



HIV Patients and Weight Loss:

Optimizing Care to Improve Outcomes

Faculty



Robert Demling, MD



Donald Kotler, MD



Christine Wanke, MD

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Program Description

HIV-associated wasting was first identified by the Centers for Disease Control and Prevention as an AIDS-defining condition in 1987. With the advent of highly active antiretroviral therapy, it was hoped that control of viral count would result in the elimination of wasting as a major sequela of HIV infection. This has turned out not to be the case. HIV wasting remains a serious, debilitating, and sometimes life-threatening condition. Care providers need to be vigilant to identify and properly treat patients who suffer from this disorder.

This monograph reviews the pathogenesis of protein energy malnutrition in general and its relation to the etiology of HIV-related weight loss. Also included are the epidemiology of HIV-associated wasting and the treatment options available.

Author

Duke Duguay, PhD, Assistant Medical Director at ArcMesa Educators.

Faculty Advisors

Dr. Robert Demling, Professor of Surgery at Harvard Medical School and Director of the Burn-Trauma Center at Brigham and Women's Hospital.

Dr. Christine Wanke, Professor of Medicine and Public Health and Director of the Division of Nutrition and Infection at Tufts University School of Medicine.

Dr. Donald Kotler, Professor of Medicine at Columbia University College of Physicians and Surgeons and Chief of the Division of Gastroenterology and Liver Disease at St. Luke's Roosevelt Hospital Center.

Faculty Disclosure Declarations

Robert Demling, MD
Nothing to Disclose

Donald Kotler, MD
Grants/Research Support recipient, Speakers' Bureau,
Consultant – EMD Serono Laboratories

Christine Wanke, MD
Nothing to Disclose

Author

Duke Duguay, PhD
Nothing to Disclose

Staff Disclosure Declarations

The staff of ArcMesa Educators have nothing to disclose relative to this activity.

Program Overview

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Educational Objectives

Upon completion of this activity, participants should be able to:

- List physiologic factors affecting energy intake and metabolic abnormalities that may lead to weight loss in HIV-positive patients

- Discuss the need for pharmacologic and nonpharmacologic approaches to improve weight in HIV-positive patients
- Examine the impact of HIV-related weight loss on patient outcomes
- Develop management strategies to address weight loss in HIV-positive patients

Target Audience

This activity is intended for physicians, pharmacists, and nursing professionals involved with the care of patients with HIV.

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HIV PATIENTS AND WEIGHT LOSS: Optimizing Care to Improve Outcomes

Human immunodeficiency virus (HIV)-associated wasting was first recognized by the Centers for Disease Control and Prevention as an acquired immunodeficiency syndrome (AIDS)-defining condition in 1987. With the introduction of highly active antiretroviral therapy (HAART), it was hoped that control of viral replication would result in the elimination of wasting as a major sequela of HIV infection. Unfortunately, HIV wasting remains a serious, debilitating, and sometimes life-threatening condition. Care providers need to be vigilant about identifying and properly treating their patients who suffer from this disorder. The pathogenesis of protein energy malnutrition is an important aspect of the etiology of HIV-related weight loss or wasting. The epidemiology of HIV-associated wasting and the treatments available for this condition are reviewed in this continuing medical education monograph.

Background

Body composition can be divided into 2 main components: lean body mass and fat body mass. Typically, lean body mass makes up about 75% of body weight and consists of about 70% water and contains all of the protein in the body.¹ Lean body mass is metabolically active and is essential for survival. All the muscle and visceral structures are included in the lean body mass component. The other component is fat mass, which is composed of adipose tissue and usually makes up about 25% of total body weight. Fat is a pure energy store. Adipose tissue is much less metabolically active than muscle. Fat mass increases when the intake of caloric energy exceeds caloric expenditure and decreases when caloric intake is lower than caloric expenditure.

During the digestive process, food is broken down into its constituent macronutrients (proteins, carbohydrates, and fats). The majority of ingested protein is used for protein synthesis, with very little being used for fuel. Carbohydrates and fats are used for energy. Any additional energy is stored in the fat depot. The size of the protein compartment is dependent on the balance between anabolism and catabolism. Under most circumstances, energy intake is adequate and the size of the protein compartment is stable. With starvation, in the absence of other stresses, the small amount of carbohydrate stored as glycogen is rapidly depleted and the body utilizes energy

from the fat and protein stores.² Lipids from the fat compartment normally represent the main source of energy. Fat has a much higher energy density than proteins or carbohydrates and can be almost completely depleted to cover energy requirements. Proteins, by contrast, can be only partially depleted because of their required structural, mechanical, and enzymatic functions. For these reasons, lean mass is preferentially preserved to prevent the breakdown of protein for fuel.

