General Nutrition, Weight Loss, and Wasting Syndrome

Tables and Recommendations

Key to Abbreviated Terms Within Guidelines			
ACTH	adrenocorticotropin hormone	**GERD**	gastroesophageal reflux disease
ATP	adenosine triphosphate	**HAART**	highly active antiretroviral therapy
BCM	body cell mass	**IL**	interleukin
BIA	bioelectric impedance analysis	**LBM**	lean body mass
BUN	blood urea nitrogen	**PRE**	progressive resistance exercise
BW	body weight	**rhGH**	recombinant human growth hormone
CI	caloric intake	**REE**	resting energy expenditure
CMV	cytomegalovirus	**TBW**	total body weight
CPK	creatine phosphokinase	**TEE**	total energy expenditure
DEXA	dual energy x-ray absorptiometry	**TNF**	tumor necrosis factor
DT	dietary thermogenesis	**TPN**	total parenteral nutrition
EEA	energy expenditure of activity	**UBW**	usual body weight
EM	extracellular material	**VAT**	visceral adipose tissue
Fat	fat compartment	**VLDL**	very low density lipoprotein

I. Introduction

Recommendation:

The clinician should ensure that patients with HIV-associated weight loss are receiving effective ARV therapy (see Chapter 4: *Guidelines for the Use of Antiretroviral Therapy*)**.**

> **Key Point:**
> Weight loss is a symptom that warrants a carefully executed diagnostic evaluation for correctable or treatable confounding conditions.

II. Assessment of Body Composition

Recommendation:

The clinician should measure and record the weight of HIV-infected patients at each visit.

See Table 1.

> **Key Point:**
> The clinician should be vigilant for HIV-associated malnutrition, even in patients who appear to be maintaining their usual body weight. Weighing the patient should not be the sole method used to detect nutritional deficiencies.

Table 1 Clinical Determination of Changes in Body Composition			
Change in Body Composition	**History**	**Physical Examinations**	**Laboratory**
↓**Body Cell Mass**	Fatigue, weakness, decreased exercise tolerance	Proximal muscle wasting, weakness of deltoids/ iliopsoas, peripheral edema	↑CPK (if myopathy present) ↑BUN/creatinine ↓albumin
↓**Extracellular/** ↓**Intravascular** H_2O	Orthostatic dizziness, polydipsia, dry skin and xerostomia, alimentary difficulty, polyuria, diarrhea	Orthostatic hypotension, decreased skin turgor, dry mucosa	↑or ↓Na ↑BUN/creatinine ↓HCO_3 ↓K, Mg
↓**Fat**	Change in body habitus	Prominent venous pattern/extremities, facial wasting	↑triglycerides

III. Assessing Nutritional Status

Recommendation:

A careful nutritional assessment should be conducted by a registered dietitian for any patient who has involuntary weight loss of at least 5% of the UBW, demonstrates clinical evidence of LBM loss, or follows a restrictive diet involving major food groups.

> **Key Point:**
>
> A thorough medical history and a focused physical examination are the most valuable tools in assessing nutritional status.

IV. Energy Expenditure

> **Key Point:**
>
> Resting energy expenditure in all stages of HIV/AIDS may be increased by >10% when compared with non-HIV-infected individuals.[5]

V. Weight Loss

A. Pathophysiology

1. Decreased Nutrient Intake

Recommendations:

When patients present with dysphagia or odynophagia, the clinician should evaluate for causes of neoplasms, stomatitis, and/or esophagitis, especially when the patient's CD4 count is <200 cells/mm^3.

After active opportunistic diseases have been excluded in patients with voluntary restricted caloric intake, clinicians should consult with or refer the patient to a dietitian, psychiatrist/psychologist, or social worker.

> **Key Point:**
>
> Dietary restrictions for some HAART regimens pose significant barriers to adequate caloric intake and good nutrition. It may be necessary to consider a change in HAART under these circumstances (see Table 2).

