

The Effect of Protease Inhibitor Therapy on Growth and Body Composition in Human Immunodeficiency Virus Type 1-Infected Children

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ABSTRACT. *Objective.* To determine the effect of protease inhibitors (PIs) on growth and body composition in children with human immunodeficiency virus type 1 (HIV-1) infection.

Background. HIV-1-infected children have chronic problems with both linear growth and weight gain. Viral load may directly influence growth and nutritional status of HIV-1-infected children with reduction of viral load improving the nutritional condition.

Design/Methods. Data from 67 patients who initiated PI therapy between 1996 and 1999 and who were enrolled in a prospective, longitudinal study of growth and nutrition in HIV-1-infected children were analyzed. Outcomes included pre-PI versus post-PI measures of height, weight, weight-for-height, triceps skinfold thickness, and arm muscle circumference. Predictor covariates included age, race, gender, Tanner stage, CD4 z score, Centers for Disease Control and Prevention stage, route of infection, plasma HIV-1 RNA, other antiretroviral therapy, recommended daily allowances for calories, treatment with megestrol acetate, and PI therapy.

Results. Sixty-seven children were followed for a median of 2.4 years with a total of 362 visits (median: 5 visits; range: 1–12). During follow-up, they received PIs for a median of 5 months. Fifty-one percent were girls, 54% black, 15% Hispanic, and 25% white. The mean age at first visit was 6.8 years. In a univariate analysis, weight z score (–0.67 to –0.35) and weight/height z score (0.25–0.76) improved on PI therapy. Using repeated-measures regression analysis, controlling for the above named covariates, PI treatment showed a significant effect on weight z score (increase in z score by 0.46), weight/height z score (increase in z score by 0.49), and arm muscle circumference (increase in percentile by 11.5). A borderline effect was found for height z score (increase in z score by 0.17) and no effect was found for triceps skin-

fold thickness. In a separate analysis, PI therapy increased CD4 counts twofold and reduced plasma HIV-1 RNA copies by 79%.

Conclusion. In addition to a significant reduction in viral load, PI therapy in children has a positive effect on several growth parameters, including weight, weight/height, and muscle mass. *Pediatrics* 2001;107(5). URL: <http://www.pediatrics.org/cgi/content/full/107/5/e77>; *human immunodeficiency virus, protease inhibitor, growth, body composition, children.*

ABBREVIATIONS. HIV-1, human immunodeficiency virus type 1; AIDS, acquired immunodeficiency syndrome; HAART, highly active antiretroviral therapy; PI, protease inhibitor; AMC, arm muscle circumference; TSF, triceps skinfold; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; CDC, Centers for Disease Control and Prevention; SD, standard deviation; SE, standard error; RDA, recommended dietary allowance.

Despite dramatic gains in reducing the incidence of vertically acquired human immunodeficiency virus type 1 (HIV-1) infection, an estimated 20 000 children, including adolescents, are living with HIV-1 or the acquired immunodeficiency syndrome (AIDS) in the United States.¹ Survival time and quality of life for children living in countries with access to highly active antiretroviral therapy (HAART) have improved because of advances in medical therapy. Indeed, the goal of therapy in the United States has shifted from delayed disease progression to indefinite viral suppression.^{2–4} With these developments, new questions relating to long-term changes in growth and body composition in both adults and children have arisen.

Understanding the link between nutrition and the new therapeutic options available is critical, because nutritional status has been shown to be associated with pediatric HIV-1 disease progression.^{5,6} Growth patterns before HAART therapy of HIV-1-infected children in developed countries are fairly well established,^{7–11} although the exact mechanisms of these growth abnormalities are not as well understood. HIV-1-infected children in developed countries have similar birth weights compared with noninfected groups, but quickly diverge in both weight and height within the first months of life.^{7–10} These differences tend to be stable, although weights can de-

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cline with the onset of an acute event, such as pneumonia (unpublished data). Interventions, such as enteral^{12,13} or parenteral supplementation¹⁴ and appetite stimulants¹⁵ known to improve nutritional status in other children, can improve weight in children with HIV-1 infection but have little effect on height over the short term.