Pathogenesis of Protein Energy Malnutrition in HIV/AIDS

The Centers for Disease Control and Prevention defined HIV wasting as an involuntary weight loss of 10% or more from baseline plus either chronic diarrhea, or chronic weakness and fever.³ In patients severely ill with advanced HIV infection, weight loss is generally due to protein energy malnutrition, which is a pathological state that results in a depletion of lean body mass. This may or may not be associated with a significant loss of body fat or total body weight. Protein energy malnutrition is the most common nutritional deficiency seen in hospitalized patients in the United States.⁴ The loss of lean body mass associated with this disorder may be due to inadequate intake of dietary protein and energy, or to metabolic problems leading to excess protein catabolism. It is important to stress that this loss of lean body mass may occur in the absence of weight loss.

Pathology of Protein Energy Metabolism

Chronic infections such as HIV stimulate an immune response that increases the demand for metabolically derived energy and substrates, leading to a catabolic disease state.⁵ The resulting loss of lean body mass can lead to increased disability, decreased activity, discomfort with moving, and decreased appetite. These factors, especially the decrease in appetite, promote disease progression. Significant loss of lean body mass also causes immune deficiency and may increase susceptibility to infection. As an illustration, bacterial pneumonia is one of the leading causes of death for people with severe protein energy malnutrition from any cause.⁶ In addition, patients may develop spontaneous and chronic wounds that are unable to heal. The epidermis becomes very thin and breaks down rela-

tively easily (Figure 1). Tissue damage may result from minimal trauma, such as the movement of a finger across the skin. Superficial Stage I and II pressure ulcers, and also deeper Stage III and IV pressure ulcers, are common among patients with severe protein energy malnutrition.

Metabolic Effects of the Stress Response

Any bodily threat, whether psychological or physiological, can trigger a stress response leading to hypermetabolism, catabolism, and in the extreme, immune deficiency. In this process, the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system play essential roles in an effort to maintain homeostasis.⁷ There is a profound increase in the serum concentrations of catecholamines. Hypermetabolism, or an abnormal increase in the metabolic rate, often follows. A simultaneous increase in cortisol and decrease in circulating anabolic hormones leads to a catabolic state where body tissue, including protein, is metabolized. In protein energy malnutrition, there is an increased utilization of protein for energy. Up to 20% to 25% of the body's energy production may be derived from protein. This leads to a decrease in the size of the protein compartment, but not necessarily a decrease in total body weight.²

Diagnosis of Protein Energy Malnutrition

Some patients may present with signs of protein energy malnutrition. A subjective global assessment is a valuable clinical technique for assessing a patient's nutritional status based on aspects of the patient's history and physical examinations.⁸ This assessment includes a discussion of the patient's nutritional intake and daily activities. The physical examination should include a search for hair loss, decreased skin turgor, and muscle wasting. Functional



Figure 1. Pressure Ulcers. (This is a clinical example of some of the symptoms of protein energy malnutrition. Notice the thinning of the skin caused by the removal of most of the collagen from the dermis.)

abnormalities should be noted at each visit to ascertain if the patient is losing muscle mass or function over time. It is important to measure changes in body composition using anthropometric measurements, such as weight history, body mass index (BMI), skinfold thickness, and physical circumferences or girth. BMI is the most commonly used anthropometric measurement. It is calculated by dividing the patient's body weight in kilograms by the square of the patient's height in meters. BMI represents a general assessment of a patient's body composition relative to the overall population. Alternative techniques may provide a more quantitative measurement of lean body mass. These include bioelectrical impedance analysis, dual energy x-ray absorptiometry, computed tomography and magnetic resonance imaging, and hydrodensitometry.^{9,10} However, these tests may be difficult to interpret and are expensive. Currently, third-party payers are not likely to cover these imaging techniques.

In some cases, it may be hard to make a relative determination of the change in lean body mass for a particular patient. At an initial visit, a prior reading is not available for comparison, so clinicians must interpret the absolute number obtained from a quantitative measure of body weight and composition. Serum prealbumin concentration can be used as a reliable and specific biochemical indicator of protein energy malnutrition.¹¹ The biological half-life of prealbumin is 2 to 3 days. Therefore, the serum prealbumin concentration is valuable because it represents the patient's physiological status over the previous several days. Prealbumin concentrations can be used to classify a patient as being within the normal range, having mild to moderate malnutrition, or having severe malnutrition.

