Severity of Human Immunodeficiency Virus Infection Is Associated with Decreased Phase Angle, Fat Mass and Body Cell Mass in Adults with Pulmonary Tuberculosis Infection in Uganda[1]

Snehal Shah,* Christopher Whalen,† Donald P. Kotler,** Harriet Mayanja,‡ Alice Namale,‡ George Melikian,§ Roy Mugerwa‡ and Richard D. Semba[2,§]

*The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA; †Tuberculosis Research Unit, Department of Epidemiology, Case Western Reserve University, Cleveland, OH; **Division of Gastroenterology, Department of Medicine, St. Luke's-Roosevelt Hospital Center, New York, NY; §Department of Ophthalmology, Johns Hopkins School of Medicine, Baltimore, MD; and ‡Department of Medicine, Makerere University, Kampala, Uganda

ABSTRACT Although coinfection with tuberculosis and human immunodeficiency virus (HIV) is emerging as a major problem in many developing countries, nutritional status has not been well characterized in adults with tuberculosis and HIV infection. We compared nutritional status between 261 HIV-positive and 278 HIV-negative adults with pulmonary tuberculosis in Kampala, Uganda, using anthropometry and bioelectrical impedance analysis. Among 163 HIV-positive and 199 HIV-negative men, intracellular water–to–extracellular water (ICW:ECW) ratio was 1.48 ± 0.26 and 1.59 ± 0.48 ($P = 0.006$) and phase angle was 5.42 ± 1.05 and 5.76 ± 1.30 ($P = 0.009$), respectively. Among 98 HIV-positive and 79 HIV-negative women, ICW:ECW was 1.19 ± 0.16 and 1.23 ± 0.15 ($P = 0.11$) and phase angle was 5.35 ± 1.27 and 5.43 ± 0.93 ($P = 0.61$), respectively. There were no significant differences in BMI, body cell mass, fat mass or fat-free mass between HIV-positive and HIV-negative adults. Among HIV-positive subjects, BMI, ICW:ECW, body cell mass, fat mass and phase angle were significantly lower among those with $CD4^+$ lymphocytes ≤ 200 cells/μL compared with those who had >200 cells/μL. In sub-Saharan Africa, coinfection with pulmonary tuberculosis and HIV is associated with smaller body cell mass and intracellular water, but not fat-free mass, and by large differences in ICW:ECW and phase angle α. J. Nutr. 131: 2843–2847, 2001.

KEY WORDS: • *acquired immune deficiency syndrome* • *AIDS* • *human immunodeficiency virus infection* • *HIV* • *malnutrition* • *body composition* • *bioelectrical impedance* • *tuberculosis*

There are an estimated 1.86 billion individuals, or nearly one-third of the world's population, infected with *Mycobacterium tuberculosis*, and the majority of these individuals live in developing countries where human immunodeficiency (HIV)[3] is a major public health problem (1). Tuberculosis accounts for three million deaths a year, making it the leading infectious cause of death, far surpassing measles (two million deaths per year) and malaria (one million deaths per year) (2). In 1997 there were 7.96 million new cases and 16.2 million existing cases of tuberculosis, and 8% of incident cases of tuberculosis were coinfected with HIV (1). Among the major infectious diseases, tuberculosis has long been associated with malnutrition, a factor that is known to play a role in the reactivation of latent tuberculosis infection (3).

In sub-Saharan Africa, tuberculosis is one of the most common opportunistic infections among HIV-infected adults (4). Although malnutrition is associated with tuberculosis, there have been few studies addressing nutritional status in HIV-infected adults with tuberculosis. These studies have been limited to assessment of body weight (5) and serum albumin concentrations (6). A recent study from Burundi among adults with tuberculosis, including pulmonary, extrapulmonary and disseminated infection, suggests that those infected with HIV have significantly lower weight, BMI and fat-free mass compared with individuals without concurrent HIV infection (7). Moreover, there appears to be a relationship between BMI, host immune function and the natural history of HIV in adults with tuberculosis (8).

