

Total Energy Expenditure in Human Immunodeficiency Virus-Infected Men and Healthy Controls

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Total daily energy expenditure (TEE) has been reported to be slightly decreased in weight-stable acquired immune deficiency syndrome (AIDS) patients. This conclusion is based on a comparison of TEE measurements to the data reported by others. We measured TEE in nine weight-stable human immunodeficiency virus (HIV)-infected homosexual men (Centers for Disease Control [CDC]-II to -IV) without active opportunistic disease and nine age-, sex-, and height-matched healthy controls using the doubly labeled water technique for 2 weeks, and resting energy expenditure (REE) using the ventilated-hood technique. TEE in HIV-infected patients was not significantly different from that in healthy controls (221 ± 12.5 and 210 ± 9 kJ · kg lean body mass [LBM]⁻¹ · d⁻¹, respectively, NS). REE was approximately 10% higher in HIV patients than in healthy controls (134 ± 4 and 125 ± 4 kJ · kg LBM⁻¹ · d⁻¹, respectively, $P = .02$). The energy spent in relation to physical activity was not different between HIV-infected patients and the controls (66 ± 10 and 64 ± 5 kJ · kg LBM⁻¹ · d⁻¹, respectively, NS). In conclusion, REE is increased by about 10% in weight-stable HIV-infected men without active opportunistic disease. TEE and the energy spent during physical activity are not different in this group of patients versus healthy controls. This is in contrast to the previously reported decrease of TEE in weight-losing AIDS patients. Therefore, the energy requirements of stable HIV-infected patients are not decreased compared with those of healthy subjects.

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LOSS OF BODY WEIGHT is one of the striking symptoms of human immunodeficiency virus (HIV) infection. Weight loss is by definition the consequence of a negative energy balance and is due to reduced energy intake and/or increased energy requirement. Reduced intake of food has been shown to be the major factor causing weight loss in acquired immune deficiency syndrome (AIDS). Physical activity and therefore total daily energy expenditure (TEE) are decreased in weight-losing AIDS patients.¹⁻⁴ However, the data on TEE in weight-stable AIDS patients are incomplete. In a group of weight-stable patients, mean TEE was slightly lower than reported in the literature.⁵ In another study, TEE was also lower in weight-stable AIDS patients, again compared with data from the literature.⁶

The main components of TEE are resting energy expenditure (REE) and energy expenditure related to physical activity. In sedentary people, REE accounts for about 70% of TEE. Despite the suggested decrease in TEE in HIV infection, REE is consistently increased by 8% to 10% in weight-stable HIV-infected patients.⁷⁻¹⁰ Therefore, the above-mentioned uncontrolled data suggest that energy expenditure related to physical activity is decreased in HIV-infected patients. To evaluate energy expenditure in clinically stable HIV infection in more detail, we measured TEE and REE in clinically stable male

AIDS patients and in age- and height-matched control subjects. TEE was measured by the doubly labeled water technique, which does not interfere with habitual daily activity. REE was measured by the ventilated-hood technique.

SUBJECTS AND METHODS

Subjects

Twelve HIV-seropositive men were recruited from our outpatient clinic. They were classified according to the 1993 criteria of the Centers for Disease Control (CDC) as CDC-II/III ($n = 6$) and CDC-IV ($n = 6$), respectively. All subjects were free of active opportunistic disease and had stable weight (<1.5 kg change of weight in the 3 months preceding the study). The level of physical activity, defined as the type of employment and the time spent on sports, had to be unchanged for at least 2 years. Patients with known neurological, endocrine, or gastrointestinal disease or abnormal plasma concentrations of transaminases, alkaline phosphatase, bilirubin, and creatinine were excluded. For each patient, an age- and height-matched healthy male volunteer was studied as a control. The study protocol was approved by the institutional Medical Ethics Committee and Research Committee, and written informed consent was obtained from all subjects.

Protocol

After enrollment, weight was measured and the patients were instructed by an experienced dietician to record their food intake in a diary. Subsequently, TEE was measured with the doubly labeled water technique under free-living conditions at home for 14 days. Total body water (TBW) was measured by ²H dilution with an overnight equilibration interval of approximately 10 hours on day 1 and day 14. Lean body mass (LBM) was calculated as $TBW/0.73$. At the end of the study, day 15, weight was measured again and REE was measured in the postabsorptive state.