Epidemiology of HIV-Related Weight Loss in the HAART Era

The hope of HIV care providers was that patients treated with HAART would not experience HIV wasting/weight loss. However, recent analyses suggest that weight loss remains a frequent problem in the HAART era.¹² The Nutrition for Healthy Living Cohort includes approximately 450 HIV-infected adults who have been followed every 6 months for changes in nutritional and metabolic parameters. In one study, wasting was defined as a loss of 10% of body weight over the course of the study, a >5% loss of body weight over 6 months, or a BMI <20 kg/m². Among this group of patients, 48% were receiving HAART when they met one of the definitions of wasting. Moreover, 31% of the individuals who were on

stable HAART subsequently met at least one definition of wasting. The fact that these patients developed a wasting condition while on HAART may be indicative of failure of HAART or the development of viral resistance, but their physicians had not yet changed their HAART regimen in response. Surprisingly, 26% of those who had early disease (ie, they had not progressed to the point of requiring HAART) also met one definition of HIV-associated wasting. This suggests that people with early disease, people newly initiating successful HAART, and those individuals with disease progression while on HAART may all suffer from HIV-related weight loss.

Pathogenesis of HIV-Related Weight Loss in the HAART Era

Surprising results from a retrospective analysis of HIV-infected patients on HAART revealed that individuals who were not trying to lose weight were significantly more likely to lose 5% of their body weight over 6 months ($P = .002$) in the more recent-HAART era (1998-2003) than in the early-HAART era (1995-1997).¹³ While the causes of the more frequent weight loss were not determined, these patients often began at a much higher BMI and may have been able to maintain a reasonable BMI even after some weight loss. These data emphasize the fact that there may be ongoing nutritional problems in HIV-infected patients who are appropriately treated with HAART. This result is of continuing concern because even a 5% loss of weight over 6 months was shown to significantly increase the risk of death in a study performed in the pre-HAART era.¹³ A study of HIV patients who died from wasting early in the epidemic evaluated body cell mass, a body compartment closely related to lean body mass.¹⁴ In these patients, wasting was

progressive until death (Figure 2). The body weight at death was about one third below ideal body weight, a result similar to what has been seen in classic starvation studies.¹⁴ Body cell mass at the time of death was 50% to 55% of normal in this study.

In a study by Tang et al, simple weight loss as measured by loss of body weight alone, loss of lean body mass, or loss of fat mass were all able to predict an increased risk of death over the course of HIV infection.¹⁵ Probably because HIV-infected individuals are losing both fat and lean body mass, simple weight loss was found to be the strongest predictor of death. Those individuals who had lost more than 10% of their body weight had a nearly 6-fold increased risk of death over the course of their HIV infection. Those individuals who had a 5% to 10% loss of body weight had a 4-fold increased risk of death during the course of their HIV infection. This translates to a 1% loss of body weight being associated with an 11% increase in the risk of death. Thus, the impact of weight loss on HIV survival, even in the era of well-controlled viral replication with HAART, is still significant.

Weight loss or the loss of lean body mass negatively affects the quality of life (QOL). In a study published by Wilson et al, there was a significant linear association between increasing lean body mass and increasing QOL in male patients infected with HIV.¹⁶ A higher amount of lean body mass was significantly associated with higher QOL, including physical functioning and general health perception, as well as significantly fewer days spent in bed during the last month. Interestingly, the same association was not observed in women. There was no significant difference in QOL in the women in this study. Women, no matter what their BMI, had a uniformly lower QOL. This

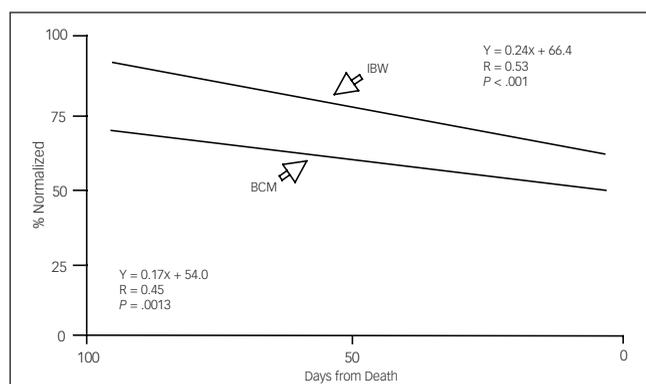


Figure 2. Comparison of the Relationships of Normalized Body Cell Mass (BCM) and Body Weight as Percent of Ideal Body Weight (IBW) at the Time of Death¹⁴