Preliminary evidence in pediatric HIV-1 research suggests that combination antiretroviral therapies have a positive effect on mean weight, height, growth velocity, appetite, and well-being.¹⁶⁻¹⁹ Chronic viral activity is likely to alter growth patterns for any child.²⁰ Thus, inducing viral suppression may potentially shunt energy utilization from a chronic immunologically activated state to positive nitrogen balance, with improved gains in both weight and height. Because protease inhibitor (PI) therapy can profoundly affect viral load in children with HIV-1 infection, we sought to examine the effect of PIs on growth and body composition.

METHODS

Patient Population

HIV-1-infected children enrolled in a prospective, longitudinal study on growth and nutrition and who initiated PI therapy between 1996 and 1999 at the Children's Hospital AIDS Program, Boston and the University of Rochester Pediatric HIV Program were included in this analysis. The institutional review boards at both institutions approved the research protocol. The diagnosis of HIV-1 infection was confirmed by repeatedly positive serum enzyme-linked immunosorbent assay in conjunction with Western blot assays (older children) or, for infants, repeatedly positive HIV-1 RNA or DNA polymerase chain reaction or HIV-1 culture. Children had acquired HIV-1 infection perinatally or from blood products. Children enrolled in blinded AIDS Clinical Trials Group protocols with a PI component were included only if the study drugs were unblinded at the time of data analysis. No children received enteral or parenteral nutrition during the study.

Outcome Measurements

The main outcomes of this study were age- and gender-adjusted anthropometric measurements, compared before and after PI therapy. These measurements included height, weight, weight-for-height, arm muscle circumference (AMC), and triceps skinfold thickness (TSF). Weight (recorded to the nearest 0.01 kg) and recumbent length (children <2 years old) or standing height (children >2 years old; recorded to the nearest 0.01 cm) were recorded by using recommended techniques.²¹ TSF (a measure of fat stores) and mid-arm muscle circumference were measured with standard techniques and used to derive AMC (a measure of muscle mass).²² Age- and sex-adjusted percentiles for AMC and TSF were derived from the Ten-State Nutrition Survey for infants and children.²³

Data Collection/Covariates

Clinical and laboratory data were collected from simultaneous visits that followed the study protocol. Children were evaluated every 3 to 6 months. Additional information was abstracted retrospectively from the medical records as needed. Baseline information included age, sex, Tanner stage, race, and route of HIV-1 infection. In addition, CD4 T lymphocyte cell count, antiretroviral therapy (PI, nucleotide reverse transcriptase inhibitor [NRTI], and/or nonnucleotide reverse transcriptase inhibitor [NNRTI]) and Centers for Disease Control and Prevention (CDC) HIV stage²⁴ were recorded at each study visit. CD4⁺ T cell counts were expressed as age-adjusted z scores.²⁵ Plasma HIV-1 RNA concentration was measured on samples by quantitative HIV-1 RNA polymerase chain reaction using Amplicor HIV-1 Monitor test (Roche Diagnostic Systems, Branchburg, NJ). Energy intake, expressed in kilocalories per kilogram per day and adjusted for age, was determined at each study visit and was presented as the percentage of expected. Dietary intakes were determined by an

interviewer-administered 24-hour recall of the previous day's intake from the primary provider of the child or patient, if deemed reliable. Megestrol acetate use as an appetite stimulant was recorded. All longitudinal data for each child were included in the dataset before PI therapy. PI therapy was defined as drug therapy with at least 1 PI, including nelfinavir, indinavir, saquinavir, or zidovudine for >2 months. If the PI was discontinued for any reason, data collection was stopped for that child at that point in time.

Statistical Analysis

Simple descriptive statistics (means, standard deviations [SDs], and percentages) were used to define the characteristics of the study cohort at the time of their first visit in this database. All weights, heights, and weight-for-heights are expressed as z scores²⁶ to adjust for age and sex. The z scores were calculated by subtracting from each observed data point the age/sex-appropriate normal predicted value, and then dividing by 1 SD (as determined by the normative population). If a z score is zero, then the child is exactly at the age/sex-appropriate value. If a z score is above (below) 2 (-2), then the child is in the upper (lower) 2.5% extreme of the normative population. AMC and TSF were age- and sex-adjusted and expressed as percentages, with 50% indicating normal for age and sex.