Measurement of Energy Expenditure

TEE. TEE was measured according to previously reported methods.¹¹ In summary, ²H₂O (~ 0.1 g/kg body weight) plus H₂ ¹⁸O (~ 0.2 g/kg body weight) was swallowed by the participants at 10 PM. Urine samples were collected before ingestion of the doubly labeled water and in the morning (second voiding) and evening of the first, seventh, and fourteenth day after ingestion. In the evening of day 14, after voiding, a second dose of ²H₂O (~ 0.1 g/kg body weight) was administered, and urine from the second voiding the next morning (~ 10 hours after

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ingestion of the isotope) was used to measure TBW at the end of the observation period. The levels of the isotopes ^2H and ^{18}O were measured in duplicate with isotope ratio mass spectrometry (Aqua Sira, Middlewich, Cheshire, UK). The rate of production of CO_2 was calculated from the difference between the elimination rate constants for ^2H and ^{18}O . The resulting value was multiplied by the heat equivalent of CO_2 to yield TEE. Data were corrected for changes in TBW over the observation period, assuming these changes were linear. The respiratory quotient was individually calculated from dietary intake during the observation period. A dietary history was taken in advance, and the subjects were asked to keep a food diary during the whole period. The diary was checked against the dietary history. Intake of nutrients was calculated with a computer program (VOEDING; Basis, Leiden, The Netherlands) using the Dutch Food Table (NEVO table, Voorlichtingsbureau voor de voeding, The Hague, The Netherlands, 1996). All dietary calculations were performed by the same dietitian.

REE. REE was measured by indirect calorimetry using a ventilated hood with a mass flow meter, a zirconium O_2 sensor, and an infrared-absorption CO_2 analyzer (model 2900; Sensor Medics, Anaheim, CA). Calibration of the mass flow meter and O_2 and CO_2 analyzers was verified before each measurement. O_2 consumption and CO_2 production were measured continuously for 20 minutes. Before and after the 20-minute measurement period, blood gas analysis was performed in arterialized blood samples to exclude changes in pCO_2 and HCO_3^- due to hyperventilation. To allow for adaptation to the ventilated hood, the results of the first 10 minutes were discarded.

Energy expenditure related to physical activity. Energy expenditure related to physical activity was calculated as the difference between 90% of TEE and REE. Dietary-induced thermogenesis was assumed to be 10% of TEE in healthy subjects and AIDS patients. Dietary-induced thermogenesis has been reported to be unaltered in weight-stable AIDS patients.¹²

Statistics

Data are expressed as the mean \pm SE. Physical characteristics of the study groups were compared by the unpaired Student *t* test after testing for normality. Intraindividual changes in physical characteristics during the observation period were tested by the Student *t* test for paired observations. To correct for differences in energy expenditure attributable to differences in fat-free mass (FFM), REE and TEE were compared by analysis of covariance with FFM as the covariate. Statistical significance was established at *P* less than .05. Statistical analysis was performed using the Number Cruncher Statistical System software package (NCSS, Kaysville, UT).

RESULTS

Subjects

The data for three of 12 patients in the study could not be evaluated. One patient stopped collaboration within 1 week after ingestion of the doubly labeled water because of a serious event in his private life. Another patient was excluded because of a *herpes zoster ophthalmicus* infection in the first week of the study that required hospitalization. The third patient completed the study, but ^2H and ^{18}O enrichment was detected in the urine samples taken at day 1 but not at days 7 and 14, indicating that the patient provided urine other than his own on these days. Physical characteristics of the nine HIV-infected subjects (CDC-II/II, *n* = 5; CDC-IV, *n* = 4) and nine healthy controls are listed in Table 1. Baseline characteristics were not different between the groups. The weight of the patients did not change between the start and end of the 2-week observation period (from 77.8 ± 2.2 to 77.4 ± 2.4 kg).

Table 1. Physical Characteristics of the Study Population

Characteristic	HIV Patients (<i>n</i> = 9)	Controls (<i>n</i> = 9)
Age (yr)	34.0 \pm 1.9	32.6 \pm 1.5
Height (cm)	183 \pm 2	182 \pm 1
Weight (kg)	77.4 \pm 2.1	78.1 \pm 1.6
BMI (kg \cdot m ⁻²)	23.1 \pm 0.8	23.6 \pm 0.5
FFM (%)	80 \pm 2	78 \pm 2
FFM (kg)	61.9 \pm 2.0	60.6 \pm 1.6

Abbreviation: BMI, body mass index.