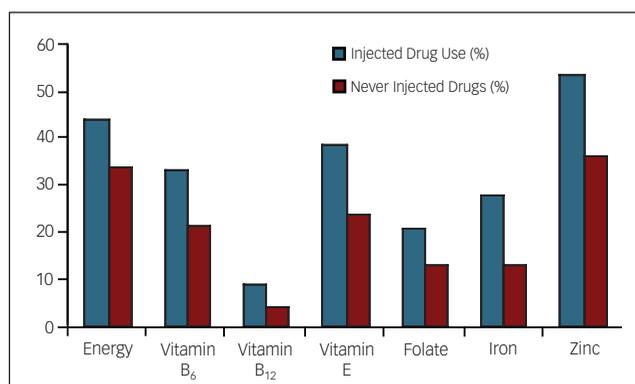


Figure 3. Percentages of HIV-infected Patients with Inadequate Dietary Intake: Significant Differences Between Injected Drug Users and Nonusers ($P < .05$ for all variables, $n = 614$)⁸

indicates that the issues of nutritional status may have different implications in men and women.

Causes of HIV-Related Weight Loss

There are 2 main categories of people who involuntarily lose weight due to HIV infection.¹⁷ The first includes those individuals who are assimilating too few calories to support their metabolic needs. This can be due to complications of HIV, which can lead to anorexia, nausea, physical problems with taking in food, oral ulcers, and dysphagia. In addition, depression and socioeconomic barriers to accessing appropriate amounts of food may be present. A variation on this theme consists of patients with malabsorption, who may consume a normal number of calories, but cannot absorb them due to a digestive disorder. The other category of patients with HIV-associated wasting includes those individuals who may be taking in sufficient amounts of energy but have an altered metabolism which promotes lean mass depletion. HIV infection, as well as both infectious and neoplastic complications, affect intermediary metabolism in a number of ways. This leads to skeletal muscle depletion and the acute phase response. When weight loss occurs despite attempts at maintaining normal caloric intake, the possible presence of opportunistic infections and malignancies should be investigated.

An analysis of data from the Nutrition for Healthy Living Cohort investigated whether weight loss in HIV-positive drug users was related to drug use or HIV infection.¹⁸ This study compared the intake of individuals who used injectable drugs with the intake of individuals who never injected drugs (Figure 3). The study found that approximately 44% of HIV-infected active drug users had inadequate energy intake compared with about 34% of those who had never used drugs ($P = .04$). In addition, the percentage of patients who had insufficient intake of iron and zinc was much higher in patients who injected drugs than in patients who did not ($P < .001$ for both elements). Similarly, patients who used injectable drugs were significantly more likely to have insufficient intake of vitamin B₆, vitamin E, and folate than patients who did not ($P < .05$ for each vitamin). Both groups had adequate intake of vitamin B₁₂. The use of injectable drugs is one factor affecting dietary intake in patients with HIV disease. This may be due to socioeconomic reasons.

Increased awareness has led to an increased rate of detection of hormonal deficiencies that may contribute to the loss of weight or loss of lean body mass in patients

TABLE 1

	<200 cells/ μ L (n = 30)	200-499 cells/ μ L (n = 63)	\geq 500 cells/ μ L (n = 37)
Weight, kg	62.8	69.3*	72.8*
BMI, kg/m ²	23.8	26.9*	27.2*
Fat, %	31.5	35.2	34.6
Lean, %	68.5	64.8	65.4

* $P < .05$.
BMI = body mass index.

with HIV.¹⁹ Low testosterone or thyroid hormone levels may contribute to loss of weight or lean body mass in these patients.²⁰ A more complex phenomenon is HIV-related cytokine dysregulation, which affects cytokine production and cytokine homeostasis and may contribute to poor food intake. There is evidence that the increased resting energy expenditure in HIV-infected patients may be the result of cytokine activation.²¹

The altered metabolism contributing to weight loss in HIV-infected patients may also contribute to subcutaneous fat atrophy, and may be very difficult to distinguish from lipodystrophy associated with HAART.²² Lipodystrophy may also produce weight loss and may resemble HIV wasting due to morphologic changes produced by fat redistribution. One possible way to distinguish fat atrophy from lipodystrophy is by looking at the level of lean body mass. HIV wasting typically produces a progressive loss of both lean and fat body mass, whereas lipodystrophy is only associated with loss of subcutaneous fat.

