

NUTRITION AND HIV/AIDS

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OBJECTIVES

1. Describe the complex interactions between nutrition and human immunodeficiency virus (HIV)/AIDS.
2. Describe the risk factors that contribute to malnutrition in HIV/AIDS.
3. Explain how to conduct a nutritional assessment of children and adults.
4. Explain how to determine nutrient needs of children and adults.
5. Describe how to classify malnutrition.
6. Describe nutrition intervention strategies for adults and children with HIV/AIDS.

KEY POINTS

1. HIV infection can often result in nutritional deficiencies and growth failure.
2. Malnutrition associated with HIV/AIDS can severely affect an already compromised immune system, leading to increases in rates of opportunistic infections and a decreased survival rate.
3. A nutritional assessment is an indispensable component of the comprehensive management of HIV-infected individuals.
4. One must monitor and maintain adequate nutritional status in HIV-infected children and adults.
5. The management of moderately and severely malnourished HIV-infected individuals includes both aggressive nutritional support according to well-accepted protocols and antiretroviral medications.
6. Routine vitamin A supplementation and distribution of antihelminth medications are important contributions to good nutrition in many settings.

OVERVIEW

Severe weight loss and wasting were some of the earliest recognized signs of human immunodeficiency virus (HIV) infection, and in many African countries HIV was

called “slim disease” because of the prominence of this feature. Wasting and weight loss are common features of HIV infection, especially in resource-limited settings, with some studies showing 40%-44% of adults and 59% of children having wasting and malnutrition as a part of their disease manifestations. There is a complex relationship between nutrition and HIV infection. Malnutrition, even without HIV, can compromise the immune system, and CD4 T cells can be decreased in malnourished, HIV-negative individuals. Nutritional status may indicate disease severity and may help indicate response to antiretroviral therapy (ART). Both macronutrient and micronutrient deficiencies are important in HIV-infected patients. For all these reasons, an assessment of nutritional status should be a routine part of the care of every HIV-infected patient. Prevention and management of nutritional deficiencies and malnutrition are crucial parts of the comprehensive management of HIV-infected children and adults. Metabolic abnormalities, usually related to ART, are common but will not be discussed in this chapter (see the chapter on metabolic abnormalities).

REASONS FOR MALNUTRITION/ GROWTH PROBLEMS IN HIV-INFECTED INDIVIDUALS

HIV contributes to malnutrition in many different ways and can directly or indirectly result in decreased caloric intake, increased loss of nutrients, and increased use of nutrients/energy. Factors thought to contribute to wasting and malnutrition in people with HIV/AIDS include metabolic alterations, infection, fever, gastrointestinal (GI) changes and illnesses, developmental/neurological problems, and economic and psychosocial issues. HIV also seems to affect lean body or muscle mass more aggressively than other infections, resulting in a disproportionate loss of muscle compared with fat during the development of malnutrition.

Any infection, and HIV infection in particular, alters the metabolism of energy, carbohydrates, fats, proteins, vitamins, and minerals, increasing the body's need for these nutrients. Fever may increase protein utilization and increases calorie needs by 12% for each degree Celsius above normal and 7% for each degree Fahrenheit above normal. Though there is some controversy, it is thought that HIV infection may increase resting energy expenditure (the amount of energy that the body uses to run basic cell and tissue functions at rest), which could lead to wasting. An increased production of cytokines in HIV infection may also contribute to wasting in HIV infection.

The interaction of HIV with the GI tract (see chapter on GI manifestations of HIV) can profoundly affect nutritional status. Diarrhea increases caloric needs by 25% and often leads to a decreased oral intake. Malabsorption, the inability of the body to absorb nutrients from the GI tract, may be associated with diarrhea or occur without diarrhea because of metabolic changes associated with HIV. It can lead to vitamin, mineral, protein, fat, and carbohydrate losses as well as a decrease in oral intake. Dehydration from diarrhea may result in an acute loss of weight from water loss and can be a life-threatening complication of diarrhea (see the chapter on GI manifestations of HIV infection

for recommendations on treating dehydration). Severe oral candidiasis (yeast), esophageal candidiasis, herpes gingivostomatitis, viral esophagitis, and gastritis can make eating difficult and painful, leading to decreased oral intake or feeding refusal (see chapter on opportunistic infections for recommendations on treating these infections). Nausea and vomiting caused by drugs, infection, and/or illness can result in poor oral intake, dehydration, and loss of nutrients.

Children and adults with HIV/AIDS can develop feeding problems, often due to neurological deterioration related to HIV infection, leading to inadequate intake of nutrients. Infants with HIV can have a weak suck, resulting in inadequate intake of breast milk or formula. Older children may develop poor chewing and feeding skills. Difficulty swallowing can lead to poor oral intake or refusal to eat. There is a risk of aspiration and pneumonia with swallowing problems.

Economic issues leading to inadequate nutrient intake are a frequent contributor to malnutrition in many settings. These issues include a limited food supply, loss of household income or livelihood (such as farming) due to illness, and limited cooking and storage facilities. HIV-infected adults may be too ill or uninterested to care for themselves and their children. Depression in an adult or child can also lead to decreased appetite and poor nutrient intake.

IMPORTANCE OF MALNUTRITION AND WASTING IN HIV/AIDS

The interaction between malnutrition and HIV is complex. Recognizing malnutrition is important because it may predict disease progression and higher risk of morbidity and mortality. The presence of malnutrition is a predictor of worse outcomes in both HIV-infected adults and children. In HIV-infected children, measurements such as height growth velocity and low weight for age predict survival and disease progression. Malnutrition may be a secondary result of advanced HIV disease. Primary malnutrition may also



A Ugandan girl drinks formula by cup.

accelerate HIV disease progression. Malnutrition independent of HIV infection has a high morbidity and mortality, and this effect may be exaggerated in HIV-positive individuals.

Recognizing malnutrition is also important so that specific treatments directed at improving nutritional status can be used. Control of HIV infection using antiretroviral (ARV) medications and interventions directed at nutritional deficiencies, such as nutritional supplements, are often both necessary to adequately care for infected individuals. Use of ARVs without nutritional support, or nutritional support without ARVs, will often result in poor treatment responses and outcomes. With ARV medications and improvement in CD4 count and viral load, weight and some lean body mass can be restored. However, some patients see little to no improvement in lean body mass, so one must try to maintain good nutritional status in HIV-positive patients from the time of diagnosis.

NUTRITION ASSESSMENT

A nutrition assessment is a critical part of evaluating every HIV-infected patient and has three major components:

1. A history and physical examination, including a diet and feeding history, to identify the causes that may be contributing to a patient's current wasting or malnutrition, or risk factors for the development of nutritional problems in the future
2. Assessing objective measures of growth (height, weight, mid-upper arm circumference [MUAC], head circumference, weight gain, and linear growth) and comparing them to expected norms
3. A laboratory assessment when available and appropriate

History, Physical Examination, Diet/Feeding History

The history and physical examination in a nutrition assessment should focus on identifying symptoms and signs of malnutrition as well as any specific causes that are currently contributing or might contribute to malnutrition. The previous section discusses some of the more common factors contributing to malnutrition in HIV-infected patients. The physical exam should assess for pitting edema because this may be a sign of severe malnutrition, often without low weight or visible wasting. Signs of common micronutrient deficiencies are shown in **Table 1**.

Table 1. Clinical signs of vitamin/mineral deficiencies

Vitamin or mineral	Clinical signs
B12	Macrocytic (larger than normal red blood cells) anemia, neurologic disturbances, altered mental status
C	Bleeding gums, petechial hemorrhages (small, purplish spots on the skin)
A	Night blindness, xerophthalmia (dryness of the eyes), loss of appetite
B6, niacin, riboflavin	Cheilosis (fissures, redness, sores around lips)
Iron	Thin, brittle, concave fingernails, microcytic anemia
Zinc	Growth retardation, dermatitis (inflammation of the skin evidenced by itching, redness, and lesions), diarrhea, hair loss
Selenium	Cardiomyopathy (abnormalities of the heart muscles)

Dietary intake and feeding history are important aspects of a nutrition assessment. The adequacy of nutrient intake can be assessed based on a 24-h patient diet recall (a list of what the patient normally eats and/or ate in the past 24 h) or a 3-day food intake record (kept in writing by the patient or a caretaker). One must interview the patient/caretaker to find out the types and estimated amounts of foods, formula, fluids, and breast milk consumed. For those giving infant formula, determine how they are mixing the formula: over- and underdilution are common and potentially serious problems. Other important information includes how long it takes the patient to eat; the patient's appetite; any chewing, sucking, or swallowing problems; presence of nausea, vomiting, diarrhea, and abdominal pain; and any feeding refusal, food intolerance, allergies, and fatigue. If the patient is a child, know who provides the food for the child, who feeds the child, and whether there is an adequate supply of food daily or intermittently.

Objective Measures of Growth

Weight, length or height, head circumference/frontal-occipital circumference (FOC), and MUAC are important objective measures of nutritional status. Body weight is one of the most fundamental ways to assess nutritional status in infants and children, especially when evaluated over time, and weight alone is adequate to assess growth when no other measurements are available. Dehydration

can affect weight, so determining whether the patient is dehydrated is important. Recent acute weight loss could indicate infection and/or changes in intake. Weight loss of more than 2% in one week, 5% in one month, 7.5% in 3 months, and 10% in 6 months are considered significant. One must take the time and effort to measure these values accurately (see chapter on growth). For children, rate of weight gain and linear growth are also important components of a nutrition assessment, and one should plot weights, heights, and FOCs on appropriate growth charts (see chapter on growth).