Energy Expenditure

Parameters of energy metabolism were not different between subjects classified as CDC-II/III and those classified as CDC-IV, and therefore, the data of all HIV-infected subjects are combined in Table 2. REE corrected for body weight was about 10% higher in HIV-infected men compared with healthy controls (95% confidence interval [CI], +2% to +18%, *P* = .02). TEE corrected for body weight was not significantly different between the groups (95% CI for the difference between HIV-positive and healthy subjects, -7% to +25%, NS). The relative contribution of REE to TEE was not different between HIV-infected subjects and healthy controls (95% CI, -9% to +9%, NS). The energy expenditure attributed to physical activity was not different between the two groups (95% CI, -14% to +29%).

DISCUSSION

The results of this study confirm previous observations^{1,3,7-10} that REE is increased by approximately 10% in clinically stable HIV-infected patients. However, TEE was not significantly different between HIV-infected subjects and matched controls. The absolute values for TEE in HIV-infected men in this study (~ 13.7 MJ \cdot d⁻¹) are in line with the data from Macallan et al¹ in their subgroup of 12 HIV-infected patients with stable weight ($\sim 3,250$ kcal/d = 13.6 MJ \cdot d⁻¹) and are considerably higher than the values they found in rapidly weight-losing AIDS patients ($\sim 2,180$ kcal/d = 9.1 MJ \cdot d⁻¹). Reference data obtained by Macallan et al from the literature⁵ indicated slightly higher values for TEE in healthy volunteers ($\sim 3,420$ kcal \cdot d⁻¹ = 14.3 MJ \cdot d⁻¹). TEE is a function of age, body weight, and physical activity. Therefore, comparisons between TEE values from different groups should be made after correction for age and body weight and parameters of physical activity.^{13,14} The present study documents that TEE in HIV-infected patients with an unchanged pattern of physical activity

Table 2. Energy Metabolism (mean \pm SE)

Parameter	HIV Patients (<i>n</i> = 9)	Controls (<i>n</i> = 9)
Total daily energy expenditure (MJ \cdot d ⁻¹)	13.7 \pm 0.7	12.7 \pm 0.5
Resting energy expenditure MJ \cdot d ⁻¹	8.2 \pm 0.2*	7.5 \pm 0.2
% of TEE	61.3 \pm 2.7	61.1 \pm 1.3
Physical activity-related energy expenditure (MJ \cdot d ⁻¹)	4.1 \pm 0.6	3.9 \pm 0.3

**P* < .05 v healthy controls by analysis of covariance with FFM as covariate.

was not less than TEE in age- and height-matched healthy controls.

Paton et al⁶ found a mean value for TEE of about 183 kJ · kg LBM⁻¹ · d⁻¹ in HIV-infected patients, which is less than the values we found in HIV-infected patients and healthy controls (221 and 210 kJ · kg LBM⁻¹ · d⁻¹, respectively). This discrepancy can be explained by methodological and clinical differences. TEE in their study was measured with the bicarbonate-urea method, which is likely to interfere with daily activity due to continuous subcutaneous infusion and frequent urine sampling. Another difference is that the majority of their patients reported a sedentary life-style due to advanced disease. Therefore, the data reported by Paton et al. cannot merely be extrapolated to HIV-infected patients with an unaltered life-style.

REE corrected for body weight or LBM in this study was approximately 10% higher in clinically stable HIV-infected subjects than in healthy controls, in line with previous data obtained in both CDC-II/III and CDC-IV HIV-infected patients.^{1,3,7-10} Therefore, the increase in REE observed in the present study is in good agreement with the consistently reported 8% to 10% increase in all stages of HIV infection in the absence of active opportunistic disease.

The interindividual variation of TEE is much larger than that

of REE, mainly due to variation in physical activity.¹³ Intraindividual variation in TEE, reflected by the difference between TEE in week 1 and week 2, was 3% ± 4% in this study. The analytical precision of the isotope ratio measurements is 0.2 ppm for ²H and 0.4 ppm for ¹⁸O.¹⁵ Therefore, intraindividual and interassay/intraassay variation did not substantially contribute to the variation in TEE results.

We cannot exclude the possibility that TEE is slightly higher in HIV-infected patients. However, due to the variability in TEE between subjects, we were not able to document such a small difference in the present study. Nonetheless, this does not invalidate our conclusion that TEE is not decreased in clinically stable HIV-infected patients.

The difference between TEE and REE was not different between HIV-infected patients and controls. Our data therefore indicate that a more or less similar amount of energy was spent for physical activity in both groups. Because only patients with an unaltered life-style were included in the study, our conclusions cannot be extended to patients with a sedentary life-style due to advanced disease.

In conclusion, TEE in clinically stable HIV-infected men is not significantly different from TEE in healthy subjects. Therefore, energy requirements are not affected by HIV infection in the absence of concomitant opportunistic disease.

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