Table 2 Manufacturers' Guidelines Combining Antiretroviral Medication and Food				
ARV Drug	**To be taken on empty stomach**	**To be taken with food**	**No known food interactions**	**Special Considerations**
Abacavir (ABC)			X	
Amprenavir (APV)				Avoid meals with >50 g fat. Avoid vitamin E supplements. Do not take antacids 1 hour before or after taking APV.
Atazanavir (ATZ)		X		
Delavirdine (DLV)			X	Take with acidic beverage. Do not take antacids or magnesium supplements 1 hour before or after taking DLV.
Didanosine (ddI)	X			When taken with TDF, ddI can be taken with a light meal. Alcohol may exacerbate toxicity. Avoid acidic beverages when taking ddI. Do not take aluminum- or magnesium-containing antacids.
Efavirenz (EFV)	X			Avoid meals with >40-60 g fat.
Emtricitabine (FTC)			X	
Enfuvirtide (T-20)			X	
Fosamprenavir (f-APV)			X	
Indinavir (IDV)	X			Take on empty stomach 1 hour before or 2 hours after meals. Drink plenty of fluids (8-10 cups/day). Grapefruit juice may affect absorption.
Lamivudine (3TC)			X*	
Lopinavir/ ritonavir (LPV/r)		X		To increase absorption, take with a meal containing >15 g fat
Nelfinavir (NFP)		X		To increase absorption, take with a meal containing >15 g fat
Nevirapine (NVP)			X	
Ritonavir (RTV)		X		Take with food that contains both protein and fat. To increase absorption, take with a meal containing >15 g fat
Saquinavir (SQV)		X		Take within 2 hours of high-fat meal or snack (>50 g). Grapefruit juice may increase retention.
Stavudine (d4T)			X	
Tenofovir (TDF)			X	
Zalcitabine (ddC)	X			
Zidovudine (ZDV)			X	Avoid high-fat meals when taking ZDV.

Data are from manufacturers' information and Fields-Gardner C, Salomon S, Davis M. *Living Well With HIV and AIDS: A Guide to Nutrition*. Chicago, IL: The American Dietetic Association, 2003.

* Although absorption is decreased with food, systemic availability is not affected.

2. Decreased Nutrient Absorption

RECOMMENDATIONS:

For all patients with chronic diarrhea, the clinician should examine for and treat gastrointestinal opportunistic infections (*Mycobacterium avium* complex, bacterial pathogens such as *Salmonella*, *Cryptosporidium*, microsporidia, *Isospora*, *Giardia*, *Entamoeba*, *Clostridium difficile*), as well as assess for ARV-induced diarrhea.

The clinician should evaluate patients with chronic diarrhea in the setting of weight loss for malabsorption by 3-day fecal fat measurement, D-xylose absorption studies, and jejunal and/or colon biopsy.

3. Disturbances of Metabolism

RECOMMENDATIONS:

The clinician should perform a comprehensive medical evaluation when rapid unintentional weight loss (≥10% of the UBW) occurs over weeks to months because it is frequently associated with a life-threatening opportunistic infection or neoplasm.

Clinicians should consider measuring total and free testosterone levels in all HIV-infected men with changes in libido, loss of LBM, or fatigue.

Key Point:

Because women lose a disproportionate amount of body fat at all stages of HIV infection, malnutrition should be suspected in women demonstrating fat loss.

TABLE 3
METABOLIC ABNORMALITIES ASSOCIATED WITH WEIGHT LOSS IN HIV/AIDS

- Abnormal energy expenditure/hypermetabolism
- Cytokines—the cachectin theory
- Cytokine induction of other catabolic agents
- Futile cycling
- Inappropriate substrate usage
- Protein wasting
- Endocrine factors
- Fat redistribution/"lipodystrophy"
- HAART-associated hypercholesterolemia, hypertriglyceridemia, and insulin resistance/hyperglycemia
- Myopathy due to HIV and/or nucleoside mitochondrial toxicity

Key Point:

When weight loss is associated with profound fatigue, postural hypotension, hyperkalemia and/or hyponatremia, clinicians should consider adrenal insufficiency, especially in cases of disseminated *M. avium* complex and CMV infection.

B. Management of Gradual HIV-Associated Weight Loss (see Figure 1)

1. Nutritional Supplementation

RECOMMENDATIONS:

Although nutritional supplementation is indicated for all patients with weight loss, the clinician should not supplement caloric intake without first addressing reversible causes of weight loss.