The MUAC is another objective measure of nutritional status that is becoming more widely used, especially in resource-limited settings. It is a simple, cheap, and less error prone method by which to assess for wasting, and MUAC might be a better indicator of mortality risk associated with malnutrition than weight for height (discussed in the following section). Many malnutrition programs in developing countries have moved toward using MUAC as the preferred measure for identifying/screening for acutely malnourished children, and health practitioners need to be familiar with its use. Because muscle mass is more affected in HIV than in primary malnutrition, for which MUAC norms were developed, there is a tendency to overestimate the degree of malnutrition with this technique. This is probably an advantage during the acute management of wasting in these children but may result in the maintenance of therapies longer than necessary. By convention the MUAC is usually taken on the left arm. With the patient's arm bent at 90° at the elbow, use the MUAC band (a simple tape measure can be used) to measure the length of the upper arm, from shoulder bone to elbow, and mark the midpoint with a pen. Then, with the arm straightened, wrap the MUAC band around the child's arm at the midpoint, such that all of it is in contact with the child's skin. It should be neither too tight nor too loose. Read the MUAC, in millimeters or centimeters, to the nearest millimeter.

Other, more specialized, objective measures of determining body composition, such as the triceps skin fold, can be useful in a nutritional assessment but are outside the scope of this chapter. However, pinching the skin as part of the physical exam is an easy way to estimate the amount of subcutaneous fat and can help in determining the degree of acute malnutrition.

Laboratory Assessment

The laboratory component of a nutrition assessment in both children and adults when available should include evaluation of the complete/full blood count, total protein, albumin (dehydration can lead to falsely elevated serum levels), and prealbumin (which has a half-life of several days versus about 2 weeks for albumin). Albumin and prealbumin assess visceral protein status (muscle mass), with prealbumin, because of its shorter half-life, reflecting more recent protein intake.

CLASSIFICATION OF MALNUTRITION

After having done an in-depth nutritional assessment, one must know how to interpret the results. To assess growth, the health care provider should plot the patient's weight, height/length, and FOC on a growth chart. Any prior weights and lengths that are available, including birth weight, are helpful to plot trends in the patient's growth (see the growth chapter).

Professionals often use *z* scores to define the presence and severity of malnutrition. The *z* score is the measure of distance in standard deviations that a value is from the mean. Tables of *z* scores facilitate identification of malnutrition. In most resource-limited settings, the World Health Organization (WHO)-published *z* scores are the most widely used standards for determining levels of childhood malnutrition. For completeness, this chapter also includes other well-accepted methods of defining malnutrition. The Waterlow criteria use the percentage of expected length/height for age and the percentage of expected weight for height to define malnutrition. Using standard growth charts, one can calculate the percentage of expected height for age and weight for length/height.

Chronic Malnutrition

Chronic malnutrition is indicated by the presence of stunting—when a child's length/height is much lower than that of other children of the same age. Though used as a measure of chronic malnutrition, stunting has other causes, including chronic disease, genetic abnormalities, and endocrine disorders. Stunting may also be constitutional (short parents). The length/height-for-age *z* score is one way to determine the presence and severity of stunting. Stunting is considered to be moderate when the length/height-for-age *z* score is between -2 and -3 , and severe when the *z* score is less than -3 . Stunting may also be determined by a patient's percentage of expected height for age (**Table 2**).

Acute Malnutrition

Acute malnutrition is indicated by the presence of nutritional edema and/or wasting. Wasting is almost always the result of nutritional deprivation. The only exception is in primary muscle wasting diseases such as AIDS, in which case one must use clinical judgment. Determining whether wasting is related to nutritional deprivation or HIV/AIDS can be difficult, and managing both aggressively usually makes sense—with nutrition support as well as treatment directed at the patient’s HIV infection.

Edema is quantified as grade 1+ (mild, both feet/ankles), grade 2++ (moderate, feet plus lower legs, hands, or arms), or grade 3+++ (severe, generalized, including feet, legs, hands, arms, and face). The presence of nutritional edema of any grade indicates severe acute malnutrition. One can define the presence and severity of wasting by the weight-for-height z score. Wasting is considered to be mild when the weight-for-height z score is between -1 and -2, moderate when it is between -2 and -3, and severe when it is less than -3 (**Table 3**). One may also use MUAC to determine wasting. MUAC z scores are available by age for both males and females, but for simplicity many malnutrition programs consider a MUAC of less than 110 mm to be severe wasting and 110-125 mm to be moderate wasting for children aged 6-59 months.

The Waterlow criteria use percentage of expected weight for height to define wasting (**Table 2**). If one uses the percentage of the median weight for height, less than 70% would be considered severe wasting and 70%-80%, moderate wasting. One may use the Gomez criteria when a height measurement is unavailable, though they might be less accurate because they do not account for length/height (**Table 2**). One can also use the body mass index (BMI) to classify malnutrition, and doing so might be useful in adolescents and adults. BMI curves and z scores for age are available. For an adult, malnutrition can be defined as involuntary weight loss greater than 10% or weight less than 90% of ideal weight. To assess the nutritional status of an adult, a formula for estimating

Table 2. Waterlow and Gomez criteria

Waterlow criteria—chronic malnutrition		
Stunting:	$\frac{\text{Actual ht (cm)}}{\text{Expected ht (cm) for age at 50\%ile}} \times 100$	
Stage 0 (normal)	>95%	
Stage I (mild)	90%–95%	
Stage II (moderate)	85%–90%	
Stage III (severe)	<85%	
Waterlow criteria—acute malnutrition		
Wasting or acute malnutrition:	$\frac{\text{Actual wt (kg)}}{\text{Expected wt (kg) at patient's ht center}} \times 100$	
Stage 0 (normal)	>90%	
Stage I (mild)	80%–90%	
Stage II (moderate)	70%–80%	
Stage III (severe)	<70%	
Gomez criteria—acute malnutrition		
% of ideal body wt:	$\frac{\text{Actual wt (kg)}}{\text{Expected wt for age (kg) at 50\%ile}} \times 100$	
1st degree (mild)	75%–85%	
2nd degree (moderate)	64%–74%	
3rd degree (severe)	<64%	
Estimating ideal body wt for adults		
Male: 48 kg + 1.07 kg/cm if ht is over 152 cm		
Female: 45.5 kg + 0.9 kg/cm if ht is over 152 cm		

ideal body weight is available in **Table 2**.

Wasting Syndrome

Wasting syndrome is an AIDS-defining condition and is a WHO Clinical Stage 4 diagnosis for both adults and children. In adults, the WHO defines HIV wasting syndrome as unexplained involuntary weight loss (>10% of baseline body weight), with obvious wasting or BMI less than 18.5, plus

- unexplained chronic diarrhea (loose or watery stools more than three times daily) reported for more than 1 month or
- reports of fever or night sweats for more than 1 month without other cause and lack of response to antibiotics or antimalarial agents.

For children, WHO defines wasting as follows:

- persistent weight loss not explained by poor or inadequate feeding or other infections; and/or
- visible wasting of muscles, with or without edema of both feet; and/or

Table 3. WHO/NCHS normalized reference values for weight-for-length and weight-for-height

Boy's Weight (kg)					Length* (cm)	Girl's Weight (kg)				
-4 SD	-3 SD	-2 SD	-1 SD	Median		Median	-1 SD	-2 SD	-3 SD	-4 SD
1.8	2.1	2.5	2.8	3.1	49	3.3	2.9	2.6	2.2	1.8
1.8	2.2	2.5	2.9	3.3	50	3.4	3.0	2.6	2.3	1.9
1.8	2.2	2.6	3.1	3.5	51	3.5	3.1	2.7	2.3	1.9
1.9	2.3	2.8	3.2	3.7	52	3.7	3.3	2.8	2.4	2.0
1.9	2.4	2.9	3.4	3.9	53	3.9	3.4	3.0	2.5	2.1
2.0	2.6	3.1	3.6	4.1	54	4.1	3.6	3.1	2.7	2.2
2.2	2.7	3.3	3.8	4.3	55	4.3	3.8	3.3	2.8	2.3
2.3	2.9	3.5	4.0	4.6	56	4.5	4.0	3.5	3.0	2.4
2.5	3.1	3.7	4.3	4.8	57	4.8	4.2	3.7	3.1	2.6
2.7	3.3	3.9	4.5	5.1	58	5.0	4.4	3.9	3.3	2.7
2.9	3.5	4.1	4.8	5.4	59	5.3	4.7	4.1	3.5	2.9
3.1	3.7	4.4	5.0	5.7	60	5.5	4.9	4.3	3.7	3.1
3.3	4.0	4.6	5.3	5.9	61	5.8	5.2	4.6	3.9	3.3
3.5	4.2	4.9	5.6	6.2	62	6.1	5.4	4.8	4.1	3.5
3.8	4.5	5.2	5.8	6.5	63	6.4	5.7	5.0	4.4	3.7
4.0	4.7	5.4	6.1	6.8	64	6.7	6.0	5.3	4.6	3.9
4.3	5.0	5.7	6.4	7.1	65	7.0	6.3	5.5	4.8	4.1
4.5	5.3	6.0	6.7	7.4	66	7.3	6.5	5.8	5.1	4.3
4.8	5.5	6.2	7.0	7.7	67	7.5	6.8	6.0	5.3	4.5
5.1	5.8	6.5	7.3	8.0	68	7.8	7.1	6.3	5.5	4.8
5.3	6.0	6.8	7.5	8.3	69	8.1	7.3	6.5	5.8	5.0
5.5	6.3	7.0	7.8	8.5	70	8.4	7.6	6.8	6.0	5.2
5.8	6.5	7.3	8.1	8.8	71	8.6	7.8	7.0	6.2	5.4
6.0	6.8	7.5	8.3	9.1	72	8.9	8.1	7.2	6.4	5.6
6.2	7.0	7.8	8.6	9.3	73	9.1	8.3	7.5	6.6	5.8
6.4	7.2	8.0	8.8	9.6	74	9.4	8.5	7.7	6.8	6.0
6.6	7.4	8.2	9.0	9.8	75	9.6	8.7	7.9	7.0	6.2
6.8	7.6	8.4	9.2	10.0	76	9.8	8.9	8.1	7.2	6.4
7.0	7.8	8.6	9.4	10.3	77	10.0	9.1	8.3	7.4	6.6
7.1	8.0	8.8	9.7	10.5	78	10.2	9.3	8.5	7.6	6.7
7.3	8.2	9.0	9.9	10.7	79	10.4	9.5	8.7	7.8	6.9
7.5	8.3	9.2	10.1	10.9	80	10.6	9.7	8.8	8.0	7.1
7.6	8.5	9.4	10.2	11.1	81	10.8	9.9	9.0	8.1	7.2
7.8	8.7	9.6	10.4	11.3	82	11.0	10.1	9.2	8.3	7.4
7.9	8.8	9.7	10.6	11.5	83	11.2	10.3	9.4	8.5	7.6
8.1	9.0	9.9	10.8	11.7	84	11.4	10.5	9.6	8.7	7.7