The effect of PIs (both individually and collectively) on each of the 5 study outcomes (weight, height, weight-for-height, TSF, and AMC) was examined through repeated-measures linear regression. The models were fit through the GENMOD procedure in the SAS statistical software program (SAS Institute, Cary, NC). To account for the correlation between serial measures on the children, the GENMOD procedure adjusted all standard errors (SEs) for correlation that was initially assumed to diminish as the time interval between the measurements increased (first-order autoregressive). Initially, we started with a simple unadjusted comparison of growth before the use of PIs with growth at least 2 months after the initiation of PIs. Next, we adjusted the PI comparison for % recommended dietary allowance (RDA) caloric intake, sex, Tanner stage, age, race, route of HIV-1 infection, megestrol acetate, NRTI, NNRTI use, CDC stage, amount of time HIV-1-infected, plasma HIV-1 RNA, and CD4 z score. To avoid assuming linear effects, the percent of expected energy intake, age, plasma HIV-1 RNA, and CD4 z score were divided into quartiles and entered into models through indicator variables. Also, because PI use, megestrol acetate use, CDC stage, Tanner stage, other antiretroviral use, time HIV-1-infected, plasma HIV-1 RNA, and CD4 count were collected within 1 week of each study visit, all of these variables were allowed to change over time in the longitudinal analyses. Finally, we added 1 additional covariate into the fully adjusted models: a 0/1 variable indicating whether a particular time point was the first measure of growth after the initiation of PI use. In this way, we could try to examine whether PI use had a brief singular effect on growth or whether the effect was persistent throughout the course of therapy.

To verify the expected effect of PI use on disease, we also ran the same fully adjusted repeated-measures regression models with CD4 counts and z scores and plasma HIV-1 RNA as outcome variables. Because the distributions of CD4 counts, z scores, and plasma HIV-1 RNA are highly skewed and nonnormal, these endpoints were first transformed to a log scale, so that the impact of PIs will necessarily be presented as percent change rather than as additive change in disease burden.

All presented P values are 2-sided and a value of .05 or less is considered to be significant.

RESULTS

Patient and Study Characteristics

Sixty-seven children were followed a median of 2.4 years (range: 0-3.8 years), with a total of 362 visits over this time (median: 5 visits; range: 1-12). Six children who received PI therapy and who had insufficient follow-up (ie, <2 months) were included for information on predrug treatment only. Sixteen children with data exclusively on PI therapy were included for information during drug treatment only. Forty-five children had longitudinal follow-up

before and after PI therapy. There was a median of 4 visits before PI therapy (range: 1–11) with a median of 2.2 years (range: 0–3.7) of follow-up. There was a median of 2 visits (range: 1–6) while on PI therapy with a median of 0.4 years (range: 0–1.6) of follow-up.

The initial patient characteristics at study entry are shown in Table 1. There was an equal distribution of girls and boys (51% girls). The children represented a broad spectrum of HIV stage with 24% being CDC class C1, C2, C3, and the mean CD4 T lymphocyte count was 748 (SD = 710) and CD4 z score was -1.80 (SD = 1.31). Ninety-four percent of the children acquired HIV-1 vertically. In general, the children were below standard in weight (z score: -0.6 ; SD: 1.2; $P < .001$ vs z score: 0) and height (z score: -1.1 ; SD: 1.4; $P < .001$ vs z score: 0), with elevated weight-for-height (z score: $+0.4$; SD: 1.0; $P = .01$ vs z score: 0). TSF percentiles were below standard (mean: 39%; SD: 31; $P = .01$ vs 10%). Mean AMC percentiles were normal at 55%. Children were consuming greater than the RDA for both kilocalories and protein (125% and 324%, respectively).

Univariate Analysis of Nutritional Outcomes With PIs

An uncontrolled analysis of PI effects on growth and nutritional outcomes is shown in Table 2. There was a significant improvement in weight z score with mean measures improving from -0.67 while off PI therapy to -0.35 while on therapy ($P = .001$). Weight-for-height measures improved as well, with mean weight-for-height z score of 0.25 improving to 0.76 ($P = .02$) after PI therapy. No significant differences were found for height, AMC percentile, or TSF percentile in this uncontrolled analysis.

