Energy expenditure in HIV infection

Lisa Kosmiski

ABSTRACT

Energy intake recommendations for adults should be based preferably on direct measurements of total daily energy expenditure (TDEE) in corresponding populations who are maintaining healthy body weight and satisfactory physical activity levels. During adolescence, pregnancy, and lactation, energy requirements should be based on TDEE plus the additional energy required to advance these physiologic states. With illness, energy expenditure and energy intake change, but nutritional intervention is not necessarily beneficial. This article reviews data on energy expenditure in HIV infection with a focus on adults, adolescents aged ≥14 y, and pregnant and lactating women. Resting energy expenditure (REE) in adults with untreated asymptomatic HIV is ~10% higher than in healthy control subjects. In asymptomatic adults receiving antiretroviral therapy, REE may be similarly increased. HIV wasting and secondary infections are also associated with increased REE. In contrast, TDEE is typically normal in asymptomatic HIV and decreased in HIV wasting and secondary infection. No direct measurements of REE or TDEE are available in adolescents or in pregnant or lactating women with HIV. On the basis of current data, energy intake may need to increase by ~10% in adults with asymptomatic HIV to maintain body weight. In adolescents and in pregnant and lactating women with asymptomatic HIV, energy requirements should approximate recommendations for their uninfected counterparts until further data are available. In the resource-rich world, the energy expenditure changes associated with HIV are unlikely to contribute to significant weight loss. More data are needed on energy expenditure in HIV-infected populations from developing nations, where concurrent malnutrition and coinfections are common.

INTRODUCTION

The optimal energy requirements of persons who suffer from chronic disease, such as HIV infection, are poorly understood. Relatively few studies have directly measured TDEE in chronic disease, despite the fact that energy requirements must match TDEE when weight maintenance is the goal. In addition, various factors are likely to influence energy requirements in disease, including the nature, severity, and phase of the disease; concurrent malnutrition; available treatments; and the level of associated inactivity. Furthermore, the illness is often accompanied by significant anorexia, which may be adaptive in some circumstances but not in others. Finally, nutritional support is not necessarily beneficial and may even be harmful (1) during certain disease processes.

The calculation of energy requirements for adolescents and pregnant and lactating women with disease is even more complex. During these periods EI must exceed TDEE for optimal outcomes. In adolescents extra energy is required to support growth (2). Normal-weight pregnant and lactating women also require energy in excess of TDEE to sustain optimal fetal growth and milk production, respectively (3, 4).

There are 3 components to TDEE: REE, diet-induced thermogenesis, and physical activity energy expenditure (5). REE accounts for 60–70% of TDEE and is the energy expended at rest to maintain normal bodily functions. REE is largely determined by the amount of lean body mass (5, 6). Diet-induced thermogenesis is the energy required to digest and assimilate food and accounts for 5–10% of TDEE. Physical activity energy expenditure is quite variable but typically accounts for 20–30% of TDEE. Importantly, REE may be increased in disease without a concomitant increase in TDEE because physical activity levels often decrease dramatically during illness.

HIV infection is a chronic disease, but its course is often punctuated by more acute processes, such as opportunistic infection or malignancy (7). Its prevalence is high in populations that also suffer from chronic malnutrition. Also, many individuals are not treated with antiretroviral therapy at the time the infection is discovered. Instead, initiation of treatment often depends on viral load and immune function (8). In the current era of antiretroviral therapy, a substantial number of HIV-infected individuals will develop the HIV lipodystrophy syndrome (9), which may also alter energy expenditure. Finally, many patients with HIV are coinfected with other pathogens, such as hepatitis B and C, as well as malaria and tuberculosis, which have their own effects on energy balance (10–12).

To our knowledge, only 5 studies have directly measured TDEE in HIV-infected subjects. In other studies TDEE must be inferred from estimates of daily EI in the study population. If caloric intake is increased in a weight-stable population, then it can be cautiously inferred that TDEE is also increased. However, numerous studies have measured REE in HIV infection and have...
done so under a variety of clinical circumstances. Together, these studies, along with others on nutritional interventions in HIV infection, can form the basis for EI recommendations in some HIV-infected populations under certain clinical circumstances.

In the following pages I have attempted as nearly as possible to present the data on energy expenditure in HIV infection by the distinct clinical categories recognized today. If an HIV-infected group in a particular study included individuals with important clinical differences, an attempt has been made to point this out.