Bioelectrical impedance analysis (BIA) has been proposed for nutritional studies in HIV-infected individuals and has been shown to be sufficiently precise for clinical investigation (9). Phase angle α, the relationship between two vector com-

[1] Financial support for this study was provided by The National Institute of Allergy and Infectious Diseases (AI32414, AI41956), the National Institute of Child Health and Human Development (HD32247, HD30042), and the Fogarty International Center, the National Institutes of Health and the United States Agency for International Development (Cooperative Agreement HRN A-0097-00015-00).

[2] To whom correspondence should be addressed.
E-mail: rdsemba@jhmi.edu.

[3] Abbreviations used: BCM, body cell mass; BIA, bioelectrical impedance analysis; ECW, extracellular water; FFM, fat-free mass; HIV, human immunodeficiency; ICW, intracellular water; MHC, major histocompatibility complex; TBW, total body water; TNF-α, tumor necrosis factor-α.

Manuscript received 19 March 2001. Initial review completed 7 June 2001. Revision accepted 9 August 2001.

ponents of resistance and reactance that is considered to indicate water distribution between extra- and intracellular spaces, has been shown to be an independent predictor of mortality during HIV infection (10,11). Body cell mass also appears to be an independent predictor of mortality among HIV-infected adults in the era before highly active antiretroviral therapy (12). To gain further insight into body composition in adults with pulmonary tuberculosis, we conducted a study that compared nutritional status between HIV-infected and uninfected adults with pulmonary tuberculosis in Kampala, Uganda using BIA.

MATERIALS AND METHODS

The study population consisted of adults who presented with sputum-positive pulmonary tuberculosis to the National Tuberculosis and Leprosy Program at the Tuberculosis Clinic of Old Mulago Hospital, Kampala, Uganda between February 1999 and January 2000. Subjects were offered HIV testing and were screened for HIV-1 antibodies after oral informed consent. All subjects were given appropriate pre- and post-test HIV counseling and AIDS education. At enrollment, basic demographic information and a medical history were collected, and a standardized physical examination was conducted by a medical officer. Subjects received standard four-drug chemotherapy for tuberculosis per guidelines of the Ugandan Ministry of Health. Adults with a previous history of treated pulmonary tuberculosis were excluded. The study was approved by the institutional review boards at Case Western Reserve University and the Ugandan National AIDS Research Subcommittee, with final approval by the Office for Protection from Research Risk of the National Institutes of Health.

Single-frequency BIA was performed at 50 kHz and 800 μA (RJL Systems, Detroit, MI) with standard tetrapolar lead placement (13). Before performing measurements on each subject, the BIA instrument was calibrated using the manufacturer's recalibration device. The resistance (R) and reactance (X_c) are based on measures of a series circuit (9). BIA measurements were performed in triplicate for each subject. The reproducibility of the R and X_c measurements on repeated measurement in the clinic was <1%. Body weight was determined to the nearest 0.1 kg using a SECA adult balance, and standing height was determined to the nearest 2 mm. Triceps skinfold thickness was measured using Holtain calipers. Total body water (TBW), body cell mass (BCM), fat-free mass (FFM) and intracellular water (ICW) were calculated from BIA measurements using equations that were previously cross-validated in a sample of patients (white, black and Hispanic) with and without HIV infection (9). Extracellular water (ECW) was calculated as TBW minus ICW, and fat mass (FM) was calculated as body weight minus FFM. HIV-1 infection was diagnosed on the basis of a positive enzyme-linked immunosorbent assay for HIV-1 antibodies (Recombigen; Cambridge Biotech, Cambridge, MA). At enrollment, a complete blood count and differential white blood cell count were done using an automated cell counter (T540 Coulter, Hialeah, FL), and $CD4^+$ lymphocytes were measured using standard two-color flow cytometry (14).

Student's t test was used to compare normally distributed variables between groups. Men and women were analyzed separately. Exact and χ^2 tests were used for comparisons of categorical variables between groups. HIV-infected adults were divided into two groups based upon $CD4^+$ lymphocyte count above and below 200 cells/μL, per convention. BMI < 19 kg/m^2 was considered consistent with malnutrition (15). Phase angle $\alpha < 5.3°$ was used because this cutoff was previously shown to be predictive of mortality in HIV-infected adults (11).