Effects of Advanced HIV Disease

Data suggest that the degree of advancement of HIV disease contributes to the nutritional status of HIV-infected individuals. Women who had lower CD4+ T-cell counts had lower body weights and consistently lower BMI.²³ When looking across CD4+ strata, HIV-infected women in the HAART era were able to maintain lean body mass. Although they had lower body weights and BMI, they were proportionately lower in both fat and lean body mass (Table 1). The data in men mirrored these data in women. Men with more normal (\geq 500 cells/ μ L), intermediate (200-499 cells/ μ L), and low (<200 cells/ μ L) CD4+ counts were proportionate for fat and lean body mass.

A study of HIV-infected patients showed that a change in viral load had an impact on body weight and BMI.²⁴

TABLE 2**Effect of Anti-cytomegalovirus Therapy on Body Composition²⁷**

	Untreated	Treated	P Value
Body weight, g/d	-132 ± 29	49 ± 19	<.001
BMI, mEq/d	-6.4 ± 2.7	2.8 ± 1.1	<.005
BCM, g/d	-58	26	
Body fat, g/d	-36 ± 20	23 ± 14	<.05
Albumin, g/d	-0.3 ± 0.1	0.1 ± 0.1	<.02
Energy, kJ/d	-1554	1075	

BMI = body mass index; BCM = body cell mass.

Among patients with HIV disease that was not advanced enough to require the use of HAART, each 10-fold increase in viral load was associated with a 0.92-kg decrease in body weight ($P = .003$). However, if the HIV viral load was stable, there was no predictable impact of viral load on weight. Change (increase) in viral load was a statistically significant predictor of weight loss ($P = .01$). For individuals who were on HAART, there did not appear to be an association between changes in viral load and weight, but there was a significant association between changes in CD4+ count and changes in weight ($P < .001$). Increases in CD4+ count resulted in increases in weight, and decreases in CD4+ count resulted in decreases in weight.

In the early part of the HIV pandemic, it was presumed that the AIDS-defining illnesses from which a patient with HIV suffered were the major contributors to weight loss. Over time, there has been an opportunity to reevaluate this presumption and look at the role of AIDS-defining illnesses in the HAART era. There is an association between the acute occurrence of an AIDS-defining illness and a weight-loss outcome.²⁵ There is also a linear association between the number of AIDS-defining illnesses suffered by a patient and the risk of losing weight. There are fewer cases of opportunistic infections and AIDS-defining illnesses in the HAART era, reducing the risks associated with weight loss.²² Interestingly, when patients with an AIDS-defining illness were compared with patients who were AIDS-defined by CD4+ counts below 200 cells/ μ L, the frequency of weight loss was the same.²⁵ Weight loss and wasting occurred in these HIV-infected patients treated with HAART, whether or not they had an AIDS-defining illness.

Management of HIV-Associated Wasting

Even in the HAART era, patients with HIV infection are often not taking antiviral therapy.²⁶ Many patients are

unaware that they are HIV-positive. Even among patients with known HIV infection, up to one third are not receiving care. The use of HAART may be limited by toxicity or tolerability. Of those who are taking antivirals, some may be taking them incorrectly, and some may be infected with a resistant virus strain. For these reasons, the association of HIV infection with appropriate antiviral therapy is still not 1:1. This lack of appropriate and adequate treatment for HIV infection may be a serious contributing factor, partially explaining the continued existence of wasting and other side effects associated with HIV infection. Treatment options for the management of HIV wasting have included nutritional therapy, treatment of HIV infection and opportunistic infections, dietary counseling, appetite stimulants, enteral feeding, semielemental diets, and complementary therapies.

Nutritional Therapy

The overall goal of providing nutritional support to an HIV-infected patient is to prevent the critical level of depletion at which mortality rises, and is not different from the goal in any other patient suffering from wasting. The specific aims are to try to preventively maintain functional capacity and to preserve, if not enhance, immune function. The latter is normally dependent on adequate intake of micronutrients. In all patients with protein energy malnutrition, related to HIV or otherwise, the goal is to slow disease progression.