SD: standard deviation score (or Z-score). Although the interpretation of a fixed percent-of-median value varies across age and height and generally the two scales cannot be compared, the approximate percent-of-median values for -1 and -2 SD are 90% and 80% of median, respectively (Gorstein et al. Issues in the assessment of nutritional status using anthropometry. *Bulletin of the World Health Organization*, 1994, 72:273-283).

*Length is measured for children below 85 cm. For children 85 cm or more, height is measured. Recumbent length is on average 0.5 cm greater than standing height; although the difference is of no importance to individual children, a correction may be made by subtracting 0.5 cm from all lengths above 84.9 cm if standing height cannot be measured.

Table 3. WHO/NCHS normalized reference values for weight-for-length and weight-for-height (continued)

Boy's Weight (kg)					Height* (cm)	Girl's Weight (kg)				
-4 SD	-3 SD	-2 SD	-1 SD	Median		Median	-1 SD	-2 SD	-3 SD	-4 SD
7.8	8.9	9.9	11.0	12.1	85	11.8	10.8	9.7	8.6	7.6
7.9	9.0	10.1	11.2	12.3	86	12.0	11.0	9.9	8.8	7.7
8.1	9.2	10.3	11.5	12.6	87	12.3	11.2	10.1	9.0	7.9
8.3	9.4	10.5	11.7	12.8	88	12.5	11.4	10.3	9.2	8.1
8.4	9.6	10.7	11.9	13.0	89	12.7	11.6	10.5	9.3	8.2
8.6	9.8	10.9	12.1	13.3	90	12.9	11.8	10.7	9.5	8.4
8.8	9.9	11.1	12.3	13.5	91	13.2	12.0	10.8	9.7	8.5
8.9	10.1	11.3	12.5	13.7	92	13.4	12.2	11.0	9.9	8.7
9.1	10.3	11.5	12.8	14.0	93	13.6	12.4	11.2	10.0	8.8
9.2	10.5	11.7	13.0	14.2	94	13.9	12.6	11.4	10.2	9.0
9.4	10.7	11.9	13.2	14.5	95	14.1	12.9	11.6	10.4	9.1
9.6	10.9	12.1	13.4	14.7	96	14.3	13.1	11.8	10.6	9.3
9.7	11.0	12.4	13.7	15.0	97	14.6	13.3	12.0	10.7	9.5
9.9	11.2	12.6	13.9	15.2	98	14.9	13.5	12.2	10.9	9.6
10.1	11.4	12.8	14.1	15.5	99	15.1	13.8	12.4	11.1	9.8
10.3	11.6	13.0	14.4	15.7	100	15.4	14.0	12.7	11.3	9.9
10.4	11.8	13.2	14.6	16.0	101	15.6	14.3	12.9	11.5	10.1
10.6	12.0	13.4	14.9	16.3	102	15.9	14.5	13.1	11.7	10.3
10.8	12.2	13.7	15.1	16.6	103	16.2	14.7	13.3	11.9	10.5
11.0	12.4	13.9	15.4	16.9	104	16.5	15.0	13.5	12.1	10.6
11.2	12.7	14.2	15.6	17.1	105	16.7	15.3	13.8	12.3	10.8
11.4	12.9	14.4	15.9	17.4	106	17.0	15.5	14.0	12.5	11.0
11.6	13.1	14.7	16.2	17.7	107	17.3	15.8	14.3	12.7	11.2
11.8	13.4	14.9	16.5	18.0	108	17.6	16.1	14.5	13.0	11.4
12.0	13.6	15.2	16.8	18.3	109	17.9	16.4	14.8	13.2	11.6
12.2	13.8	15.4	17.1	18.7	110	18.2	16.6	15.0	13.4	11.9

SD: standard deviation score (or Z-score). Although the interpretation of a fixed percent-of-median value varies across age and height and generally the two scales cannot be compared, the approximate percent-of-median values for -1 and -2 SD are 90% and 80% of median, respectively (Gorstein et al. Issues in the assessment of nutritional status using anthropometry. *Bulletin of the World Health Organization*, 1994, 72:273-283).

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- weight for height of -3 standard deviations from the mean, as defined by the WHO Integrated Management of Childhood Illness guidelines; and
- not adequately responding in 2 weeks to standard therapy.

Wasting causes loss of lean body mass. Wasting has declined in many countries since the introduction of ART but is still a frequent complication of HIV, especially in resource-limited and food-insecure environments.

NUTRITION INTERVENTIONS

The level of nutritional support for HIV-infected patients should be guided by their current nutritional status as well as by the presence of risk factors for malnutrition. Causes of malnutrition and risk factors for the development of worsening nutritional status should be comprehensively addressed. Preventing malnutrition through education and increased caloric intake is the goal

for patients with no malnutrition. Patients with moderate or severe acute malnutrition need aggressive inpatient or outpatient management depending on available resources and country-specific guidelines. Although other interventions to address muscle wasting/malnutrition in HIV-infected patients exist, such as administration of testosterone, growth hormone, or anabolic steroids, these are not widely available in most settings.

Address Causes of an Individual’s Malnutrition

To treat nausea and vomiting, recommend small frequent meals; cold foods and beverages; low-fat foods; and bland, nonspicy foods. See the chapter on GI manifestations for an in-depth approach to managing diarrhea. For oral lesions and esophageal pain, recommend smooth-textured, nonspicy foods; cold foods; drinking through a straw to bypass sores; and mild sauces and gravies on

foods to make swallowing easier. Treat the underlying cause of the oral or esophageal lesions/pain if possible. When a patient has developmental delay or neurological deterioration, conduct a feeding and swallowing evaluation if possible. If the patient has problems chewing or swallowing, it may help to purée the food. Enteral (tube) feedings may be the best option if a patient cannot eat.

Foodborne illness can cause serious problems for HIV-infected patients, and patients and caregivers should be educated on simple techniques to avoid these. Teach patients and caretakers to wash their hands before and during food preparation, especially if handling raw meat; to wash fresh produce with clean water; to cook foods thoroughly; to avoid raw meat, fish, and eggs; to avoid unpasteurized dairy products and soft cheeses; to boil bottles and nipples if used (cups should be used, even

Table 4. Equations to estimate energy requirements based on 2006 dietary reference intakes

Infants and young children	
Estimated energy requirement (kcal/day) = total energy expenditure + energy deposition	
0-3 mo	EER ^a = (89 × weight (kg) – 100) + 175
4-6 mo	EER = (89 × weight (kg) – 100) + 56
7-12 mo	EER = (89 × weight (kg) – 100) + 22
13-35 mo	EER = (89 × weight (kg) – 100) + 20
Children and adolescents 3–18 yrs	
Boys	
3-8 yrs	EER = 88.5 – (61.9 × age [yr]) + PA ^b × [(26.7 × weight [kg]) + (903 × height [m])] + 20
9-18 yrs	EER = 88.5 – (61.9 × age [yr]) + PA × [(26.7 × weight [kg]) + (903 × height [m])] + 25
Girls	
3-8 yrs	EER = 135.3 – (30.8 × age [yr]) + PA × [(10.0 × weight [kg]) + (934 × height [m])] + 20
9-18 yrs	EER = 135.3 – (30.8 × age [yr]) + PA × [(10.0 × weight [kg]) + (934 × height [m])] + 25
Adults 19 yrs and older	
Men	EER = 662 – (9.53 × age [yr]) + PA × [(15.91 × weight [kg]) + (539.6 × height [m])]
Women	EER = 354 – (6.91 × age [yr]) + PA × [(9.36 × weight [kg]) + (726 × height [m])]
Pregnancy	
Estimated energy requirement (kcal/day) = nonpregnant EER + pregnancy energy deposition	
1st Trimester	EER = Nonpregnant EER + 0
2nd Trimester	EER = Nonpregnant EER + 340
3rd Trimester	EER = Nonpregnant EER + 452
Lactation	
Estimated energy requirement (kcal/day) = nonpregnant EER + milk energy output – weight loss	
0-6 mo postpartum	EER = Nonpregnant EER + 500 – 170
7-12 mo postpartum	EER = Nonpregnant EER + 400 – 0

These equations provide an estimate of energy requirement. Relative body weight (i.e., loss, stable, gain) is the preferred indicator of energy adequacy.