RESULTS

There were 278 HIV-negative and 261 HIV-positive adults with pulmonary tuberculosis enrolled in the study, and demographic characteristics and some laboratory variables are shown in **Table 1**. Among both men and women with pulmonary tuberculosis, HIV-positive individuals were older and had a lower mean $CD4^+$ lymphocyte count, serum albumin level and hemoglobin level than HIV-negative individuals. A larger proportion of HIV-positive individuals with pulmonary tuberculosis were female compared with HIV-negative individuals. $CD4^+$ lymphocytes, serum albumin and hemoglobin were not measured on 5, 15 and 5 of the 539 total participants in the study, respectively, because of lack of availability of an adequate blood sample for analysis.

BMI and body composition in HIV-negative and HIV-positive adults with pulmonary tuberculosis are shown in **Table 2**. Among both men and women, there were no significant differences in BMI or the proportion of individuals with BMI < 19 kg/m^2 by HIV status. Intracellular to extracellular water ratio (ICW:ECW) and phase angle α were significantly lower in HIV-positive than in HIV-negative men with pulmonary tuberculosis. The proportion of adults with phase angle $\alpha < 5.3°$ was significantly higher in HIV-positive compared with HIV-negative men. There were no significant differences in BMI or indicators from BIA between HIV-positive compared with HIV-negative women.

BMI and body composition were compared among 259 HIV-infected adults with pulmonary tuberculosis who had $CD4^+$ lymphocyte counts ≤200 and >200 cells/μL (**Table 3**). Among both men and women, those with $CD4^+$ lymphocyte counts ≤200 cells/μL had significantly lower mean BMI, re-

TABLE 1

Characteristics of HIV-positive and HIV-negative adults with pulmonary tuberculosis

	Men			Women		
Characteristic	HIV-negative	HIV-positive	*P*	HIV-negative	HIV-positive	*P*
n	199	163		79	98	
Age, *y*	28.6 ± 7.4	32.4 ± 6.7	0.0001	26.4 ± 7.9	28.6 ± 6.6	0.001
$CD4^+$ lymphocytes,[2] *cells/μL*[2]	596 ± 217	270 ± 222	0.0001	770 ± 271	307 ± 251	0.0001
Serum albumin,[3] *g/L*	32.3 ± 4.7	29.2 ± 4.1	0.0001	33.2 ± 3.7	28.5 ± 4.6	0.0001
Hemoglobin,[2] *g/L*	122 ± 20	113 ± 30	0.002	110 ± 19	98 ± 17	0.002
Anemic,[4] %	42.6	62.6	0.0002	67.9	85.5	0.006

[1] Values are means ± SD for continuous variables.
[2] No $CD4^+$ lymphocyte count or hemoglobin measurements for two HIV-negative and one HIV-positive men, one HIV-negative and one HIV-positive women.
[3] No serum albumin measurement for five HIV-negative and seven HIV-positive men, one HIV-negative and two HIV-positive women.
[4] Hemoglobin <120 g/L for females, <130 g/L for males.

TABLE 2

BMI and body composition in HIV-positive and HIV-negative adults with pulmonary tuberculosis