TABLE 1. Patient Characteristics at Initial Visit ($n = 67$)

Sex	
Female	51%
Male	49%
Race	
Black	54%
Hispanic	15%
White	25%
Other	6%
CDC stage	
N (1–3)	5%
A (1–3)	25%
B (1–3)	46%
C (1–3)	24%
Route of infection	
Vertical	94%
Blood products	6%
Age, mean	6.8 y
	(SD: 3.7 y)
CD4 count, mean	748 cells/mm ³
	(SD: 710)
CD4 z score, mean	-1.80 (SD = 1.31)
Viral load, median	25 471 copies
	(range: 359–688 116)
Megesterol acetate use	10%
Height z score	-1.1 (SD = 1.4)
Weight z score	-0.6 (SD = 1.2)
Weight-for-height z score	0.4 (SD = 1.0)
TSF percentile	39 (SD = 31)
AMC percentile	55 (SD = 29)

Multivariate Analysis of Nutritional Outcomes With PIs

Using repeated-measures regression, the adjusted effects of PIs on growth and body composition were determined. The analyses controlled for age, sex, Tanner stage, race, route of HIV-1 transmission, time with HIV-1 infection, CDC stage, CD4 z score, plasma HIV-1 RNA, caloric intake, and megesterol acetate, NRTI, and NNRTI therapy. The results shown in Table 3 reveal that PIs significantly improved weight z score by nearly one half SD ($P < .001$), weight-for-height z score by nearly one half SD ($P = .016$), and AMC percentile by 11.5% ($P = .003$). There was a borderline effect on height, increasing the z score by 0.17 SD ($P = .10$). No effect was found on TSF percentiles. Analysis of individual effects of PIs showed similar results (Table 3). We note that in additional analyses, PI use was not associated with a change in caloric intake ($P = .86$). When the adjusted analysis was confined to only those children with both pretreatment and posttreatment data ($n = 45$), we found similar results with a significant improvement in weight ($P < .001$), weight-for-height ($P = .014$), and AMC ($P = .001$). A borderline effect was found on height ($P = .066$), and no effect was found on TSF ($P = .90$).

When the repeated-measures regression model was expanded to adjust for a marker of the first instance of PI use (Table 4), we found that the previous positive effects of PI therapy on weight and AMC remained essentially unchanged and were sustained throughout the follow-up period. We found that there was a trend toward an improvement in height z score by 0.26 SD ($P = .065$), which occurred subsequent to the first follow-up after initiation of PI therapy. Similarly, TSF percentile improved by 6.8% ($P = .15$) subsequent to the first follow-up after initiation of PI therapy. Because height increased, the gain in weight-for-height z score was reduced to 0.43 SD and did not reach significance ($P = .07$). This analysis shows that weight and AMC increase immediately after PI initiation, while there is a trend that height and TSF may show a delayed response to PIs.

The repeated-measures analysis evaluating the effect of PIs on CD4 counts showed that PI use increased CD4 counts twofold (95% confidence interval: 1.4,2.8; $P < .001$), after adjusting for percent RDA calories, sex, Tanner stage, age, race, route of infection, megesterol acetate, NRTI, NNRTI use, CDC stage, and amount of time HIV-1-infected. The median absolute CD4 count increased from 378 (range: 0–3822) cell/mm³ pretherapy to 496 (range: 24–2273) cell/mm³ posttherapy. Similarly, the median CD4 z score increased from -2.40 (range: -3.9 – -1.9) to -2.06 (range: -3.9 – -2.2). A similarly adjusted analysis demonstrated that PIs reduced plasma HIV-1 RNA by 79% (95% confidence interval: 58%, 90%; $P < .001$), with median HIV-1 RNA decreasing from 25 644 (range: 359 000–750 000) to 14 336 (range: 0–750 000) copies.

TABLE 2. Growth Measures While Off and On PIs

	Mean*† While off PIs	Mean*† While on PIs	P Value†
Parameter			
Height z score	-1.11 (0.17)	-1.05 (0.18)	.470
Weight z score	-0.67 (0.15)	-0.35 (0.14)	.001
Weight/height z score	0.25 (0.17)	0.76 (0.20)	.022
AMC percentile	54 (3.6)	56 (3.6)	.430
TSF percentile	35 (3.5)	38 (3.5)	.440

* Results reported as weighted means and SEs.

† Means and *P* values were calculated from a repeated-measures regression with protease inhibitor use as the sole predictor. By adjusting for correlation between serial measurements of growth, multiple observations on the same child are effectively down-weighted when calculating means, SEs, and *P* values.