^aEstimated energy requirement.

^bPhysical activity coefficient (see Table 5).

Adapted from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: Institute of Medicine, National Academies Press, 2006.

Table 5. Physical activity (PA) coefficients for use in EER^a equations

Sex and age group	Sedentary (PAL ^b 1.0–1.39)	Low Active (PAL 1.4–1.59)	Active (PAL 1.6–1.89)	Very Active (PAL 1.9–2.5)
	Typical daily living activities (e.g., household tasks, walking to the bus)	Typical daily living activities plus 30-60 min of daily moderate activity (e.g., walking at 5-7 km/h)	Typical daily living activities plus at least 60 min of daily moderate activity	Typical daily living activities plus at least 60 min of daily moderate activity plus an additional 60 min of vigorous activity or 120 min of moderate activity
Boys 3–18 yrs	1.00	1.13	1.26	1.42
Girls 3–18 yrs	1.00	1.16	1.31	1.56
Men 19+ yrs	1.00	1.11	1.25	1.48
Women 19+ yrs	1.00	1.12	1.27	1.45

^a Estimated energy requirement.

^b Physical activity level.

Adapted from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: Institute of Medicine, National Academies Press, 2006.

Table 6. Dietary reference intakes for total protein by life stage group (g/kg/day)

Life stage group	EAR ^a		RDA ^b		AI ^c
	Males	Females	Males	Females	
0-6 mo					1.52 (9.1)
7-12 mo	1.0	1.0	1.2 (11) ^d	1.2 (11)	
1-3 yrs	0.87	0.87	1.05 (13)	1.05 (13)	
4-8 yrs	0.76	0.76	0.95 (19)	0.95 (19)	
9-13 yrs	0.76	0.76	0.95 (34)	0.95 (34)	
14-18 yrs	0.73	0.71	0.85 (52)	0.85 (46)	
19-30 yrs	0.66	0.66	0.80 (56)	0.80 (46)	
31-50 yrs	0.66	0.66	0.80 (56)	0.80 (46)	
51-70 yrs	0.66	0.66	0.80 (56)	0.80 (46)	
>70 yrs	0.66	0.66	0.80 (56)	0.80 (46)	
Pregnancy		0.88 ^e		1.1 (71) ^e	
Lactation		1.05		1.3 (71)	

^a Estimated average requirement. An EAR is the average daily nutrient intake level estimated to meet the requirements of half the healthy individuals in a group.

^b Recommended dietary allowance. An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals in a group.

^c Adequate intake. If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breastfed infants, the AI is the mean intake.

^d Values in parentheses are examples of the total grams/day of protein calculated from grams/kilograms/day of reference weights.

^e EAR and RDA for pregnancy are only for second half of pregnancy. For first half of pregnancy protein requirements are the same as those of nonpregnant women.

Adapted from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: Institute of Medicine, National Academies Press, 2006.

for very small infants, rather than bottles); and to store foods at proper temperatures.

Preventing Malnutrition by Increasing Calories/Improving Diet

A healthful diet for everyone should include adequate amounts of essential macronutrients (protein, carbohydrates, and fat) and micronutrients (vitamins and minerals). To appropriately advise patients on increasing their caloric intake, knowing what their energy needs are is helpful. Equations to estimate energy requirements, along with adjustments for level of physical activity, are available in the Tables 4 and 5. These are starting points and need to be adjusted for fever, sepsis, lack of weight gain/growth, or continued weight loss. HIV/AIDS can also increase losses of protein. To help estimate protein requirements, **Table 6** gives the dietary reference intakes for total protein intake, including estimated average requirements and recommended dietary allowance (RDA). For children with HIV/AIDS, protein may need to be increased to twice the RDA for protein but should not exceed 4 g/kg of body weight/day to prevent azotemia (too much urea in the blood). Adults with HIV should start with 2-2.5 g/kg/day of protein.

Because of time constraints, calculating the individual nutrient needs of each patient may not always be possible. The WHO recommends increasing the daily caloric intake of asymptomatic HIV-infected infants and children by 10% from the RDA for age and by 20%-30% if they are symptomatic or recovering from acute infections. This is a reasonable estimate, though some patients will have higher caloric needs.

If an illness is causing increased energy and/or protein needs, one must treat the underlying illness. One must also provide a high-calorie, high-protein diet and to teach the family how to increase nutritious foods in the diet that are high in vitamins and minerals. Foods high in calories help to maintain body weight and promote weight gain. Starchy foods make up a large part of the diet and are a good, inexpensive source of calories. These foods include bread, pap, porridge, mealies, sorghum, rice, potatoes, sweet potatoes, samp, millet, and pasta.

Foods high in protein help maintain muscle mass. Sources of protein include, meat (beef, mutton, pork), organ meats, fish, chicken, eggs, milk, dairy products such as yogurt and cheese, and mopani worms and other

insects. Inexpensive sources of protein include legumes such as beans and peas, nuts, peanut butter, and seeds, as well as grains such as rice, maize, barley, oats, wheat, rye, sorghum, millet, and corn. Because the proteins of grains and legumes are low in selected amino acids, they have a lower biologic value than that of meat or dairy. Grains and legumes need to be combined to supplement each other or eaten with another protein source, such as meat, on the same day, or the protein they provide cannot be totally used to synthesize body protein and will be converted into energy. Vegetables and fruits are important sources of essential vitamins and minerals, especially vitamins A and C, and need to be eaten daily.

Fats and oils are also an important part of the diet, providing calories and essential vitamins and fatty acids. Sources of fat include butter, margarine, cooking oils, nuts, avocados, mayonnaise, and salad dressings.

Sugar, sweets, sodas, and desserts are good sources of calories but should not be used in place of more nutritious foods. They can be used in addition to a healthful diet to provide extra calories.

Patients with HIV/AIDS often lack vitamins and minerals because of inadequate dietary intake, infection, and malabsorption. The water-soluble vitamins, such as vitamin C and the B vitamins, need to be included in the diet daily. The fat-soluble vitamins, such as vitamin A, need to be consumed at least every other day. Vitamin D, important for bone development, can be obtained by spending at least 15 min in the sun every other day. Calcium, important in bone development, comes from milk and other dairy products, beans, and leafy green vegetables. Vitamins A, C, E, and B are important for immune system function. Vitamins A and C are important for wound healing, and vitamin A is important for vision. The B vitamins are also important for energy production, red blood cell production, and growth. Vitamin E is important in red blood cell production and as an antioxidant. Minerals such as zinc and selenium are important in immune system function and, along with other minerals such as iron, magnesium, potassium, phosphorus, and copper, are often depleted in association with HIV infection. Because vitamins and minerals play such an important role in the body, a daily multivitamin/mineral supplement can benefit both asymptomatic and symptomatic HIV-positive patients. If giving a vitamin is not feasible, it is especially critical to promote a healthful

Table 7. Sources of vitamins and minerals

Vitamin or mineral	Source
Vitamins A and C	Fruits and vegetables including cabbage, dark green leafy vegetables, spinach, guava, carrots, beetroot, avocado, pumpkin, squash, potatoes, sweet yams, sweet potatoes, tomatoes, oranges, mangoes, pineapple, melons, papaya, and lemons
Vitamin B	Meats, whole grains, milk, eggs, and legumes
Vitamin E	Vegetable oils, dark green leafy vegetables, legumes, and nuts
Zinc	Meat, legumes, and whole-grain cereals
Selenium	Meat, seafood, and cereals
Iron	Meat, fish, poultry, whole-grain cereals, dark green leafy vegetables, and legumes
Magnesium	Green leafy vegetables, legumes, and whole grains
Potassium	Meats, poultry, fish, fruits and vegetables including bananas, potatoes, carrots, tomatoes, and oranges
Phosphorus	Meats, milk, and whole-grain cereals
Copper	Organ meats, shellfish, legumes, nuts, and whole-grain cereals

diet with a variety of foods. **Table 7** lists important vitamins and minerals and their sources.

Inpatient Management of Severe Acute Malnutrition

Severe acute malnutrition is an extremely serious condition, with substantial morbidity and mortality. Severely malnourished HIV-infected adults and children are at even higher risk of poor outcomes. Severe acute malnutrition has been considered a condition best managed in the inpatient setting, though this view is beginning to change (see the following section on outpatient management of severe acute malnutrition). The WHO has developed widely accepted protocols for the inpatient management of severe acute malnutrition that, if properly implemented, can result in less than 5%-10% mortality. HIV-infected children can be managed according to these same protocols, though they may gain weight more slowly than HIV-negative children.

An in-depth review of the inpatient management of severe acute malnutrition is beyond the scope of this chapter, and country-specific guidelines based on international standards should be followed. Commercially available preparations of therapeutic milks (F-75/F-100) and rehydration solution (ReSoMal) are in use in many places, but when this is not available these solutions can be made from easily obtained ingredients according to the recipes in **Table 8**. The following is an overview of the steps in managing severe malnutrition.

1. Treat/prevent hypoglycemia. If unable to test the blood glucose level, assume that all severely malnourished children are hypoglycemic and treat

accordingly. If the dextrostix is less than 3 mmol/L, treat with intravenous (IV) glucose (50-mL bolus of 10% glucose) if available or a 10% oral sucrose solution, with initiation of feeds within 30 min. Repeat the dextrostix if the initial one is low or if the child develops hypothermia or altered level of consciousness.