ENERGY EXPENDITURE IN ASYMPTOMATIC HIV/AIDS UNTREATED WITH COMBINATION ANTIRETROVIRAL THERAPY

Over the years, very few studies have measured energy expenditure in what would now be defined as asymptomatic HIV infection. In one of the earliest studies REE was increased by 8% in 11 asymptomatic HIV-infected subjects with a mean CD4 count of 600 cells/μL compared with healthy control subjects (13). In another study REE was increased by 7–8% in 57 HIV-infected patients with a CD4 count >200 cells/μL, also compared with healthy control subjects (14). Finally, in 20 HIV-infected patients naive to combination antiretroviral therapy, REE was ~15% higher than in healthy control subjects (15).

Many more studies have measured energy expenditure in subjects who meet the current criteria for asymptomatic AIDS. In a 1992 study, when AIDS was defined by a history of opportunistic infection or malignancy, but not by CD4 count, REE was shown to be ~25% higher in AIDS patients compared with healthy control subjects (16). However, in the same study REE was increased by only 11% in “HIV+” subjects with a mean CD4 count of 184 cells/μL. In another study done in the same time period with the same definition of AIDS, REE was 9% higher in subjects with AIDS compared with healthy control subjects, but the AIDS group included individuals with and without significant weight loss (17). In a 1996 study REE was 9% greater in 23 subjects with AIDS and a CD4 count of 100–200 cells/μL, but REE in the 24 subjects with a CD4 count <100 cells/μL was not significantly different from that of healthy control subjects (14). Finally, in one other study REE was ~25% higher in 17 AIDS patients compared with healthy control subjects (15).

Two recent but small studies have shown REE to be 14% and 20% higher in men with untreated HIV infection/AIDS compared with healthy control subjects (18, 19). In both, the mean CD4 count of the HIV-infected group was <200 cells/μL, an AIDS-defining category, but subjects with significantly higher CD4 counts were also included.

Four studies have directly measured TDEE in asymptomatic HIV or AIDS untreated with combination antiretroviral therapy. In each, TDEE was either similar to that of healthy control subjects (20–22) or similar to predicted values (23). In another study TDEE was not measured directly, but reported caloric intake was ~15% greater in the HIV-infected population compared with healthy control subjects (14). These caloric intake data came from subjects with both HIV and AIDS. More recently, a small study showed caloric intake to be ~50% greater in treatment-naive men with a mean CD4 cell count of 153 cells/μL (range: 68–578), compared with healthy control subjects (18).

In summary it appears safe to conclude that REE is increased by ~10% in asymptomatic HIV/AIDS untreated with combination antiretroviral therapy. In contrast, directly measured TDEE has been consistently normal in this clinical setting. However, caloric intake data in a few studies suggest that TDEE may also be increased in some patients. Importantly, these energy expenditure studies were done in resource-rich nations, where it appears that most individuals with HIV/AIDS who are naive to combination antiretroviral therapy can maintain body weight through the reduction of physical activity or by an increase in EI. These adaptations, however, may not be possible for individuals who live in resource-poor settings. Therefore, it seems prudent to recommend a caloric intake increase by ≥10% in normal-weight individuals with untreated HIV/AIDS, especially those in resource-poor settings. In those with chronic malnutrition, caloric needs will of course be greater, depending on the degree of malnutrition and other factors such as demands for physical activity.

ENERGY EXPENDITURE IN ASYMPTOMATIC HIV-INFECTED ADULTS RECEIVING COMBINATION ANTIRETROVIRAL THERAPY

In HIV-infected individuals receiving combination therapy the data with regard to energy expenditure are less consistent, and fewer studies have been done. In a large cohort, antiretroviral therapy was shown to have an independent effect on REE: adjusted REE was 339 kJ/d higher in those who reported use of highly active antiretroviral therapy, compared with nonusers (24). In another large cohort study also done in this era of therapy, REE was increased by ~5% in 91 HIV-infected adults without lipodystrophy, compared with healthy control subjects (25). In the same study caloric intake was similar to that of control subjects, and significantly less physical activity was reported by the HIV-infected subjects. Finally, a small study that included 13 HIV-infected subjects on combination antiretroviral therapy showed REE to be ~25% higher than that in healthy control subjects (19).

In other studies, however, REE in patients on combination antiretroviral therapy has been shown to be similar to that in healthy control subjects (26, 27). In these studies the HIV-infected subjects had complete viral suppression, which may account for the normal REE findings, because REE has been shown to correlate with viral load in HIV-infected subjects (28). Also, in a study of both HIV-infected and AIDS subjects starting therapy, REE normalized as viral load declined with treatment (15). Only one study has measured TDEE in HIV-infected subjects on antiretroviral therapy (27). TDEE was measured with the use of whole-room calorimetry and was shown to be similar to that in healthy control subjects.

