



Special Nutritional Requirements for People Living with HIV/AIDS



Question

What specific nutritional requirements do people living with HIV need to maintain their health, even if they have not experienced weight loss?

Key Take-Home Messages

- The 'recommended dietary allowance' (RDA) of vitamins and minerals, as defined by the US Food and Nutrition Board³⁰, is most often not sufficient for people living with HIV/AIDS (PHAs)¹⁵
- In comparison with HIV-negative individuals, PHAs have lower serum levels of the following micronutrients: zinc,^{1,5,12,13,15,17} magnesium,¹⁷ iron,²⁰ selenium,^{2,5,13,14,15,17} prealbumin,¹⁷ Vitamin A,^{4,5,7,13,14,15,16,17} Vitamin E,^{4,5,7,14,15,16,17} Vitamin C,^{4,5,15,16,17} B-6,^{4,5,15,17} and B-12 Vitamins.^{4,5,13,15,17}
- Findings from several studies suggest that there is an association between low serum levels of these nutrients and faster disease progression to AIDS^{5,15,16,17}
- Supplementation of vitamins and minerals has been found to slow disease progression significantly in some studies.^{4,10} However, other studies have stated that is unclear if supplementation with micronutrients has any measurable impact on the progression of HIV disease.¹¹
- Malnutrition should be detected, treated and monitored early, in order to improve a PHA's chances of survival and their quality of life.⁴
- Data from the literature cannot be used to develop specific evidence based dietary guidelines for micronutrients because of methodological limitations in several studies.⁵

EVIDENCE INTO ACTION

The OHTN Rapid Response Service offers HIV/AIDS programs and services in Ontario quick access to research evidence to help inform decision making, service delivery and advocacy. In response to a question from the field, the Rapid Response Team reviews the scientific and grey literature, consults with experts, and prepares a brief fact sheet summarizing the current evidence and its implications for policy and practice.

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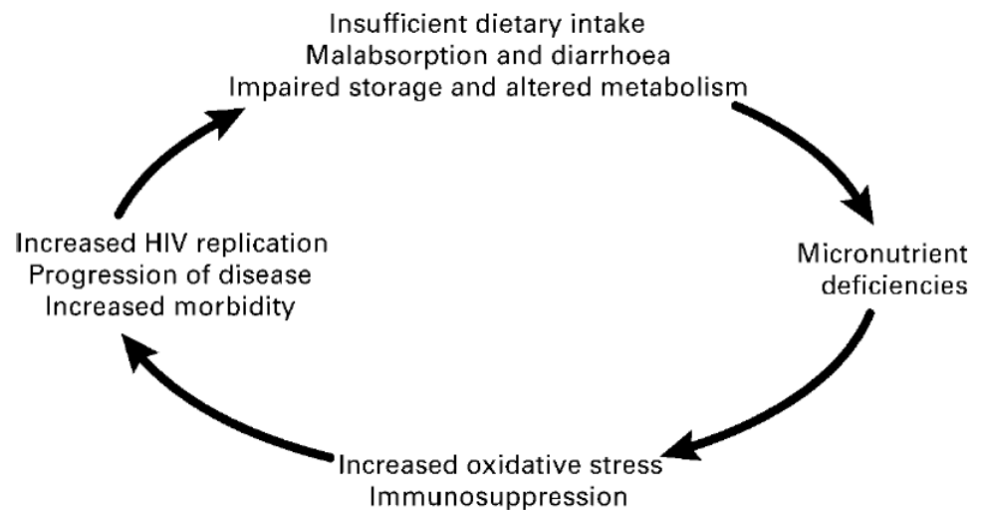
The Issue and Why It's Important

It has been found people living with HIV/AIDS (PHAs) do not always consume the recommended daily allowance for certain micronutrients¹⁵. Additionally, studies of energy balance in HIV-infected individuals have found that weight loss in PHAs is the consequence of reduced energy intake¹⁶. This reduced micronutrient and energy intake in PHAs may occur for a variety of reasons: loss of appetite, aversion to food, dysphagia, nausea, vomiting, and chronic fatigue¹⁵. It could also be because of diarrhea, malabsorption of fats, carbohydrates and some micronutrients, impaired storage of micronutrients, and altered metabolism of micronutrients¹⁵ (see figure 1). All of these issues are common in all stages of HIV¹⁵. Furthermore, HIV-infected patients with severe malabsorption consequently have a lower food intake¹⁹.