2. Treat/prevent hypothermia. Hypothermia can be the result of sepsis or lack of insulating fat. May need active rewarming, if rectal temperature is less than 35.5°C (95.9°F), by using warmed blanket, incandescent lamp, or heater; or put the child on mother's bare chest (skin to skin). Ensure that the child is covered at all times, especially at night.

3. Treat/prevent dehydration. Dehydration can be difficult to reliably assess in severely malnourished children, and the mental state, moisture of mouth/tongue/tears, and skin pinch may not be reliable indicators of dehydration in these children. A history of diarrhea along with thirst, hypothermia, sunken eyes, weak or absent radial pulses, and cold hands and feet are usually reliable signs of dehydration—but may also indicate septic shock. Avoid IV fluids except for shock. Give ReSoMal (not ORS) orally or with nasogastric tube 70-100 mL/kg over 12 h (start at 5 mL/kg every 30 min for the first 2 h and then 5-10 mL/kg/h for the next 10 h). Stop ReSoMal if there are any signs of overhydration, which would include increased respiratory rate and pulse rate, engorged jugular veins, or increasing edema.

4. Correct electrolyte imbalance. Provide extra potassium and magnesium and a low-sodium diet

at first. Most commercially available preparations of F-75/F-100 contain adequate amounts of these electrolytes, but when these preparations are not available, make and give an electrolyte-mineral solution as described in **Table 8**.

5. Treat/prevent infection. Infection is common, especially when hypothermia or hypoglycemia is present, though fever may be absent. Measles vaccine should be given if the child is not vaccinated

and is more than 6 months old. Give broad-spectrum antibiotics with oral trimethoprim-sulfamethoxazole or amoxicillin if no complications are present, or IV ampicillin and gentamicin if the child is severely ill or there are signs of infection. Giving an antimalarial is important in malaria-endemic areas.

6. Correct micronutrient deficiencies. Ensure that vitamin A, multivitamin, folate, and adequate amounts of zinc and copper are given at recom-

Table 8. Recipes for therapeutic feeds and other fluids

Ingredient	Amount	
Recipe for ReSoMal		
Water (boiled and cooled)	2 L	
WHO-ORS	One 1-L packet	
Sugar	50 g	
Electrolyte/mineral solution	40 mL (see recipe below)	
Recipe for F-75		
Dried skim milk	25 g	
Sugar	100 g	
Vegetable oil	30 g (or 35 mL)	
Electrolyte/mineral mix	20 mL	
Water	Make up to 1 L or add 860 mL	
Contents per 100 mL: energy, 75 kcal; protein, 0.9 g; lactose, 1.3 g; potassium, 4.0 mmol; sodium, 0.6 mmol		
Recipe for F-100		
Dried skim milk	80 g	
Sugar	50 g	
Vegetable oil	60 g (or 70 mL)	
Electrolyte/mineral mix	20 mL	
Water	Make up to 1 L or add 810 mL	
Contents per 100 mL: energy, 100 kcal; protein, 2.9 g; lactose, 4.2 g; potassium, 6.3 mmol; sodium, 1.9 mmol		
Recipe for electrolyte mineral solution		
	Quantity (g)	Content of 20 mL
Potassium chloride	224	
24 mmol		
Tripotassium citrate (C ₆ H ₅ K ₃ O ₇ H ₂ O)	81	2 mmol
Magnesium Chloride (MgCl ₂ .2H ₂ O)	76	3 mmol
Zinc Acetate, Zn(CH ₃ COO) ₂ .2H ₂ O	8.2	300 µmol
Copper Sulphate, CuSO ₄ .5H ₂ O	1.4	45 µmol
Water	To make up to 2500 mL	
If available, also add 0.028 g of sodium selenate (NaSeO ₄ .10H ₂ O) and 0.012 g of potassium iodide (KI). Dissolve in cooled boiled water and store in sterile bottles in refrigerator.		
Alternative if electrolyte mineral mix unavailable		
Potassium—make a 10% stock solution of potassium chloride (100 gm KCl in 1 L of water)		
For ReSoMal—add 45 mL of stock KCl instead of electrolyte mineral mix		
For F-75/F-100—add 22.5 mL of KCl stock solution instead of 20 mL of electrolyte mineral mix		
Zinc—Make a 1.5% solution of zinc acetate (15 g of zinc acetate in 1 L of water)		
Give this solution orally at a dose of 1 mL/kg/day		
Magnesium—Give a dose of 0.3 mL/kg (to a maximum of 2 mL) of 50% magnesium sulfate intramuscularly one time only		

Adapted from Ashworth A, Khanum S, Jackson A, Schofield C. *Guidelines for the inpatient treatment of severely malnourished children*. World Health Organization, 2003.

mended doses. Iron should not be started initially but should be given once the appetite returns and the child is gaining weight.

- 7. Start cautious feeding.** Give feeds with F-75 as soon as possible, at a total daily volume of 130 mL/kg/day. Children with severe edema should be started on feeds with F-75 at a lower volume—100 mL/kg/day. Feed every 2 h for the first 1-2 days and then every 3 h for about 3 days. Feeding every 4 h should start at day 6-7. As feeding frequency decreases, feeding volume should increase so that the child continues to receive 130 mL/kg/day. This schedule can be sped up for children with good appetites.
- 8. Achieve catchup growth.** When the appetite improves, replace the F-75 with the same volume of F-100 for 48 h. If after 2 days the feeds are well tolerated without any signs of heart failure, then increase each feeding by 10 mL until some of the feeding remains uneaten, and continue at that volume. Solid foods can be reintroduced when the child has been tolerating feeds within a range of 150-220 mL/kg/day for a few days. Weight gain of greater than 10 g/kg/day is optimal.
- 9. Provide sensory stimulation and emotional support.** Provide tender-loving care, a cheerful environment, structured play 15-30 min/day, and physical activity as soon as the child is capable.
- 10. Prepare for follow-up after recovery.** Prepare for discharge when weight for height approaches -1 standard deviation (-1 z score) of NCHS/WHO reference values. Nutrition education for parents will help to prevent relapse. Children recovering from AIDS will have greater stunting (height for age) than that of uninfected children and because of muscle wasting will appear to have some degree of prolonged wasting (weight for height) when plotted on standard reference weight-for-height or BMI charts.

Outpatient Management of Acute Malnutrition

Despite the well-documented effectiveness of inpatient protocols, the mortality of pediatric severe acute malnutrition remains high in many resource-limited settings. There are many reasons for this, including patient overcrowding, inadequate staff to implement the relatively labor-intensive protocols, poor infection control practices resulting in a high rate of hospital-acquired infections, and the limited number of hospitals and inaccessibility of inpatient treatment to large parts

of the population. The high costs to caregivers who must leave their jobs, home responsibilities, and other children/family to care for a sick child in the hospital often result in caregivers' postponing treatment until the malnutrition is far advanced and thus more difficult to treat and associated with worse outcomes. Therefore, focus has shifted to developing outpatient management strategies for pediatric severe acute malnutrition. Ready-to-use therapeutic food (RUTF) has allowed the outpatient management of acute malnutrition and thus resulted in fewer hospital-acquired infections, increased accessibility to the general public, decreased burden on inpatient facilities, and decreased costs to families previously associated with inpatient treatment, resulting in earlier presentation for care, decreased levels of defaulting from care, and thus substantially improved outcomes. Outpatient management of malnutrition is most effective within the framework of a community-based therapeutic care model, which is becoming the basis for many countries' malnutrition programs.

RUTF is an oil-based, energy dense, mineral/vitamin-enriched food used in the management of acute malnutrition in children. It is a type of therapeutic food that can be used in place of therapeutic milk such as F-100. There are many advantages to using RUTF over therapeutic milks. RUTF does not require preparation, may be stored at room temperature with minimal risk of contamination, and has a shelf life of up to 24 months. It is easier to administer than therapeutic milk, facilitates shorter time to discharge from the hospital, and allows ongoing treatment of malnutrition at home.

Outpatient management has also brought about a new classification of malnutrition—complicated versus uncomplicated. Children with acute malnutrition and complications—such as severe pneumonia, severe dehydration, severe anemia, hypo- or hyperthermia, poor appetite, severe (grade 3+++ edema)—are admitted to an inpatient facility to start their treatment. Once these complications have been adequately treated, the children may be transitioned to RUTF and discharged to complete their treatment as outpatients. Acutely malnourished patients without complications who have a good appetite can be prescribed a ration of RUTF on the basis of their weight and then followed up as outpatients. The specific outpatient protocols for the use of RUTF in outpatient malnutrition are beyond the scope of this chapter. Where RUTF is available, local protocols should be followed.

Table 9. Vitamin A supplementation

Schedule of high-dose vitamin A distribution	Dose (IU)
Infants <6 mo	
Non-breastfed infants	50,000, orally
Breast-fed infants whose mothers did not receive vitamin A supplementation	50,000, orally
Infants 6–12 mo	100,000, orally, every 4–6 mo
Children >12 mo	200,000, orally, every 4–6 mo
Mothers	200,000, orally, within 8 wks of delivery

Adapted from World Health Organization. *Vitamin A supplements: a guide to their use in treatment and prevention of vitamin A deficiency and xerophthalmia*. World Health Organization, 1997.