Nutritional therapy is intended to minimize the loss of weight, lean mass, and fat; to improve QOL; and to enhance functional capacity. The goal is not necessarily to restore normal weight, body composition, or function, as these goals may be difficult or impossible to achieve. More importantly, nutritional support in patients with disease complications provides time for medical or surgical therapies to be effective, in which case, nutritional repletion will occur spontaneously. There are many nutritional therapies. They can be divided into the following categories: treating the underlying disease; providing food, formula, or some form of dietary counseling; stimulating appetite; and providing food nonvolitionally (ie, tube-feeding). If these strategies are not sufficient, complementary therapies to increase anabolism or inhibit catabolism should be considered.

Treating Opportunistic Infections

Malnutrition has multiple causes. Poor food intake can be the result of infections such as *Candida esophagi-*

tis or *Herpes esophagitis*, which cause swallowing to be painful. Malabsorption in the gut can be due either to partial or complete villus atrophy or to CD4+ cell depletion–related infections such as *Cryptosporidia*, microsporidia, and *Isospora belli* that lead to gut dysfunction. Additionally, the body’s acute stress response can be triggered by the systemic inflammatory immune response that occurs from infections such as cytomegalovirus (CMV) colitis, *Clostridium difficile* toxin–associated colitis, or others. Management strategies for treating wasting should include targeting the primary cause of malnutrition.

Data from a study evaluating ganciclovir, a guanosine analogue that inhibits CMV replication, for the treatment of systemic CMV infection in HIV-infected patients were analyzed to determine the effect of treatment on body composition (Table 2).²⁷ The changes in body weight, body cell mass, body fat, and energy balance all significantly and dramatically favored the patients treated with ganciclovir over untreated patients. These patients did not get nutritional support per se; however, improvement in body composition was observed with ganciclovir therapy. These results support the concept of treating the underlying cause of weight loss rather than just the symptoms. A similar argument could be made for antiretroviral therapy itself, where it has been demonstrated that weight loss occurs in the absence of antiretroviral therapy and weight gain occurs early during treatment with antiretroviral agents.²⁸ This result emphasizes the importance of treating the underlying cause of weight loss rather than focusing exclusively on the weight loss itself.

Dietary Counseling

Patients who are not severely ill may do well with dietary counseling, including instruction on what and how to eat.²⁹ Conversely, patients who are quite ill may not respond sufficiently to dietary counseling alone, as they often suffer from anorexia, not a lack of food.³⁰ There may also be food insecurity or hunger. However, in the presence of serious infection, weight loss may occur from anorexia even with adequate access to food.

Appetite Stimulants

Appetite stimulants may help some patients. Megestrol acetate, dronabinol, and cyproheptadine are treatment options available to help gain weight.³¹ Much of the weight gain is the result of an increase in body fat. In terms of megestrol acetate, the fat gain in men may be related to hypogonadism caused by this synthetic deriva-

tive of progesterone suppressing serum testosterone levels. Low serum testosterone levels may contribute to weight loss, and this is primarily due to depletion of lean body mass. Weight loss may even be associated with an increase in fat mass.^{32,33}

Enteral Feeding

Enteral feeding can also be used to improve nutritional status in patients with HIV infection. In one study, a group of patients, mainly with neurologic disease that impaired swallowing, were fed by gastrostomy.¹⁷ In this 2-month study, weight gain occurred with some increase in body cell mass, but there was a much greater increase in fat mass. Perhaps the most illustrative study looking at the effect of feeding on nutritional status involved a prospective longitudinal study involving patients who received total parenteral nutrition (TPN) because of malnutrition.³⁴ This study was conducted before the HAART era and included patients with active HIV infections. About half of the patients had systemic infections, CMV, or mycobacterial disease; the other half had malabsorption secondary to parasitic infections. Weight gain was observed in all patients during follow-up, which averaged 3 months. However, the weight gain was due almost entirely to an increase in body fat with almost no increase in body cell mass. In general, the patients were heavier, but not rehabilitated. However, the 2 subgroups responded quite differently to the TPN. Although the patients with systemic infections and those with malabsorption received the same amount of protein and non-protein calories, the malabsorbing patients had a very substantial improvement in body cell mass, whereas those with systemic infection had a progressive depletion ($P = .02$). The authors concluded that the response to TPN was more closely related to the nature of the underlying disease responsible for weight loss than the amount or composition of the nutritional support solution.