Normal-weight HIV-infected individuals on combination antiretroviral therapy may therefore have more variable caloric needs. Some may require no energy supplementation, whereas others may require a ≥10% increase to maintain body weight and their usual pattern of physical activity.

ENERGY EXPENDITURE IN HIV WASTING

In general, HIV wasting has been defined as the loss of 10% of body weight in the absence of another illness or condition that can
explain the weight loss (29). Adhering strictly to this definition, there have been few measurements of energy expenditure in this setting. One study showed REE to be elevated by ~12% in HIV-infected subjects with “progressive wasting,” compared with healthy control subjects (30). However, the HIV-infected group included subjects with opportunistic infections and malignancies. In another early investigation, REE was measured in 165 “malnourished” AIDS patients with and without an “evolving secondary infection” (31). REE was 11% greater in those without symptoms of secondary infection, compared with healthy control subjects. In another study, which excluded those with opportunistic infection, HIV-infected women with “early and late wasting” were compared with healthy control subjects (32). REE was not significantly elevated in the subjects with wasting, but there was a trend for REE to increase with the severity of wasting when expressed as energy expended per kilogram of body weight.

TDEE has been measured in HIV-infected subjects with weight loss, but patients with malignancy or secondary/opportunistic infections were included, along with subjects who more nearly fit the definition of HIV wasting. For example, TDEE was measured by doubly labeled water in HIV-infected men with and without weight loss (>3 kg/mo), and comparisons were made with HIV-infected men with stable weight and with healthy historical control subjects (23). The subjects with significant weight loss included 4 individuals with secondary infection and 3 with probable HIV wasting. REE was not elevated in the subjects with weight loss, and TDEE was significantly decreased by ~30% compared with the weight-stable subjects. Furthermore, physical activity energy expenditure was reduced by ~60% and caloric intake by ~50% in the men with weight loss. Clearly, the weight loss in these subjects was not due to an increase in TDEE but instead was due to a marked reduction in caloric intake. Reduced physical activity likely limited the weight loss experienced by these patients.

In summary, REE appears to be increased in HIV wasting, but TDEE is significantly decreased because of reductions in physical activity. Weight loss is instead due to marked reductions in caloric intake. In HIV wasting there is a direct relation between weight loss and death (33). However, it has not been shown that wasting itself is the direct cause of death. In addition, nutritional intervention has not been shown to improve mortality. However, there are some data that suggest that body weight and lean body mass increase with nutritional support. In 2 studies done before the era of combination antiretroviral therapy, malnourished AIDS patients with and without secondary infection were given high-energy, high-protein liquid supplements for 12 and 6 wk, respectively (34, 35). In post hoc analysis, subjects with secondary infection did not have a significant increase in body weight or lean body mass with nutritional therapy.

As in HIV wasting, emphasis should clearly be placed on treatment of the underlying infection. In the absence of such treatment, nutritional support will not benefit the patient. Most individuals should have “catch-up” weight gain driven by their own ad libitum EI if nutritional resources are available as the secondary infection is treated.

ENERGY EXPENDITURE IN HIV WITH SECONDARY INFECTION

There are few data on energy expenditure in HIV-infected individuals with secondary infection. To our knowledge REE has been measured in only 2 studies and was 29% and 34% greater in the HIV-infected subjects with secondary infection compared with healthy control subjects (16, 31). In both studies the subjects with secondary infection were losing weight. Caloric intake was measured in one of these studies and was decreased by 36% (16). Data from a different study, which included only a few individuals with secondary infection, showed TDEE to be significantly decreased in this setting (23). It is likely that decreased EI, not changes in energy expenditure, plays the major role in the weight loss experienced by those with HIV and secondary infection.

In resource-rich settings mortality from secondary infections appears to be related to the severity of the infection and not to the malnutrition that accompanies it. At this time there is no evidence that nutritional support beyond the individual’s ad libitum EI is beneficial in HIV-infected individuals with secondary infection. First, no studies have specifically set out to determine the benefits of nutritional intervention in this setting. In separate studies done before the era of combination antiretroviral therapy (mentioned above), malnourished AIDS patients with and without secondary infection were given total parenteral nutrition or high-energy, high-protein liquid supplements for 12 and 6 wk, respectively (34, 35). In post hoc analysis, subjects with secondary infection did not have a significant increase in body weight or lean body mass with nutritional therapy.