Table 10. Deworming drugs and doses

Drug	Dose for preschool children		Comment
	12–23 mo	24 mo and older	
Albendazole 400-mg tablet	1/2 tablet	1 tablet	Single dose and no need to weigh the children
Mebendazole 500-mg tablet	1 tablet	1 tablet	
Levamisole 40-mg tablet	2.5 mg/kg	2.5 mg/kg	Correct dose should be calculated based on child’s weight
Pyrantel palmoate 250-mg tablet	10 mg/kg	10 mg/kg	

Adapted from World Health Organization. *How to add deworming to vitamin A administration*. World Health Organization, 2004. (WHO/CDS/CPE/PVC/2004.11)

Malnourished, HIV-infected children can be given RUTF per the same protocols as for HIV-negative individuals, and though the rate of weight gain may be slower, many of these children will respond well. ARV medications should be used in combination with nutritional support to have a good response (see the section on ART). Where available, RUTF can be a wonderful tool to treat malnourished, HIV-infected children.

Other Important Interventions

Vitamin A deficiency is a common micronutrient deficiency that can result in blindness as well as increased susceptibility to measles, diarrhea, and malaria. Children are the most susceptible, and in areas of high vitamin A deficiency, supplementation can reduce childhood mortality by more than 20%. In areas of high vitamin A deficiency, universal supplementation is recommended by the WHO, as described in **Table 9**.

Soil-transmitted helminths are a major public health problem in much of the world, including all of Africa.

The three most prevalent worm infections that result in significant consequences for their hosts include roundworms (*Ascaris lumbricoides*), hookworms (*Ancylostoma duodenale* and *Necator americanus*), and whipworms (*Trichuris trichiura*). Worm infection results in significant loss of micronutrients, causes malabsorption of vitamin A, and contributes to anemia and malnutrition, all of which can lead to poor cognitive development. Appropriate treatment can reverse these complications of worm infection. Preschool- and school-aged children and women of childbearing age are at the highest risk for infection and complications of infection.

Deworming treatments are safe and effective. The WHO recommends routine and regular (every 6 months) deworming starting at 1 year of age. Medications and doses for antihelminthic agents are listed in **Table 10**. These medications may occasionally cause some minor nausea and abdominal pain, but because they are poorly absorbed rarely cause serious systemic side effects. Even if children younger than 1 year are accidentally given

an antihelminth, or if older children are given multiple repeated doses, harm will rarely be caused.

ART FOR MALNOURISHED CHILDREN

HIV-infected children who are moderately or severely malnourished may benefit from ART, though the decision to initiate ARVs in these patients is complex. Little information on the safety, pharmacokinetics, or effectiveness of ART in severely malnourished children exists. The optimal timing of initiation of ARVs is not known, and studies are urgently needed. On the basis of expert opinion, the WHO recommends that severely malnourished, HIV-infected children be managed for their malnutrition according to standard protocols and reassessed after the initial management phase. Children with unexplained moderate or severe malnutrition who do not respond to standard nutritional treatment by definition have a WHO Clinical Stage 3 or 4 condition, respectively, and should receive ART. Control of HIV infection by using ARVs combined with nutritional support, will often both be necessary to adequately care for infected individuals. Use of ARVs without nutritional support, or nutritional support without ARVs, will often result in poor treatment responses and outcomes.

INFANT FEEDING IN HIV

The complex interaction between nutrition and HIV is highlighted in the issue of appropriate feeding of infants born to HIV-infected mothers. When a mother who is HIV positive breast-feeds, she risks transmitting the virus to her child. Without safe and appropriate nutritional options for infants other than breast-feeding, weaning children from breast milk can have serious consequences. See the chapter on mother-to-child transmission of HIV for more information and recommendations regarding infant feeding in HIV infection.

Supporting the nutritional needs of mothers who choose to breast-feed is crucial to the outcome of the infant. A breast-feeding mother needs at least 500 extra calories per day. If she does not get enough calories, she can become malnourished, lose bone, and have a poor milk supply. Breast-feeding, HIV-infected mothers may need nutritional support in the form of both caloric and micronutrient supplements.

REFERENCES

1. Anabwani G, Navario P. Nutrition and HIV/AIDS in sub-Saharan Africa: an overview. *Nutrition* 2005;21:96-99.
2. Andresen E, Rollins NC, Sturm AW, et al. Bacterial contamination and over-dilution of commercial infant formula prepared by HIV-infected mothers in a prevention of mother-to-child transmission (PMTCT) programme, South Africa. *J. Trop. Pediatr.* 2007;53:409-414. DOI:10.1093/tropej/fmm059.
3. Ashworth A, Khanum S, Jackson A, et al. Guidelines for the inpatient treatment of severely malnourished children. Geneva, Switzerland: World Health Organization, 2003. Available at <http://whqlibdoc.who.int/publications/2003/9241546093.pdf>. [Accessed September 30, 2005.]
4. Ball CS. Global issues in pediatric nutrition: AIDS. *Nutrition* 1998;14:767-770.
5. Campa A, Shor-Posner G, Indacochea F, et al. Mortality risk in selenium-deficient HIV-positive children. *J. Acquir. Immune Defic. Syndr. Hum. Retrovirol.* 1999;20:508-513.
6. Berhane R, Bagenda D, Marum L, et al. Growth failure as a prognostic indicator of mortality in pediatric HIV infection. *Pediatrics* 1997;100(1):E7.
7. Chandra R. Effect of macro and micronutrient deficiencies and excesses on immune response. *Food Technol.* 1985;39:91-93.
8. Chantry CJ, Byrd RS, Englund JA, et al; Pediatric AIDS Clinical Trials Group Protocol 152 Study Team. Growth, survival and viral load in symptomatic childhood human immunodeficiency virus infection. *Pediatr. Infect. Dis. J.* 2003;22:1033-1039.
9. Chantry CJ, Moya J Jr. Growth, nutrition, and metabolism, pp. 244-268. In: Zeichner S and Read J, eds. *Textbook of Pediatric HIV Care*. Cambridge: Cambridge University Press, 2005.
10. Fawzi WW, Mbise RL, Hertzmark E, et al. A randomized trial of vitamin A supplements in relation to mortality among human immunodeficiency virus infected and uninfected children in Tanzania. *Pediatr. Infect. Dis. J.* 1999;18:127-133.
11. Bahwere P, Binns P, Collins S, et al. *Community-Based Therapeutic Care (CTC): A Field Manual*. Oxford, UK: Valid International, 2006. Available at http://www.fantaproject.org/downloads/pdfs/CTC_Manual_v1_Oct06.pdf. [Accessed October 5, 2006.]

12. Gomez F, Galvan RR, Frenk S, et al. Mortality in second- and third-degree malnutrition. *J Trop Ped.* 1956;9:77-83.
13. Gorbea-Robles MC, Flores-Hernandez LM, Torres-Gonzales F, et al. Nutrition assessment in pediatric patients infected with the human immunodeficiency virus. *Nutr. Clin. Pract.* 1998;13:172-176.
14. Henderson RA, Talusan K, Hutton N, et al. Serum and plasma markers of nutritional status in children infected with the human immunodeficiency virus. *J. Am. Diet. Assoc.* 1997;97:1377-1381.
15. London School of Tropical Medicine and Hygiene. Guidelines for the inpatient treatment of severely malnourished children. June 2005. Available at <http://www.lshtm.ac.uk/nphiru/research/malnutrition.pdf>. [Accessed August 28, 2006.]
16. Long KZ, Santos JI. Vitamins and the regulation of the immune response. *Pediatr. Infect. Dis. J.* 1999;18:283-290.
17. McKinney RE Jr, Wilfert C. Growth as a prognostic indicator in children with human immunodeficiency virus infection treated with zidovudine. AIDS Clinical Trials Group Protocol 043 Study Group. *J. Pediatr.* 1994;125:728-733.
18. McMeans A. Nutrition management of HIV infections and AIDS, 2003. In: Nevin-Folino NL, ed. *Pediatric Manual of Clinical Dietetics*, 2nd edition. Chicago: Pediatric Nutrition Dietetic Practice Group of the American Dietetic Association, 2003.
19. Myatt MA, Khara T, Collins S. A review of methods to detect cases of severely malnourished children in the community for their admission into community-based therapeutic care programs. *Food Nutr. Bull.* 2006;27(3 Suppl):S7-S23.
20. Ndekha MJ, Manary MJ, Ashorn P, et al. Home-based therapy with ready-to-use therapeutic food is of benefit to malnourished, HIV-infected Malawian children. *Acta Paediatr.* 2005;94:222-225.
21. Phillips SM, Motil KJ. Measurement of growth and body composition in children. In: *UpToDate*, Rose BD, (Ed.), Waltham, MA: UpToDate, 2007.
22. Periquet BA, Jammes NM, Lambert WE, et al. Micronutrient levels in HIV-1-infected children. *AIDS* 1995;9:887-893.
23. Position of the American Dietetic Association and Dietitians of Canada: nutrition intervention in the care of persons with human immunodeficiency virus infection. *J. Am. Diet. Assoc.* 2004;104:1425-1441.
24. Schofield C, Ashworth A. Why have mortality rates for severe malnutrition remained so high? *Bull. World Health Org.* 1996;74:223-229.
25. Waterlow JC. Classification and definition of protein-calorie malnutrition. *BMJ* 1972;3:566-569.
26. World Health Organization. Antiretroviral therapy of HIV infected children in resource-limited settings: towards universal access. Recommendations for a public health approach. Geneva, Switzerland: WHO, 2006. Available at http://whqlibdoc.who.int/publications/2007/9789241594691_eng.pdf. [Accessed August 15, 2006.]
27. World Health Organization. How to add deworming to vitamin A administration. Geneva, Switzerland: WHO, 2004. (WHO/CDS/CPE/PVC/2004.11) Available at http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_PVC_2004.11.pdf. [Accessed January 12, 2008.]
28. World Health Organization. Vitamin A supplements: a guide to their use in treatment and prevention of vitamin A deficiency and xerophthalmia. Geneva, Switzerland: WHO, 1997. Available at <http://whqlibdoc.who.int/publications/1997/9241545062.pdf>. [Accessed January 12, 2008.]
29. World Health Organization. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva, Switzerland: WHO, 2006. Available at http://whqlibdoc.who.int/publications/2007/9789241595629_eng.pdf. [Accessed September 29, 2006.]