TABLE 3. Multivariate Analysis* of the Effect of PIs on Growth

Growth Endpoint	Overall PI Effect (SE)	<i>P</i> Value	Ritonavir Effect (SE)	<i>P</i> Value	Indinavir Effect (SE)	<i>P</i> Value	Nelfinavir Effect (SE)	<i>P</i> Value
Height z score	0.17 (0.10)	.10	0.30 (0.13)	.024	-0.07 (0.13)	.59	0.08 (0.11)	.48
Weight z score	0.46 (0.11)	<.001	0.41 (0.12)	.001	0.42 (0.21)	.049	0.45 (0.11)	<.001
Weight-for-height z score	0.49 (0.20)	.016	0.31 (0.31)	.32	0.88 (0.39)	.023	0.53 (0.18)	.003
AMC percentile	11.5 (3.8)	.003	8.2 (5.7)	.15	12.8 (4.7)	.006	12.1 (3.6)	.001
TSF percentile	1.9 (4.0)	.63	-2.8 (5.4)	.60	-1.4 (5.7)	.80	5.3 (4.9)	.28

* Model was adjusted for sex, age, Tanner stage, race, route of infection, CDC stage, HIV RNA PCR, CD4 z score, time with HIV infection, Megace use, NRTI, NNRTI, and energy intake.

TABLE 4. Effect of PI Therapy Over Time*

	Initial Measurement After PI Therapy (Median 4 Months)		All Time Points After Initial Measurement (Range: 7–10 Months)	
	Effect (SE)	<i>P</i> Value	Effect (SE)	<i>P</i> Value
Height z score	0.15 (0.10)	.12	0.26 (0.14)	.065
Weight z score	0.45 (0.12)	<.001	0.51 (0.21)	<.001
Weight-for-height z score	0.50 (0.20)	.014	0.43 (0.24)	.07
AMC percentile	11.3 (3.9)	.003	11.7 (5.1)	.021
TSF percentile	-1.7 (4.4)	.70	6.8 (4.7)	.15

* Analysis was compared to preprotease therapy. Model was adjusted for sex, age, Tanner stage, race, route of infection, CDC stage, HIV RNA PCR, CD4 z score, time with HIV infection, Megace use, NRTI, NNRTI, and energy intake.

DISCUSSION

In this study, we have shown that PI therapy affects weight, weight-for-height, and AMC of HIV-1-infected children, independent of the concurrent decrease in HIV-1 viral load and improved CD4 T lymphocyte counts. The immediate treatment effects are most apparent with an improvement in weight and AMC; however, there was a trend toward a delayed response in height as well. The results of this study confirm previous research on the positive effect of PIs as a component of HAART in the reduction of viral load^{2,16,17,27–29} and with a larger cohort, confirm preliminary reports that suggest a positive effect of PIs on growth.^{16,18,19,27,28,30,31} Other markers of nutrition, such as lean body mass, improved as well. Our study had the unique advantage of collecting nutritional data, including energy intake and body composition measurements, on a large cohort months before PIs were started.

PIs are highly potent antiretroviral agents that act by selectively blocking HIV-1 protease, an enzyme necessary for HIV-1 replication in the later stages of virus production.³² Studies in children suggest that PI therapy is associated with a reduction in viral load and an increase in CD4 cell count,^{2,16,17,27–29} although

longitudinal studies are essential to determine the duration of this immune response. Current pediatric treatment guidelines include a PI in the recommended combination therapy regimen for any HIV-1-infected child with: clinical symptoms (CDC class A, B, and C); immune suppression (CDC class 2 and 3); or any child diagnosed under the age of 1 year, because of the high viral load activity during this period.³³ Thus, the majority of children with HIV-1 in developed countries are exposed to these medications.

The most immediate nutritional effect in our study was a significant gain in weight that was appreciated at the first follow-up visit. There are other preliminary reports of the beneficial nutritional effect of PI therapy in children. Mueller et al¹⁷ noted a weight increase with 16 weeks of PI therapy among 79% of 54 children taking indinavir, with a >10% gain in 11 of these patients and sustained effects in most. Other investigators^{16,18,27,30} reported improved appetite, weight, and well-being on drug regimens that included a PI. Varille et al³¹ included other measures of growth beyond height and weight in a study of 13 children receiving combination therapy with a PI component. They concluded that combination ther-

apy was associated with a significant increase in growth velocity, although the resting energy expenditure remained above expected values. Fat-free mass also decreased during this 18-month period.