	Men			Women		
Characteristic[1]	HIV-negative	HIV-positive	*P*	HIV-negative	HIV-positive	*P*
n	199	163		79	95	
Weight, *kg*	52.6 ± 7.4	52.6 ± 6.5	0.99	49.3 ± 7.3	79.7 ± 9.0	0.78
Height, *cm*	170 ± 7	170 ± 6	0.99	159 ± 6	158 ± 6	0.08
BMI, *kg/m²*	18.1 ± 2.2	18.1 ± 1.8	0.98	19.3 ± 2.7	19.8 ± 3.4	0.25
BMI <19 kg/m², %	65.8	70.5	0.33	51.9	44.9	0.35
Reactance (Ω)	59.4 ± 10.9	55.7 ± 10.5	0.002	64.8 ± 10.9	62.0 ± 11.3	0.10
Resistance (Ω)	599 ± 87	592 ± 82	0.46	686 ± 79	675 ± 112	0.46
TBW, *L*	33.0 ± 4.2	33.1 ± 4.0	0.78	27.4 ± 3.0	27.3 ± 3.7	0.90
ICW, *L*	20.0 ± 3.4	19.6 ± 3.0	0.27	15.0 ± 2.1	14.8 ± 2.6	0.52
ECW, *L*	12.8 ± 1.9	13.4 ± 1.9	0.65	12.3 ± 1.4	12.5 ± 1.6	0.41
ICW:ECW	1.59 ± 0.48	1.48 ± 0.26	0.006	1.23 ± 0.15	1.19 ± 0.16	0.11
BCM, *kg*	21.9 ± 3.8	21.5 ± 3.4	0.25	16.5 ± 2.2	16.2 ± 2.8	0.56
Fat mass, *kg*	4.40 ± 3.32	4.23 ± 2.72	0.60	12.2 ± 5.4	13.0 ± 7.2	0.37
FFM, kg	48.1 ± 5.1	48.3 ± 4.8	0.69	37.2 ± 3.7	36.9 ± 4.4	0.87
Percent fat, *g/100 g*	7.8 ± 5.4	7.7 ± 4.4	0.78	23.9 ± 7.7	24.8 ± 9.5	0.46
Phase angle α, °	5.76 ± 1.30	5.42 ± 1.05	0.009	5.43 ± 0.93	5.35 ± 1.27	0.61
Phase angle α <5.3°, %	34.6	44.8	0.049	37.9	47.9	0.18

[1] Values are means ± SD for continuous variables.

actance, ICW, ICW:ECW, BCM, fat mass and phase angle α than individuals with $CD4^+$ lymphocyte counts >200 cells/μL. The proportion of individuals with BMI < 19 kg/m² and with phase angle α <5.3° was significantly higher with $CD4^+$ lymphocyte count ≤200 than >200 cells/μL among both men and women.

DISCUSSION

This study demonstrates that poor nutritional status is common among adults with pulmonary tuberculosis in Uganda. The mean BMI in this population was 18.1 among both HIV-positive and HIV-negative men and 19.8 and 19.3 among HIV-positive and HIV-negative women, respectively. In comparison, in the era before highly active antiretroviral therapy in other populations, adults with advanced AIDS in Germany in 1993 had mean BMI of 21.4 kg/m² (12), men with AIDS in San Francisco had mean BMI of 22.6 kg/m² (16) and men with advanced HIV disease in the U.K. had mean BMI of 21.4 kg/m² (17). Mean BMI and the proportion of individuals with BMI <19 kg/m² were not significantly different between HIV-positive and HIV-negative adults who were newly diagnosed with pulmonary tuberculosis in Kampala, Uganda. These findings raise the possibility that generalized malnutrition may be a greater risk factor for developing pulmonary tuberculosis than HIV infection alone.

TABLE 3

Body composition in HIV-infected adults with pulmonary tuberculosis by $CD4^+$ lymphocyte count

	Men[2]			Women[2]		
Characteristic[1]	≤200 cells/μL	>200 cells/μL	*P*	≤200 cells/μL	>200 cells/μL	*P*
n	77	85		43	54	
Weight, *kg*	51.5 ± 6.2	53.7 ± 6.5	0.03	47.2 ± 7.9	51.8 ± 9.4	0.01
Height, *cm*	171 ± 6	170 ± 7	0.62	158 ± 6	158 ± 6	0.80
BMI, *kg/m²*	17.6 ± 1.7	18.5 ± 1.8	0.003	18.9 ± 2.7	20.7 ± 3.7	0.008
BMI <19 kg/m², %	66.7	46.5	0.018	61.1	48.8	0.22
Reactance, Ω	53.7 ± 11.8	57.7 ± 9.0	0.017	59.1 ± 11.1	64.8 ± 10.8	0.016
Resistance, Ω	694 ± 96	581 ± 66	0.09	695 ± 110	660 ± 113	0.13
TBW, *L*	32.7 ± 4.3	33.6 ± 3.7	0.16	26.5 ± 3.2	27.9 ± 4.0	0.06
ICW, *L*	19.0 ± 3.3	20.2 ± 2.6	0.007	14.0 ± 1.9	15.5 ± 2.9	0.006
ECW, *L*	13.5 ± 2.1	13.3 ± 1.6	0.36	12.4 ± 1.7	12.4 ± 1.5	0.98
ICW:ECW	1.42 ± 0.31	1.53 ± 0.21	0.008	1.13 ± 0.13	1.24 ± 0.17	0.0005
BCM, *kg*	20.8 ± 3.7	22.2 ± 2.9	0.009	15.4 ± 2.1	16.9 ± 3.2	0.009
Fat mass, *kg*	3.72 ± 2.82	4.72 ± 2.54	0.02	11.1 ± 5.5	14.8 ± 7.9	0.01
FFM, *kg*	47.8 ± 5.0	48.9 ± 4.5	0.13	36.1 ± 3.8	37.5 ± 4.8	0.11
Percent fat, %	6.9 ± 4.8	8.4 ± 3.9	0.02	22.5 ± 8.3	27.1 ± 9.6	0.01
Phase angle α, °	5.12 ± 1.15	5.70 ± 0.89	0.0005	4.87 ± 0.73	5.75 ± 1.46	0.0006
Phase angle α < 5.3°, %	63.3	38.9	0.002	70.6	39.1	0.002