ENERGY EXPENDITURE IN HIV LIPODYSTROPHY

HIV lipodystrophy is characterized by the loss of subcutaneous adipose tissue in the face, extremities, and buttocks (9). Similar to other lipodystrophy syndromes, HIV lipodystrophy is associated with insulin resistance, hypertriglyceridemia, and excess fat in the liver and skeletal muscle, which likely play an important role in these metabolic disturbances.

HIV lipodystrophy may also be associated with increased REE. In some, but not all, studies, REE and sleeping metabolic rate have been shown to be significantly higher in subjects with HIV lipodystrophy, compared with both HIV-infected and healthy control subjects (26, 27). In one study REE in the lipodystrophy subjects was ~15% and 20% greater than that of HIV-infected and healthy control subjects, respectively (26). Importantly, all HIV-infected subjects had complete viral suppression. In a different study REE was measured in 2 groups of HIV-infected patients: 30 with HIV lipodystrophy and 13 without lipodystrophy (36). Both groups were on combination antiretroviral therapy, but REE was 10% higher in those with lipodystrophy. In a large cohort study HIV lipodystrophy subjects tended to have higher REE compared with HIV-infected control subjects ($P = 0.07$) (25). However, a meta-analysis has shown REE to be similar in HIV-infected subjects with and without lipodystrophy (37).
Only one study has measured TDEE in HIV lipodystrophy directly (27). With the use of whole-room calorimetry, TDEE was increased by 12% in lipodystrophy patients compared with HIV-infected control subjects and by 19% compared with healthy control subjects. In another study caloric intake was significantly higher in lipodystrophy subjects compared with HIV-infected control subjects (2289 compared with 1861 kcal/d), which suggests that TDEE was increased in the weight-stable subjects with HIV lipodystrophy (36).

Despite evidence that HIV lipodystrophy is associated with both increased REE and TDEE, it is far from clear what energy requirements should be made for affected individuals. Because storage capacity for lipid fuel is markedly decreased in lipodystrophy, increased caloric intake may lead to further triglyceride accumulation in nonadipose tissues and therefore to greater insulin resistance and hypertriglyceridemia. Some individuals with lipodystrophy may actually benefit from a decrease in caloric intake (38), but studies are needed to understand the link between energy and macronutrient intake and metabolic disturbances in HIV lipodystrophy.

ENERGY EXPENDITURE IN HIV-INFECTED ADOLESCENTS

Adolescence is an anabolic state. Therefore, energy requirements are based on TDEE plus the energy needs for continued growth (2). In general, the energy requirements of boys will be greater than girls of a given body weight because boys have a greater lean body mass (39). Energy requirements for growth can be calculated from anticipated weight gain, which, in turn, is estimated from height and weight tables of the corresponding healthy population.

To our knowledge there have been no studies on energy expenditure in adolescents aged ≥14 y with HIV infection. However, in 2005, Torun (2) published new recommendations for EI in healthy children and adolescents based on an analysis of data pooled from numerous studies that measured TDEE by doubly labeled water or heart rate monitoring in subjects from both resource-rich and resource-poor nations. He observed that quadratic polynomial equations based on body weight and sex best predict TDEE. Caloric requirements can then be calculated with the use of population references of weight for age and by adding 2 kcal to the TDEE prediction for each gram of expected weight gain during growth. Compared with the 1985 FAO/WHO/United Nations University values, Torun’s work suggests that energy requirements are ~12% higher than formerly predicted for both boys and girls aged ≥12 y (2, 40). Finally, Torun recommends that energy requirements be adjusted by ±15% in populations with more or less physical activity than an average lifestyle.

Because energy expenditure has not been measured, even in “healthy” adolescents with HIV infection, no additional recommendations with regard to energy requirements can be made for optimal growth in this population.

ENERGY EXPENDITURE IN PREGNANT WOMEN WITH HIV INFECTION

To our knowledge there have been no studies of energy expenditure in pregnant women with HIV. However, in recent years many data have been generated on energy expenditure during pregnancy in uninfected women from both resource-poor and resource-rich nations. Several important points have emerged from this work.