Even if a PHA has not lost weight, they may still have deficiencies in micronutrients. It is not until the very advanced stages of HIV, when PHAs have lost a significant amount of weight, that too many clinicians finally appreciate the extent of nutritional problems associated with their patients' HIV status⁴. For instance, some findings suggest that even PHAs who eat "good food" are likely to have vitamin and mineral deficiencies⁴. This can happen before visible signs of sickness and the development of AIDS⁴.

Micronutrient deficiencies can play a significant role in HIV disease progression and death of patients^{4,15} (see figure 1). Such deficiencies may contribute to opportunistic infections and contribute to wasting⁴. As a result, it is important for PHAs to have proper nutrition in order to maintain their health, even if they have not lost weight⁴.

Figure 1. Vicious cycle of micronutrient deficiencies and HIV pathogenesis.¹⁵



What We Found

In comparison with HIV-negative individuals, PHAs have lower serum levels of the following micronutrients: zinc,^{1,5,12,13,15,17} magnesium,¹⁷ selenium,^{2,5,13,14,15,17} prealbumin,¹⁷ Vitamin A,^{4,5,7,13,14,15,16,17} Vitamin E,^{4,5,7,14,15,16,17} Vitamin C,^{4,5,15,16,17} B-6,^{4,5,15,17} and B-12 Vitamins^{4,5,13,15,17}. In

addition, people who inject drugs have been found to be more likely to show antioxidant deficiencies than gay men, with the greatest deficiencies occurring among HIV+ females who had progressed to AIDS.¹⁷ Furthermore, it has been found that all types of immune cells and their products (ie. Interleukins, interferons, and complements) depend on metabolic pathways that use various micronutrients as critical cofactors for their actions and activities⁹. As a result, micronutrient deficiencies accelerate disease progression to AIDS is because without them, the immune system is suppressed and lacks all the necessary tools to fight off infections¹⁵ (see figure 1). In addition, a lack of micronutrients may also lead to oxidative stress, which is an imbalance between the production of reactive oxygen species and the body's ability to detoxify these harmful products and to repair cellular damage¹⁵.

The following is a list of micronutrients which are essential for proper immune system function and which are often deficient in PHAs.

Vitamin A:

This vitamin was the most commonly mentioned vitamin in the literature we identified on the relationship between nutrition and HIV. Up to one-third of adult PHAs may be vitamin A deficient.⁴ Vitamin A serves a protective role for epithelial barriers and immune function.^{7,17} It is important for the function of T and B cells and the generation of antibody responses.¹⁰ Deficiency of this nutrient can lead to night blindness, xerophthalmia and anorexia.¹⁸ Reduced levels are also associated with increased risk of mother-to-child HIV transmission, viral load in breast milk and vaginal secretions, risk of progression to AIDS, reduced adult survival, risk of infant morbidity and mortality and a decline in CD4+ lymphocyte count.^{4,9,11,16,17} Randomized trials with high dose vitamin A supplementation have resulted in reduced mortality and morbidity from diarrhea in HIV-infected children. Research has also shown that CD4+ cell counts can be reversed by correction of vitamin A deficiency¹⁷.

Vitamin B₆:

Deficiency of this nutrient can lead to hyperirritability, mouth soreness, glossitis, peripheral neuropathy.¹⁸ It has also been found that vitamin B₆ deficiency is common in PHAs who are in stage III of HIV disease (as defined by the Centre for Disease Control), even if they have adequate nutrition.¹¹

Vitamin B₁₂:

Early stages of HIV (CD4 count >500) changes the body stores of B₁₂, with middle-stage HIV disease (CD4 count 200-500) being associated with a deficiency.²⁰ Deficiency of this nutrient can lead to macrocytic anemia, and neurological abnormalities such as peripheral neuropathy, altered mental status, reduced CD4**T*-cell counts, increased bone marrow toxicity and increased mortality.^{4, 18} It has also been found that HIV+ men who have sex with men (MSM) in the US with low serum B₁₂ have significantly shorter AIDS-free survival times than those with higher B₁₂.⁴ Improvements in B₁₂ have also been found to be associated with improvements in CD4**T* cell counts⁴. Vitamin B₁₂ and folate replacement is required in the cases of deficiency²⁰.