TRADITIONAL, COMPLEMENTARY, AND ALTERNATIVE MEDICINE

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OBJECTIVES

1. Define allopathic medicine, traditional medicine, and complementary and alternative medicine (CAM).
2. Review various types of traditional therapies and CAM used in treating human immunodeficiency virus (HIV)-infected patients.
3. Discuss risks and benefits associated with the use of traditional therapies and CAM by HIV-infected patients.
4. Explore prevalent patient attitudes regarding traditional therapies and CAM.

KEY POINTS

1. Health care professionals must be knowledgeable about traditional therapies and CAM to assist patients in making informed choices regarding their use.
2. Traditional therapies and CAM are often used in conjunction with conventional treatments for HIV/AIDS patients.
3. The risks and benefits of all therapies, including traditional medicines and CAM options, should be considered by patients and health care providers prior to the start of treatment.
4. When treatment failures and adverse effects of therapy are seen, the possible influence of traditional and complementary therapies needs to be considered.

OVERVIEW

The prevention, diagnosis, and treatment of disease using conventional, Western, evidence-based medical therapies is often referred to as allopathic medicine. The diagnostic modalities and therapies described in other chapters in this curriculum reflect primarily allopathic approaches to HIV and acquired immune deficiency syndrome (AIDS). Although evidence-based approaches such as the use of licensed antiretroviral medications can have an important effect on the lives of patients with HIV/AIDS, health

care practitioners must recognize that for most patients worldwide nonallopathic beliefs and practices play a major role in health care.

In many settings, traditional medical practices are the most widely used forms of health care. These practices incorporate knowledge, beliefs, and health interventions that are based on locally available plants, animals, and minerals, as well as spiritual therapies, manual techniques, and exercises. The goals of these therapies are often similar to the goals of allopathic medicine: to diagnose, prevent, and treat illnesses and to promote well-being. In industrialized countries, adaptations of traditional therapies are termed CAM. Traditional, complementary, and alternative therapies are used by many HIV-infected patients worldwide. For simplicity, this module will use the abbreviation “CAM” to describe traditional, complementary, and alternative medicines.

The World Health Organization estimates that in Africa, North America, and Europe, three of four people living with HIV/AIDS use some form of CAM. In some populations, the numbers are even higher. For patients in many parts of the world, standard Western medical therapies are not easily accessible. In countries where conventional medicines are more readily available, the number of people using CAM therapies has nevertheless been increasing over the past few decades. The implications of the widespread use of CAM are great in terms of both potential benefits and potential risks to patients.

CAM includes a wide range of therapies not usually integrated into standard Western medical practice. These therapies are referred to as complementary when they are used in conjunction with conventional medical practices. Those used instead of conventional practices are considered alternative. A variety of approaches to diagnosis, treatment, and care that fall outside of conventional methods can be classified as CAM.

Defining CAM in a multicultural context presents certain difficulties. Because CAM includes a wide range of therapies and health systems, one must avoid generalizations. What is considered conventional in one setting may be out of the ordinary in another. The list of practices that are considered to be CAM changes as some CAM therapies that are proven safe and effective become a part of mainstream medicine. Health care providers must appreciate the CAM modalities commonly used by their patients. **Table 1** defines some commonly used CAM modalities. For some of these treatments, certain benefits and risks with regard to their use in HIV-infected adults and children have been identified through research studies. Some of these studies and their potential implications for HIV-infected patients are discussed briefly in Tables 1 and 2 and later in the chapter text.

TRADITIONAL HEALERS

In some countries, most of the population relies on traditional medicine for basic health care. Traditional healers are often the most accessible of all health care providers, especially for rural communities. In Ghana, for example, it has been estimated that there is one traditional healer for every 400 people but only one conventional medical doctor for every 12,000 people.

Surveys have shown that in Africa, about 70% of people see traditional providers first when confronted with health-related problems. A 2001 study of HIV-infected people in Cambodia revealed that most consulted a traditional healer for care.

International bodies such as the World Health Organization and UNAIDS have acknowledged and

Table 1. CAM modalities commonly used in HIV/AIDS patients—definitions and potential benefits

Therapy	Theory and Uses
Acupuncture	Acupuncture is a component of traditional Chinese medicine. It is based on the theory that vital energy circulates through the body in channels called meridians. Disease occurs when the flow of vital energy is disrupted and healing occurs when the flow is restored through stimulation of specific points along the energy meridians. Stimulation occurs through a variety of techniques, including needle insertion and cupping. Acupuncture is commonly used for the treatment of pain. Studies have shown acupuncture to be effective in relieving some HIV-related symptoms, including HIV-related peripheral neuropathy.
Bioenergetic therapies	Reiki and other forms of therapeutic touch operate on the belief that energy can be transmitted from the healer to the patient. Practitioners of this form of therapy work either by direct physical contact or through visualization and energy transfer. Some HIV-infected patients report an increased sense of well-being after bioenergetic treatments.
Chiropractic	Chiropractic is based on an association between the spine and nervous system and on the self-healing properties of the human body. Chiropractors believe that misalignment of the joints, particularly the spine, is a major source of morbidity. Through manipulations of the spine and other joints, they seek to reestablish normal body functions. Chiropractic manipulations have been used in children to treat joint and gastrointestinal symptoms and to strengthen the immune system.
Faith healing	Faith healing is a component of many traditional therapeutic modalities. Some Christian communities stress that faith in God allows miraculous healing to take place. Many studies examined the effects of faith and prayer on health outcomes. Sometimes benefits have been seen among patients using faith healing modalities.
Herbs and supplements	Many herbal remedies are used throughout the world for the maintenance of health and treatment of disease. Vitamins and mineral supplements are sometimes added to or used with herbal treatments. Many conventional medicines are derived from natural plant products. Many ongoing studies are evaluating the safety and efficacy of commonly used herbal treatments.
Homeopathy	Homeopathy is a system of medical treatment that operates based on the Law of Similars and the Law of Dilutions. The Law of Similars is the belief that a substance that would cause a symptom in a healthy person can treat the same symptom in a sick person (“like cures like”). According to the Law of Dilutions, the more a substance is diluted, the more powerful it becomes as a therapy. Thus, a very dilute solution made with poison ivy extracts would be a potential homeopathic remedy for an itchy rash. A few small studies have suggested a trend toward improvement of immune function and quality of life among HIV/AIDS patients using certain homeopathic remedies.
Massage	Several different types of massage aim to improve circulation, alleviate pain, promote relaxation, and stimulate the immune system. A study of HIV-infected children in the Dominican Republic suggested that the use of massage may enhance immune function.
Mind–body exercise	Yoga, tai chi, and qi gong are among exercises that are recommended to reduce stress and improve psychosocial function. These techniques can improve fitness and overall sense of well-being.
Traditional healers (e.g., curanderos, shamans, sangomas)	In many societies, certain people are believed to be endowed with special healing powers. Traditional healers are widely used for spiritual support, problem solving, and health care. Healing techniques are often passed from one healer to another through apprenticeships. Traditional healing may take place in the form of a community ceremony or as a private healing ritual or treatment for a sick person.

studied the role and influence of traditional healers. Many international and regional groups are working to improve collaborations between traditional healers and government-sponsored health networks. For example, in Uganda, a nongovernmental organization called Traditional Healers and Modern Practitioners Together Against AIDS (THETA) has been a regional leader in building effective partnerships between traditional and modern practitioners for the care of patients with HIV infection. Their work has included training traditional healers in modern understanding of HIV pathogenesis and treatments as well as studies to document the efficacy of selected traditional herbal remedies. In Botswana, traditional healers are organized into the Dingaka (“doctors”) Association of Botswana. Efforts to train Dingaka Association members regarding the spread of HIV have resulted in increased sexually transmitted disease prevention counseling in the communities that they serve.

The education of traditional healers in conventional medical theories and treatments can play an important role in stemming the transmission of HIV. A 3-year study of the practices of traditional healers in Nigeria revealed that 77% of their treatments involved incisions made with unsterilized blades. Herbal preparations were then rubbed into actively bleeding skin cuts, using unprotected fingers, which were in direct contact with the patient’s blood. Both healers and their patients are at great risk for contracting HIV and other infections through such practices.

As antiretroviral (ARV) medications become more widely available in areas where traditional healers work, it will be important for the healers to be trained in the basic principles of their use. The misuse of antibacterial drugs by untrained practitioners, such as the mixing of low doses of antibiotics into herbal remedies, has exacerbated the problem of antibiotic resistance. Similar practices using ARV drugs would harm patients by leading to the development of viral resistance to the ARVs.

Although the risks of some traditional medical practices are real, traditional healers often use a holistic approach that makes them especially well suited to assist with the management of symptoms and the maintenance of patients’ general well-being. By providing education and regarding traditional healers as partners in the care of HIV-infected individuals, we can maximize benefits to the

patient and minimize potential harm. Traditional healers should be sensitized to the potential risk of infection to themselves as a result of certain practices.

ATTITUDES REGARDING CAM

The use of CAM modalities is widespread among HIV-infected people around the world. Although most studies related to the use of CAM in HIV-infected patients have focused on adults, CAM practices are also known to be used to treat children with HIV. Because of the importance of CAM to families and the potential for interactions between CAM and conventional medicines, asking about CAM use should be a part of medical history taking for all pediatric HIV patients.