Maintenance of lean body mass can be problematic for all patients infected with HIV-1.^{34,35} We and others^{7,8} have found significant losses of lean body mass over time in HIV-1-infected children. Although we have found normal or increased dietary intake in stable HIV-1-infected children,³⁶ augmentation of lean body mass can be difficult in light of chronic viral activity. Although not definitively proven, energy substrates are likely shunted from normal anabolic pathways to production of acute phase reactants, as found in adults with HIV-1 infection.³⁷ Enteral supplementation has not reversed the loss of lean body mass in children,¹² and there is a dearth of information on body composition in children with HIV-1 infection. In our study, PIs caused a dramatic improvement in lean body mass, as measured by AMC, over a short interval. PIs are one of the few interventions that have improved lean body mass for HIV-1-infected children. We found no immediate influence on fat mass, although there was a trend toward increased fat mass, with longer follow-up time. Limited follow-up duration precludes determination of a definitive effect on fat mass.

In our study, there was a suggestion that height improved in the follow-up period. Although we had a sufficient number of children to detect statistically significant changes in weight, weight-for-height, and AMC, we likely had limited power to detect effects on height because of sample size. Our analysis suggests that PIs do not impact on linear growth immediately as they do weight, but there is a suggestion, although not significant association, toward a delayed improvement. This finding would not be unusual, because children with growth problems because of other chronic conditions do not typically accelerate in both height and weight simultaneously when nutritionally rehabilitated. Improvements in height are often appreciated after the improvements in weight.³⁸ There have been few interventions that have improved height growth velocity in children with HIV-1 infection. Reports of enteral supplementation^{12,13} and appetite stimulants¹⁵ show increases in weight but not height. Because HIV-1-infected children are living longer and approaching puberty, interventions to maximize growth potential will be important both medically and psychologically.

Adult HIV-1-infected patients receiving PI therapy or HAART have developed a syndrome of peripheral insulin resistance, hyperlipidemia, and lipodystrophy (truncal obesity and extremity and facial wasting).^{39–43} This entity has not been as well defined in children, although many centers are reporting anecdotal experience (S. Burchett, G. Weinberg, personal communication, 2000). Therefore, additional studies that define the distribution of fat and lean body mass of children on PIs are needed, because abnormal regionalization of fat is predictive of long-term cardiovascular and diabetes risk.⁴⁴

We have also evaluated the effects of individual PIs as well as controlling for other antiretroviral ther-

apy in this group of children. We found that, in general, nelfinavir and indinavir are similar to the combined effect of all PIs, whereas zidovudine had a slightly weaker effect on weight and AMC with a stronger effect on height. Controlling for other antiretroviral therapy did not change the overall results, suggesting that PI therapy had an independent effect on weight, weight-for-height, and AMC. Although we have tried to control for potential confounders (particularly relating to disease severity) in this analysis (ie, CDC stage, CD4 counts, age, other therapies, etc), it is possible that other unmeasured factors, like serum cytokines, which may change because of PI therapy and which can alter metabolism, contribute to the growth changes associated with PI therapy. It is likely that unmeasured factors, such as the above example, which change with PI therapy, have effects on growth outcomes, rather than PIs themselves.

One limitation of this study is the lack of a control group of children with similar characteristics, in the same time frame, and who were not exposed to PI therapy. Ethical concerns in withholding standard therapy are an issue if we were to assemble this type of control group. Instead, we have used each child as his or her own control, capturing data before and after starting PI therapy.

Practitioners and families should now become aware that in addition to the antiviral effect, PI therapy is associated with a positive effect on weight, weight-for-height, and lean body mass, with a suggestion toward longer-term improvements in height with longer follow-up. The changes in fat distribution remain to be determined. Although we have documented positive gains in some parameters of growth, this should not diminish the importance of routine dietary assessment, supplementation, and teaching to maintain growth and support of the immune system. Ball⁴⁵ noted that there is an "inextricable link" between nutrition and disease status. Future research studies will need to continue to identify biological, genetic, social, and biochemical pathways that define this link, with particular focus on fat redistribution syndrome and longer-term nutritional sequelae of HART therapy in HIV-1-infected children.

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