Semielemental Diet

Another study compared TPN with a semielemental diet in patients who had malabsorption.³⁵ There was a progressive rise in weight in both groups after therapy was given. The group receiving TPN gained more weight than the group receiving the semielemental diet on average, and they were able to tolerate more calories. Weight gain was significantly related to the total number of calories consumed and was unrelated to the mode of feeding. However, the major body composition change was an

increase in body fat. Surprisingly, the group receiving the semielemental diet actually had a better QOL response than the group that received TPN, despite a more modest increase in weight. The group receiving the semielemental diet had lower morbidity, fewer infections, and a much lower cost of treatment than the group receiving TPN.

Complementary Therapies

There is a conundrum in feeding patients with HIV-related wasting. Decreased caloric intake is a major cause of malnutrition, whether or not there are lesions that affect eating, swallowing, malabsorption, or even systemic infections. A decrease in caloric intake predicts weight loss. However, an increase in caloric intake does not reverse that condition completely because it does not replete lean mass. Cytokines and other systemic responses lead to protein breakdown, not protein synthesis. And it is on this basis that, in the early 1990s, investigators looked to anabolic agents to see if they would be of some benefit. Anabolic agents have become one of several complementary therapies, along with exercise, anticatabolic agents, and the combination of these therapies. There were multiple studies done evaluating testosterone and other anabolic agents combined with exercise in men or in women.³⁶⁻³⁸ Many of these studies demonstrated a gain in lean mass without a gain in body fat, and, in some cases, even a loss in body fat, as well as an improvement in QOL.

There were also several studies investigating the efficacy of human growth hormone for the treatment of HIV-related wasting. One study was conducted in the pre-HAART era and one in the post-HAART era.^{39,40} In both studies, there was a modest weight gain, which included significant increases in lean mass and losses in body fat. The lean mass gain was seen in both the pre-HAART and the HAART eras. In these 2 studies, not only was body composition analyzed, but a functional outcome was examined using treadmill testing or cycle ergometry. In both cases, the anabolic agent led to increases in lean mass and peak functional output compared with placebo.

Other studies looked at protein supplementation and exercise.⁴¹ One study included 30 HIV-infected women with body cell mass depletion who were treated either with a whey protein nutritional supplement, progressive resistance exercise, or the combination. Protein supplementation led to a weight gain, whereas exercise led to a slight weight loss, and the combination therapy resulted in a modest weight gain. Interestingly, all 3 treatments

led to a similar increase in body cell mass, whereas protein supplementation led to an increase in body fat, much like other feeding studies. Muscle function was monitored using the one repetition maximum method. This study revealed that exercise led to a major increase in muscle strength that was independent of protein supplementation. Protein-feeding alone did not lead to an increase in muscle strength despite increases in body cell mass. The conclusion of this study was that progressive resistance exercise, when feasible, may be a better tool than protein supplementation to improve functional capacity in patients with HIV infection.

Thalidomide acts as an anti-inflammatory and an anticatabolic agent. In a double-blind, placebo-controlled trial, weight gain was observed with 2 different doses of thalidomide, half of which was in the lean mass compartment.⁴² Although the use of high-dose thalidomide is limited by adverse reactions, 8 weeks of low-dose thalidomide led to a significant increase in body weight in patients with HIV-related wasting, with minimal side effects. These data demonstrate that blocking the catabolic response may lead to an improvement in lean body mass.

Two recently published studies investigated micronutrient supplementation. Micronutrient depletion has been documented in HIV over the past 15 years. In one study, a broad-spectrum micronutrient supplement was given in an attempt to improve neuropathy in HIV-infected patients taking HAART.⁴³ Micronutrient supplementation did not significantly improve neuropathy scores, but the investigators noted a significant 24% increase in CD4+ lymphocytes over the course of the 3-month study, compared with no change in CD4+ counts in the placebo group ($P = .01$). Additionally, a placebo-controlled trial found that selenium administration significantly increased selenium plasma concentrations ($P < .001$).⁴⁴ The increase in selenium predicted a decrease in viral load ($P < .02$), which in turn predicted an increase in CD4+ count ($P < .04$).

Conclusions

Weight loss remains a frequent complication of HIV infection even in the HAART era. It remains associated with increased morbidity and mortality. Protein energy malnutrition is the most common cause of HIV-related weight loss, resulting in a decrease in both fat mass and lean body mass. Symptomatology is important in determining which type of weight loss is occurring. HIV-related weight loss is complex and may be multifactorial. Any

specific intervention for weight loss must be tailored to the etiologies that are identified in a particular patient for treatment to be most beneficial.