[1] Values are means ± SD for continuous variables.
[2] One HIV-positive man and one HIV-positive woman did not have a $CD4^+$ lymphocyte count.

The present study was limited by not having a group of control subjects who were HIV-negative and had no pulmonary tuberculosis. However, we have previously studied a control group of 569 healthy men and women in sub-Saharan Africa using the same instrument and methods (18). Among 297 men, mean BCM (± SD), FFM and fat mass were 26.9 ± 4.3, 54.3 ± 7.2 and 10.4 ± 5.6, respectively. Among 272 women, mean BCM, FFM and fat mass were 19.7 ± 2.5, 41.7 ± 4.5 and 20.3 ± 10.5, respectively. In comparison with these healthy control subjects from sub-Saharan Africa, the men and women with pulmonary tuberculosis in the present study had lower mean BCM, FFM and fat mass.

In the present study, results were reported separately for men and women, as there are large differences in BMI, BCM, fat mass and FFM by sex (18). The results of the present study do not corroborate the findings of a previous study from Burundi, in which BMI was significantly lower in 22 HIV-positive than in 11 HIV-negative adults with pulmonary tuberculosis, but there were disproportionate numbers of men and women in each group (7). The present study compared HIV-positive and HIV-negative adults who all presented with pulmonary tuberculosis. A study from Brazil showed that BCM was significantly lower among 12 HIV-positive men with tuberculosis than among 11 HIV-positive men without tuberculosis (19).

The present study shows that among adults with pulmonary tuberculosis, the main alterations in body composition associated with concurrent HIV infection are lower ICW:ECW ratio and lower phase angle α. Among HIV-positive adults with pulmonary tuberculosis, lower BMI, lower ICW:ECW, lower phase angle α and loss of BCM and fat mass were associated with more advanced HIV infection, i.e., $CD4^+$ lymphocyte count <200 cells/μL. Depletion of BCM has been associated with an increased risk of death among adults with HIV infection (20). Body composition as reflected by a low phase angle α has been shown to be an important determinant of survival during HIV infection (10,11). The phase angle α represents that distribution of water between intracellular and extracellular spaces (11). It is still unclear why this derived indicator from BIA is such a strong predictor of survival during HIV infection. During semistarvation, the ECW does not change much (21); thus, phase angle appears to be superior to reactance or ICW alone. In healthy adults, the phase angle at 50 kHz is usually in the range of 8–15° (22). Among HIV-infected adults on triple antiretroviral therapy, the phase angle was 6.2° (23), compared with the phase angle of ~4.8–5.8° described in the present study.

Wasting is a cardinal sign of tuberculosis in both HIV-positive and HIV-negative patients, and the etiology of the wasting is unclear. Pulmonary tuberculosis appears to worsen wasting when compared with HIV infection alone in sub-Saharan Africa (18). Although the cause of wasting is likely to be multifactorial, the overexpression of tumor necrosis factor-α (TNF-α) may be involved. During tuberculosis, antigen-specific major histocompatability–restricted interaction between T-lymphocytes and macrophages induces the release of T-helper type-1–like cytokines and proinflammatory cytokines such as TNF-α (4). TNF-α activates macrophage clearance of the organism and is essential for granuloma formation. Increased concentrations of TNF-α are found in the serum and pleural fluid of patients with tuberculosis (24). Higher plasma TNF-α concentrations have been reported in HIV-positive compared with HIV-negative adults with tuberculosis (25,26). The relationship between TNF-α and wasting in tuberculosis and HIV/AIDS needs elucidation.