There are many reasons why people choose to use CAM. Commonly cited reasons for CAM use include the following:

- Ease of access
- CAM providers’ use of culturally familiar ways to explain the causes of ill health
- Perception of efficacy
- Perception of safety
- Lower cost
- Preference for natural over synthetic medicine
- Greater sense of patient autonomy and taking control over one’s health care
- Greater use of physical touch
- Belief that CAM providers can heal both the body and the spirit
- Pleasant therapeutic experiences
- Rejection of science and technology
- Failure of conventional therapy to provide a cure
- Dissatisfaction with practitioners of conventional medicine
- Frustration with side effects of conventional medicines
- Desperation

Most patients who use CAM do not discuss this use with their mainstream health care providers unless asked specifically in a nonthreatening manner. Patients cite many reasons for not discussing their CAM use with nurses, physicians, and other mainstream providers, including the following:

- They are not asked specifically about the use of CAM therapies.
- They think of the CAM therapies as separate from mainstream therapies and do not recognize that

one may change the efficacy of the other.

- They fear that mainstream providers will perceive their CAM use negatively.
- They fear that mainstream providers will provide lower quality of care if mainstream providers know of their CAM use.
- The use of CAM modalities provides them with an increased sense of control over the illness that may be compromised by disclosure to a paternalistic medical provider.

Despite the widespread use of CAM therapies, many health care providers do not routinely discuss CAM use with their patients. To best serve the interests of their patients, health care providers should establish and maintain trusting relationships with patients and their families; guard against personal biases; and provide balanced, evidence-based advice about therapeutic options. When evidence regarding the safety and efficacy of a treatment choice is lacking, the uncertainty should be discussed openly, and likely risks and benefits should be considered.

EVALUATING CAM THERAPIES

Health care providers must inform patients about known treatment-related risks and must be aware that unknown toxic effects or interactions may exist. Health care providers should seek information about CAM therapies that their patients are using. When studies related to the therapies are available, providers should review their quality and results. Health care professionals can often contact the providers of CAM therapies to help clarify the merits and the risks of the treatment approaches they recommend.

RISKS

Risks associated with the use of CAM therapies can be grouped as follows:

- Causing direct physical harm.
- Causing indirect physical harm as a result of delaying or avoiding the use of conventional treatment that is known to be effective (e.g., ARVs).

Table 2. Selected potential side effects of CAM in children with HIV/AIDS

Therapy	Common Uses	Risks of Interactions
Acupuncture	See Table 1	Complications are rare, but infections and serious tissue trauma (heart rupture, liver injury) have occurred in children.
Chiropractic manipulations	See Table 1	Upper spinal manipulations have been associated with serious adverse events in children, including paralysis, strokes, and vertebral artery dissection.
Cutting and bloodletting	Purging the body of hazardous substances, creating a dermal opening for the application of herbal remedies	Unsterile conditions and reuse of cutting instruments and other tools may lead to the spread of infections, including HIV.
Herb/food product: African potato (<i>Hypoxis</i> sp.)	Immune enhancement, anti-inflammatory	Interacts with cytochrome p450 metabolism. Because many antiretrovirals and other drugs are metabolized through the cytochrome p450 system, drug levels may be altered by concurrent use.
Herb: chaparral (<i>Larrea tridentate</i>)	Antioxidant; anti-fungal; also used for arthralgias, neuralgias, respiratory infections, rashes	Multiple cases of liver damage, including cirrhosis and fulminant liver failure, have been reported.
Herb: coneflower (<i>Echinacea</i> sp.)	Immune stimulant	Use in HIV-positive patients is controversial. Some in vitro studies suggest that it might aid progression of HIV disease.
Herb: ephedra/ma huang	Stimulant, increases energy level	Increases blood pressure, heart arrhythmias; has led to strokes and death.
Herb/food product: garlic (<i>Allium sativum</i>)	Antibacterial and antiviral properties; inhibits platelet aggregation	Decreases plasma concentrations of protease inhibitors; increases bleeding tendency.
Herb: sutherlandia	Immune booster, antioxidant, anti-inflammatory	Interacts with cytochrome p450 metabolism. Because many antiretrovirals and other drugs are metabolized through the cytochrome p450 system, drug levels may be altered by concurrent use.
Herb: St. John's wort (<i>Hypericum perforatum</i>)	Used for the treatment of mood disorders, particularly depression	Reduces the concentration of certain protease inhibitors and nonnucleoside reverse transcriptase inhibitors. (St. John's wort is a potent inducer of CYP3A4 and inhibits several other CYPs.)
Homeopathy	See Table 1	Most but not all homeopathic remedies are diluted beyond the threshold of toxicity. A case of mercury poisoning in an infant after ingestion of homeopathically diluted mercury has been reported.

- Harm may also come from financial or emotional exploitation. The issue of financial exploitation is crucial because many of those infected with HIV are financially disadvantaged.

Many herbs and supplements contain undeclared pharmaceutical drugs, heavy metals, and other contaminants. A recent study of 260 Asian patent medicines sold in the United States revealed that one-third contained undeclared pharmaceuticals and/or heavy metals. The origin, contents, and quality of all remedies ingested or applied to the body should be investigated. Care should be taken to ensure that patients are not unknowingly consuming products that are likely to be harmful to them.

Patients and health care providers should consider the potential risks and benefits of all therapies. Part of this evaluation should include reflection regarding how different therapies may interact with each other. Just as certain prescription drugs should not be given together because of potential adverse effects, some CAM therapies should not be used in conjunction with prescription medications. In HIV-infected patients on ARVs, some herbs hasten the progression of HIV infection because of the herbs' effects on ARV concentrations (**Table 2**). This effect is probably due to induction and inhibition of various cytochrome P450 enzymes involved in ARV metabolism. When patients fail to respond to prescribed therapies, health care professionals should always consider the possibility of such interactions.

Patients stand to gain much by increased understanding of the benefits and risks associated with CAM use. In 1998, the National Institutes of Health of the United States established the National Center for Complementary and Alternative Medicine (NCCAM) to help bridge some of the gaps between conventional and CAM providers. Through scientific studies, NCCAM investigates which CAM practices are effective and why. As of early 2008, 28 NCCAM trials related to the use of CAM for HIV/AIDS-related care were either completed or in progress. These included studies related to the use of acupuncture to treat chronic diarrhea in HIV patients and massage to improve immune function and quality of life in HIV-infected children. Several African and Asian countries are similarly putting considerable resources

into analyzing the benefits and risks of locally popular CAM practices and disseminating results of their studies. Patients and health care providers should look for the results of these and similar studies to guide them in the rational evaluation of CAM therapies.

REFERENCES

1. Bica I, Tang AM, Skinner S, et al. Use of complementary and alternative therapies by patients with human immunodeficiency virus disease in the era of highly active antiretroviral therapy. *J. Altern. Complement. Med.* 2003;9:65-76.
2. Bodeker G, Kabatesi D, King R, et al. A regional task force on traditional medicine and AIDS. *Lancet* 2000;355:1284.
3. Chang BL. Factors associated with complementary therapy use in people living with HIV/AIDS receiving antiretroviral therapy. *J. Altern. Complement. Med.* 2003;9:695-710.
4. Chipfakacha VG. STD/HIV/AIDS knowledge, beliefs and practices of traditional healers in Botswana. *AIDS Care* 1997;9:417-425.
5. Committee on Children With Disabilities. Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability. *Pediatrics* 2001;107:598-601.
6. Ernst E. Serious adverse effects of unconventional therapies for children and adolescents: a systematic review of recent evidence. *Eur. J. Pediatr.* 2003;162:72-80.
7. Ko RJ. Adulterants in Asian patent medicines. *N. Engl. J. Med.* 1998;339:847-848.
8. Madsen H, Andersen S, Nielsen RG, et al. Use of complementary/alternative therapies among pediatric patients. *Eur. J. Pediatr.* 2003;162:334-341.
9. Marcus D, Grollman AP. Botanical medicines: the need for new regulations. *N. Engl. J. Med.* 2002;347:2073-2076.
10. Markowitz JS, Donovan JL, DeVane CL, et al. Effect of St. John's Wort on drug metabolism by induction of cytochrome P450 3A4 enzyme. *JAMA* 2003;290:1500-1504.
11. Pappas S, Perlman A. Complementary and alternative medicine. The importance of doctor-patient communication. *Med. Clin. North Am.* 2002;86:1-10.

12. Peters EJ, Immananagha KK, Essien OE, et al. Traditional healers' practices and the spread of HIV/AIDS in south eastern Nigeria. *Trop. Doct.* 2004;34:79-82.
13. Piscitelli SC, Burstein AH, Welden N, et al. The effect of garlic supplements on the pharmacokinetics of saquinavir. *Clin. Infect. Dis.* 2002;34:234-238.
14. Power R, Gore-Felton C, Vosvick M, et al. HIV: effectiveness of complementary and alternative medicine. *Prim. Care* 2002;29:361-378.
15. Ullman D. Controlled clinical trials evaluating the homeopathic treatment of people with human immunodeficiency virus or acquired immune deficiency syndrome. *J. Altern. Complement. Med.* 2003;9:133-141.
16. Wiwanitkit V. The use of CAM by HIV-positive patients in Thailand. *Complement. Ther. Med.* 2003;11:39-41.
17. Zhou S, Gao Y, Jiang W, et al. Interactions of herbs with cytochrome P450. *Drug Metab. Rev.* 2003;35:35-98.