Weight loss is a complication of HIV and AIDS. Interventions may be used not only in patients with significant HIV-related weight loss, but preventively to delay the onset of further weight loss or wasting. Ultimately, effective control of the HIV infection will assist in stabilizing nutritional status. If nutritional depletion occurs despite suppressing viral replication, the management of weight loss does not differ in HIV-infected patients from its management in any other clinical circumstance.

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POST-TEST

To receive credit, participants can visit: www.CMEDiscussions.com/8161 or fax/mail to ArcMesa Educators, LLC, 951 State Highway 33 West, Monroe Township, NJ 08831; Fax: 609-630-6110. Answer the 10-question multiple-choice post-test below and complete the program evaluation. A statement of credit will be issued upon successful completion of the post-test with a score of 70% or higher. Credit expires April 30, 2009. No credit will be given past this date.

Exam Questions

(Choose the best answer for each question.)

Record your answers on the Answer Form on the bottom of the next page.)

1. Serum concentration of which of the following is most useful in diagnosing new patients who may have HIV-related wasting?
 - a. Albumin
 - b. Glucose
 - c. Insulin
 - d. Prealbumin
 - e. High-density lipoprotein
2. Highly active antiretroviral therapy has not reduced HIV-related wasting.
 - a. True
 - b. False
3. Which form of weight loss is of greatest concern in patients infected with HIV?
 - a. Involuntary weight loss
 - b. Protein energy malnutrition
 - c. Loss of body fat mass
 - d. Subcutaneous fat atrophy
4. A potentially dangerous loss of lean body mass is always associated with a significant loss in body weight.
 - a. True
 - b. False
5. In patients suffering from starvation, which store of energy is normally exhausted first?
 - a. Fat
 - b. Protein
 - c. Carbohydrate
 - d. Other
6. Patients with HIV-related wasting generally lose only lean body mass, not fat mass.
 - a. True
 - b. False
7. HIV-associated wasting can occur even when caloric intake appears adequate.
 - a. True
 - b. False
8. Appetite stimulants have been shown to promote weight gain in clinical studies.
 - a. True
 - b. False
9. An increase in caloric intake can generally be expected to alleviate the symptoms of protein energy malnutrition.
 - a. True
 - b. False
10. According to the data presented, exercise leads to a greater increase in muscle strength than dietary protein supplementation.
 - a. True
 - b. False

HIV PATIENTS AND WEIGHT LOSS: Optimizing Care to Improve Outcomes

Participant Data: Required information for credits and individual record retention.

(Please Print Clearly)

First Name _____ Last Name _____

Address _____

City _____ State _____ Zip _____

Daytime Phone _____ Fax _____

Specialty _____ E-mail Address _____

State License(s) _____ License # _____

Validation: I confirm that I have studied the course materials and have personally completed the course examination.

Please sign for CE/CME credit: _____

HIV Wasting Evaluation: Please provide us with your candid evaluation so that we can continue to improve these continuing education materials. We thank you for your comments and appreciate your suggestions for future courses. Please circle a phrase that best reflects your satisfaction with this activity.

To what extent did this activity assist you in meeting the following learning objectives?

1. List physiologic factors affecting energy intake and metabolic abnormalities that may lead to weight loss in HIV-positive patients
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

2. Discuss the need for pharmacologic and nonpharmacologic approaches to improve weight in HIV-positive patients
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

3. Examine the impact of HIV-related weight loss on patient outcomes
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

4. Develop management strategies to address weight loss in HIV-positive patients
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

5. Please rate the quality of the learning materials.
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

6. Please rate the effectiveness of the instructors.
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

7. Please rate the effectiveness of this activity in relation to your practice.
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

8. Was this format effective for delivering this activity?
5-Excellent 4-Very Good 3-Good 2-Fair 1-Poor

9. Did you perceive this activity to be balanced and unbiased?
Yes No

10. If no, please explain:

11. What change(s) in knowledge, competence, or performance would be encouraged by this activity?

12. What topics would best meet your needs?

13. Would you like to be contacted about future CE/CME activities?
Yes No

Answer Form

1. a b c d e
2. a b

3. a b c d
4. a b

5. a b c d
6. a b

7. a b
8. a b

9. a b
10. a b

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