Further investigation is needed to determine whether ICW:ECW and phase angle α are useful predictors of clinical outcome among HIV-infected adults with pulmonary tuberculosis. The most commonly used indicator of nutritional status during tuberculosis chemotherapy has been weight gain (4). It is unclear whether successful tuberculosis chemotherapy in HIV-infected adults is associated with improvement in BMI, BCM, ICW:ICW or phase angle α. Future studies should determine whether BIA will be useful in monitoring nutritional status during tuberculosis chemotherapy.

ACKNOWLEDGMENT

We thank the study team nurse Grace Tumesiimi; the members of the Case Western Reserve University/Makerere University collaboration staff, Jessica Milman, Michael Odi, and Duncan Smith; and the physicians and staff of the Tuberculosis Research Unit for their assistance. We thank Barbara Laughon, National Institute for Allergy and Infectious Diseases, and Ken Bridbord, Fogarty International Center, for continued encouragement and support.

LITERATURE CITED

1. Dye, C., Scheele, S., Dolin, P., Pathania, V. & Raviglione, M. C. (1999) Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. JAMA 282: 677–686.

2. Murray, C.J.L. & Lopez, A. D. (1997) Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 349: 1269–1276.

3. DeCock, K. M., Soro, B., Coulibaly, I. M & Lucas, S. B. (1992) Tuberculosis and HIV infection in sub-Saharan Africa. JAMA 268: 1581–1587.

4. Whalen, C. S. & Semba, R. D. (2001) Tuberculosis. In: Nutrition and Health in Developing Countries (Semba, R. D. & Bloem, M. W., eds,), pp. 209–235. Totowa, NJ, Humana Press.

5. Kennedy, N., Ramsay, A., Uiso, L., Gutmann, J., Ngowi, F. I. & Gillespie, S. H. (1996) Nutritional status and weight gain in patients with pulmonary tuberculosis in Tanzania. Trans. R. Soc. Trop. Med. Hyg. 90: 162–166.

6. Scalcini, M., Occenac, R., Manfreda, J. & Long, R. (1991) Pulmonary tuberculosis, human immunodeficiency virus type-1 and malnutrition. Bull. Int. Union Tuberc. Lung Dis. 66: 37–41.

7. Niyongabo, T., Henzel, D., Idi, M., Nimubona, S., Gikoro, E., Melchior, J. C., Matheron, S., Kamanfu, G., Samb, B., Messing, B., Begue, J., Aubry, P. & Larouze, B. (1999) Tuberculosis, human immunodeficiency virus infection, and malnutrition in Burundi. Nutrition 15: 289–293.

8. Whalen, C. C., Nsubuga, P., Okwera, A., Johnson, J. L., Hom, D. L., Michael, N. L., Mugerwa, R. D. & Ellner, J. J. (2000) Impact of pulmonary tuberculosis on survival of HIV-infected Ugandan adults. AIDS 14: 1219–1228.

9. Kotler, D. P., Burastero, S., Wang, J. & Pierson, R. N. Jr. (1996) Prediction of body cell mass, fat-free mass, and total body water with bioelectrical impedance analysis: effects of race, sex, and disease. Am. J. Clin. Nutr. 64(suppl):489S–497S.

10. Ott, M., Fischer, H., Polat, H., Helm, E. B., Frenz, M., Caspary, W. F. & Lembcke, B. (1995) Bioelectrical impedance analysis as a predictor of survival in patients with human immunodeficiency virus infection. J. Acquir. Immune Defic. Syndr. Hum. Retrovirol. 9: 20–25.

11. Schwenk, A., Beisenherz, A., Römer, K., Kremer, G., Salzberger, B. & Elia, M. (2000) Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment. Am. J. Clin. Nutr. 72: 496–501.

