Our study was not designed to evaluate this specifically. In addition, our sample is not population-based; thus, it is not possible to determine whether HIV truly affects growth and body composition differently in boys and girls. Prior studies, including population-based studies, have not evaluated for sex-specific differences in growth characteristics. Sex-specific effects in body composition changes in adults with AIDS have been reported. In contrast to men, women exhibit a disproportionate decrease in fat in the early stages of AIDS wasting, losing significant lean body mass in later stages. Sex differences in growth and body composition in children in response to environmental insults such as malnutrition and infection, with boys being more sensitive, have been described in developing countries. Future population-based studies are required to confirm sex differences in growth and body composition changes among children infected with HIV.

Children with HIV, especially those with GF, have decreased FFM and BCM. These functionally important compartments potentially affect both the quality of life and survival in these children. Additional studies evaluating the factors that influence growth and body composition, including the role of HIV replication on energy balance and metabolism, are required. Evaluating the effect of HIV therapies on body composition will also be important in the future.

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