First, energy requirements for pregnant women are not based on direct measures of maternal TDEE only, but on TDEE plus the cost of the ongoing tissue deposition and maintenance of that tissue as the pregnancy progresses (3). In general, TDEE increases as pregnancy advances in well-nourished women, increasing by ~15–20% in the third trimester (41, 42). The majority of this increase in TDEE is due to pregnancy-associated increases in REE. In a review of 261 women from 8 studies REE increased by ~4% in the first trimester, by 10% in the second trimester, and by 24% in the third trimester (43). In addition, recommendations with regard to EI for pregnant women should be population based because of differences in body size. In other words, the gestational weight gain that gives optimal outcomes for both the mother and baby will differ by population (44). For example, in resource-rich nations, a birth weight of 3.1–3.6 kg is associated with optimal outcomes for both the infant and the mother (45). To achieve this birth weight, women with healthy baseline body weight typically need to gain 10–14 kg over the course of their pregnancy. In general, this entails a 90 kcal increase/d in caloric intake in the first trimester, a 300 kcal increase/d in the second trimester, and a 450 kcal increase/d in the third trimester. In resource-poor nations maternal height and weight are often significantly lower than those in the resource-rich world and optimal gestational weight gain is different.

Finally, pregnancy is a time of great metabolic flexibility (46), which allows women to bear children under a wide range of nutritional conditions. For example, in a group of women from Gambia, REE actually declined significantly by week 6 of pregnancy, returned to baseline by week 18, and only increased by 117 kcal/d at week 36 (47). In the same study, TDEE did not change significantly at any time during the pregnancy. These remarkable adaptations in maternal energy expenditure allow for maternal EI to primarily fuel the growth of the baby.

It is unknown how HIV infection affects the energy requirements of pregnancy. Based on studies of asymptomatic adults with HIV infection, it is unlikely that HIV-associated changes in energy expenditure would significantly affect gestational weight gain in most women in resource-rich settings. However, studies are needed in resource-poor settings where concurrent malnutrition is common.

ENERGY EXPENDITURE IN LACTATING WOMEN WITH HIV

Again, no direct measurements of energy expenditure have been done in lactating women with HIV infection. However, there has been a good deal of work done in this area in uninfected women. Lactation is primarily a process of energy transfer, and energy requirements are not based on direct measures of TDEE during lactation but on TDEE plus the energy content of milk (4). It is assumed that ~20% of the added energy cost of lactation is due to milk synthesis and that this should be measured as part of maternal REE. However, the majority of studies have shown that both REE and TDEE are unchanged in lactation (4, 45). It is possible, therefore, that the energy cost of milk synthesis is...
compensated for by a decrease in energy expenditure in other maternal organs and/or tissues.

In resource-rich settings the energy cost of lactation is generally estimated to be ~500 kcal/d, and a 500-kcal increase in EI is generally recommended for normal-weight women who plan to breastfeed exclusively (45). This figure is based on studies of milk production and its energy content at 3 and 6 mo post-partum. A majority of women increase their caloric intake to support lactation, but well-nourished women can also mobilize energy from fat stores to support the cost of lactation.

As in pregnancy, it is unknown how HIV infection affects the energy requirements of lactation. In resource-rich settings, asymptomatic HIV infection is unlikely to significantly affect the energy requirements of lactation.

SUMMARY

In summary, alterations in REE are common in HIV infection. In asymptomatic HIV/AIDS untreated with antiretroviral therapy, REE is increased by ~10%. However, directly measured TDEE has been normal in this setting. Most individuals, therefore, maintain body weight through a reduction in physical activity and/or an increase in caloric intake. REE appears to be more variable in HIV-infected patients on combination antiretroviral therapy; only one study has measured TDEE in this setting, and it showed TDEE to be normal.

In HIV wasting, REE is significantly increased, but weight loss is driven by reductions in caloric intake because TDEE is decreased in this setting due to reductions in physical activity. Also, there is no evidence that nutritional support in the absence of effective antiretroviral therapy improves mortality. Secondary infection in HIV is associated with marked elevations in REE, but TDEE appears to be decreased. Weight loss in this setting also appears to be mainly due to reductions in caloric intake, and there is no evidence that nutritional support increases body weight or lean body mass. Finally, HIV lipodystrophy may be associated with increases in both REE and TDEE, but additional EI cannot be recommended at this time.

Unfortunately, energy expenditure has not been measured in HIV-infected adolescents or in HIV-infected pregnant and lactating women. In general, these are states that require energy in excess of TDEE for optimal outcomes. Therefore, in resource-poor settings, where concurrent malnutrition is common, energy expenditure studies could be especially helpful in shaping EI recommendations for these populations.

The author declared no conflicts of interest.

REFERENCES