FIGURE 1
MANAGEMENT OF GRADUAL WEIGHT LOSS IN HIV-INFECTED PATIENT

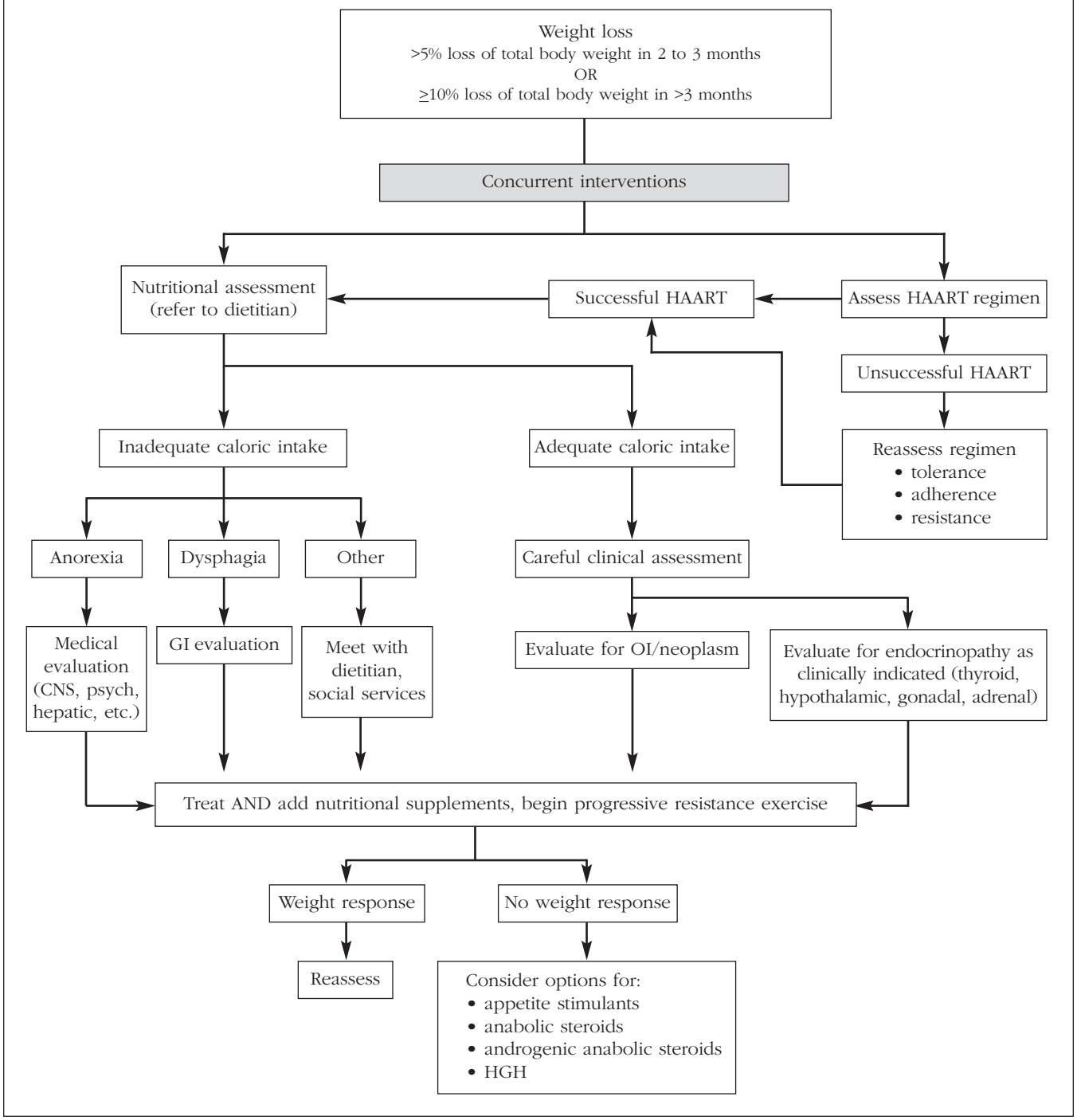


Table 4 Selected Commercially Available Liquid Nutritional Supplements*						
Products	**Calories/cc**	**% Carbo**	**% Protein**	**% Fat**	**Osmols**	**Features**
Osmolite	1.06	57%	14%	29%	300	Low residue, lactose and gluten free
Juven	90 cal/ packet	2-3 g/ packet depending on flavor	0, contains amino acids arginine and glutamine	0	450-470, depending on flavor	Contains β-hydroxy, β-methylbutyrate, a metabolite of amino acid leucine to decrease muscle protein breakdown
Glucerna shake	0.93	47%	18%	35%	530	Designed for diabetics or those with impaired glucose tolerance
Nepro	2.0	43%	14%	43%	665	Designed for patients on dialysis
Jevity	1.06	54.3%	16.7%	29%	300	High fiber, lactose and gluten free
EnsurePlus	1.5	53.3%	16.7%	30%	650	Low residue, gluten and lactose free
Criticare	1.06	82%	14%	4%	650	Low residue, low-fat elemental
Peptamen 1.5	1.0	51%	16%	33%	450	Calorically dense peptide based elemental for malabsorption
Perative	1.3	54.5%	20.5%	25%	385	Peptides and free amino acids semi-elemental for malabsorption
Suplena	2.0	51%	6%	43%	600	Designed for patients with ESRD and liver failure. Low in protein, adjusted mineral content.

* The products listed above do not represent a complete listing of the commercially available supplements.

Clinicians should recommend the use of "once daily" multivitamin supplements containing selenium (20-40 mg) for all HIV-infected patients experiencing weight loss.

Clinicians should not recommend high-dose vitamin therapy because this might exacerbate pre-existing gastrointestinal dysfunction and/or anorexia.

Clinicians should consider medical conditions, such as pancreatitis, diabetes mellitus, or renal insufficiency, in planning macronutrient balances.

2. Treatment of Anorexia

Recommendation:

When patients present with anorexia, clinicians should perform a careful review of the medication list to determine whether the anorexia is medication-induced.

3. Treatment of Non-Infectious Diarrhea

RECOMMENDATION:

When recalcitrant diarrhea occurs as a complication of HAART, clinicians should consider a change in therapy if suitable alternatives with a high likelihood of successful viral suppression are available (based on HIV resistance testing).

4. The Role of Exercise

RECOMMENDATION:

Clinicians should advise patients to participate in a fitness program that uses progressive resistance exercise.

5. Anabolic Steroids

RECOMMENDATIONS:

Clinicians should exclude specific endocrine abnormalities, such as hypothalamic hypogonadism and hyperthyroidism, before prescribing oxandrolone.

Clinicians should monitor for hypogonadism in eugonadal men who are receiving long-term nandrolone or oxandrolone.

6. Androgenic Anabolic Steroids

RECOMMENDATIONS:

Clinicians should consider short-term (several months) testosterone therapy with supraphysiologic doses, in conjunction with PRE, to achieve BCM increase in selected male patients demonstrating a rapid rate of muscle loss.

Because androgenic anabolic steroids cause virilization, a general recommendation for their use in women cannot be made until further studies have been completed.

Because androgen enhances libido, clinicians should strongly reinforce safer sexual practices for patients receiving androgenic anabolic steroids.

7. Recombinant Human Growth Hormone

RECOMMENDATIONS:

Clinicians should consider prescribing a 12-week course of recombinant human growth hormone (rhGH) after hypogonadism and active opportunistic diseases have been excluded.

Clinicians should discontinue rhGH treatment if no weight gain is observed after the initial 3 to 4 weeks of therapy.

If weight loss continues despite several weeks of rhGH therapy, the clinician should re-evaluate for co-existent opportunistic infections.