12. Süttmann, U., Ockenga, J., Selberg, O., Hoogestraat, L., Deicher, H. & Müller, M. J. (1995) Incidence and prognostic value of malnutrition and wasting in human immunodeficiency virus-infected outpatients. J. Acquir. Immune Defic. Syndr. Hum. Retrovirol. 8: 239–246.

13. Jackson, A. S., Pollack, M. L., Graves, J., & Mahar, M. T. (1988) Reliability and validity of bioelectrical impedance in determining body composition. J. Appl. Physiol. 64: 529–534.

14. Giorgi, J. V., Cheng, H. L., Margolick, J. B., Bauer, K. D., Ferbas, J., Waxdal, M., Schmid, I., Hultin, L. E., Jackson, A. L., Park, L., Taylor, J.M.G. & Multicenter AIDS Cohort Study Group. (1990) Quality control in the flow cytometric measurement of T-lymphocyte subsets: the Multicenter AIDS Cohort Study experience. Clin. Immunol. Immunopathol. 55: 173–186.

15. Andres, R., Elahi, D., Tobin, J. D., Muller, D. C. & Brant, L. (1985) Impact of age on weight goals. Ann. Intern. Med. 103: 1030–1033.

16. Mulligan, K., Tai, V. W. & Schambelan, M. (1997) Cross-sectional and longitudinal evaluation of body composition in men with HIV infection. J. Acquir. Immune Defic. Syndr. Hum. Retrovirol. 15: 43–48.

17. Paton, N. I., Elia, M., Jennings, G., Ward, L. C. & Griffin, G. E. (1998) Bioelectrical impedance analysis in human immunodeficiency virus-infected pa-

tients: comparison of single frequency with multifrequency, spectroscopy, and other novel approaches. Nutrition 14: 658–666.

18. Kotler, D. P., Thea, D. M., Heo, M., Allison, D. B., Engelson, E. S., Wang, J., Pierson, R. N., St. Louis, M. & Keusch, G. T. (1999) Relative influences of race, sex, environment, and HIV infection on body composition in adults. Am. J. Clin. Nutr. 69: 432–439.

19. Paton, N. I., Castello-Branco, L. R., Jennings, G., Ortigao de Sampaio, M. B., Elia, M., Costa, S. & Griffin, G. E. (1999) Impact of tuberculosis on the body composition of HIV-infected men in Brazil. J. Acquir. Immune Defic. Syndr. Hum. Retrovirol. 20: 265–271.

20. Kotler, D. P., Tierney, A. R., Wang, J. & Pierson, R. N. Jr. (1989) Magnitude of body-cell-mass depletion and the timing of death from wasting in AIDS. Am. J. Clin. Nutr. 50: 444–447.

21. Keys, A. (1950) The biology of human starvation. Minneapolis, MN, University of Minnesota Press.

22. Ellis, K. J. (2000) Human body composition: in vivo methods. Physiol. Rev. 80: 649–680.

23. Schwenck, A., Beisenherz, A., Kremer, G., Diehl, V., Salzberger, B. & Fätkenheuer, G. (1999) Bioelectrical impedance analysis in HIV-infected patients treated with triple antiretroviral treatment. Am. J. Clin. Nutr. 70: 867–873.

24. Barnes, P. F., Fong, S. J., Brennan, P. J., Twomey, P. E., Mazumder, A. & Modlin, R. L. (1990) Local production of tumor necrosis factor and IFN-gamma in tuberculosis pleuritis. J. Immunol. 145: 149–154.

25. Wallis, R. S., Vjecha, M., Amir-Tahmasseb, M., Okwera, A., Byekwaso, F., Nyole, S., Kabengera, S., Mugerwa, R. D. & Ellner, J. J. (1993) Influence of tuberculosis on human immunodeficiency virus (HIV-1): enhanced cytokine expression and elevated beta 2-microglobulin in HIV-1-associated tuberculosis. J. Infect. Dis. 167: 43–48.

26. Vanham. G., Edmonds, K., Qing, L., Hom, D., Toossi, Z., Jones, B., Daley, C. L., Huebner, B., Kestens, L., Gigase, P. & Ellner, J. J. (1996) Generalized immune activation in pulmonary tuberculosis: co-activation with HIV infection. Clin. Exp. Immunol. 103: 30–34.