VI. THE WASTING SYNDROME

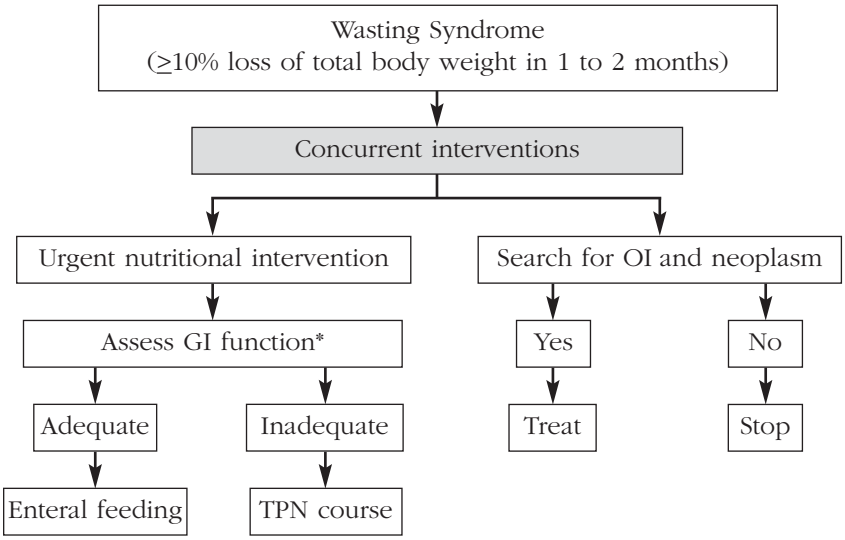
RECOMMENDATION:

Clinicians should perform a detailed evaluation for opportunistic infections or malignancies in all patients with wasting syndrome.

A. Diagnosis

See Figure 2.

FIGURE 2
MANAGEMENT OF WASTING SYNDROME



* See Section V: *Weight Loss*

B. Nutritional Intervention in the Wasting Syndrome

RECOMMENDATIONS:

The clinician should perform an immediate evaluation to determine the cause of the wasting syndrome.

For patients with conditions that prevent enteral feeding, total parenteral nutrition (TPN) may be indicated for short-term management.

The clinician should monitor supplementation with micronutrients by frequently assessing serum electrolytes and blood glucose in the first several weeks of re-feeding.

VII. FAT REDISTRIBUTION (LIPODYSTROPHY) SYNDROMES

Key Point:

Clinicians should consider the possibility of concurrent lactic acidosis and/or hepatic dysfunction in patients with lipoatrophy.

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Appendix A

Therapy for Gradual HIV-Associated Weight Loss

Table A-1
Therapy for Gradual HIV-Associated Weight Loss

	Anticipated Effects	Daily Dose Range	Comments
Appetite Stimulants			
Megestrol Acetate (Megace)	↑appetite, ↑BM, ↔BCM, ↑Fat	400-800 mg/day with meals	May ↓testosterone levels; may cause impotence; risk of thromboembolism, adrenal insufficiency
Dronabinol (Marinol)	↑appetite, ↑BM, ↔BCM, ↑Fat	2.5-10 mg bid with meals	Patients may not tolerate CNS effects
Cyproheptadine (Periactin)	↑appetite, ↑BM, ↔BCM	4-8 mg bid with meals	Can cause drowsiness, dry mouth
Anabolic Steroids			
Testosterone (Gel form, topical patch, buccal mucoadhesive, IM injection)	↑performance status, ↑appetite, ↑BCM, ↑BM, ↑mood/libido	1 gel-pak daily, or 1 patch/24 hr, or 1 buccal application q 12 hr, or 200-400 mg IM q 2-4 wk	Preferred when serum free testosterone levels are ↓; testicular atrophy; PSA should be followed Androgenic >> Anabolic
Oxandrolone (Oxandrin)	↑BM, ↑BCM, ↑appetite	5-20 mg/day	Best with resistance exercise; be vigilant for peliosis hepatitis Androgenic << Anabolic
Oxymetholone (Anadrol-50)	↑BM, ↑BCM	1-2 mg/kg/day	Best with resistance exercise; be vigilant for peliosis hepatitis Androgenic << Anabolic
Nandrolone (Deca-durabolin)	↑BM, ↑BCM	100-200 mg q2 weeks	Best with resistance exercise; be vigilant for peliosis hepatitis Androgenic << Anabolic
Growth Hormone			
Recombinant Somato-Tropin (Serostim)	↑appetite, ↑BM, ↑BCM	3-6 mg sq qHS	Expensive Usual 12-week course; can be repeated.
Cytokine Inhibitors*			
Thalidomide	↔appetite, ↑BM	100-300 mg/d	Available to registered prescribers for oral aphthae and wasting. Lowers serum TNF. Efficacy for wasting not established.
Pentoxifylline (Trental)	↔appetite, ↔BCM	400 mg tid	Lowered serum TNF in several studies. No clinical benefit.

* Because a central role of TNF in wasting has not been established, this treatment approach should be considered speculative and of unproven effectiveness.