Folic acid/Folate:

Early stages of HIV (CD4 count >500) changes the body stores of folate, with middle-stage HIV disease (CD4 count 200-500) being associated with a deficiency.²⁰ Folate works closely with B₁₂ but role in HIV is unclear.⁴

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Vitamin C:

Vitamin C plays an important role in the immune system. It stimulates the production of proteins such as interferons, antibodies, and complement which protect cells against bacterial and viral attack.⁴ Vitamin C is even capable of inhibiting HIV replication in T cell lines in the absence of other agents.⁴ One study found that 3 months of supplementation with Vitamin C (in addition to vitamin E) has been shown to reduce oxidative stress.¹⁹ Another study in Canada found that 3 months of supplementation with vitamin C and E significantly reduced HIV viral load.⁴

Vitamin E:

Vitamin E acts as an antioxidant in the immune system.¹⁴ Plasma levels of vitamin E, recorded over time, have been found to be predictive of progression to AIDS.^{4,10,15,19} Supplementation of Vitamin E (800mg/day) and C (1gm/day) in one Toronto study of PHAs reduced markers of oxidative stress.¹⁰ In another study, Vitamin E and C supplementation were found to reduce the production of proinflammatory immune products²⁴ which are associated with wasting. Specifically, when paired with a vitamin B-complex, this combination was found to significantly reduce the risk of wasting.²⁴

Iron:

Iron acts as a cofactor for antioxidant enzymes in the immune system.⁷ PHAs experience chronic anemia which can cause an iron deficiency.²⁰ Supplementation with iron may be helpful to correct for this.²⁰

Selenium:

Selenium acts as an antioxidant in the immune system.¹⁴ Low concentrations were found to cause cardiomyopathy, peripheral myopathy,¹⁸ and be associated with a faster progression to AIDS.²³ It was also associated with an increased risk of mycobacterial infections among HIV infected intravenous drug users (IVDU) in Miami.¹⁰ Other studies found that selenium deficiencies of selenium increased overall risk of mortality even when CD4 counts was factored in the analyses.^{15,17} Plasma selenium levels and mean erythrocyte glutathione peroxidase activity has also been found to have a negative correlation with HIV/AIDS disease progression²³. Selenium supplementation has been recommended for HIV-1/AIDS infected patients receiving HAART, in conjunction with N-acetyl cysteine and L-glutamine to increase CD4 cell counts.²³

Serum Albumin:

Reduced levels of serum albumin are an indicator of malnutrition.²⁰ Low levels of prealbumin were found to be a strong predictor of death, (risk of 3.2 respectively, adjusted for CD4 count)¹⁹. Visceral proteins such as albumin should be supplemented in conjunction with a high-protein diet, except in cases of renal insufficiency.²⁰

Zinc:

Zinc is a cofactor for antioxidant enzymes.⁷ Deficiency of this nutrient can cause growth retardation, alopecia, dermatitis, diarrhea, gonadal atrophy.¹⁸

Dietary Guidelines:

Data from the literature cannot be used to develop specific evidence based dietary guidelines for micronutrients because of methodological limitations in

several studies.⁵ There is one double-blinded clinical trial from Uganda which found certain supplements to be effective in delaying the progression to AIDS. The recommendations from this study can be seen in Table 1 below.²³

The following is a list of food based dietary guidelines⁵ which could be followed to try ensure proper nutrient uptake for PHAs. It should also be noted that some of the literature has stated that even PHAs on a balanced diet may still have vitamin and mineral deficiencies.⁴

The diet of a PHA, especially for children and infants, should have a variety of different foods in order to strive to meet all nutrition needs.⁵

1. **animal-source foods:** meat, poultry, fish, eggs which are high in protein, iron and zinc and which should be eaten daily⁵ Stable HIV/AIDS patients require 0.8g – 1.25g of protein per kg of body weight, in addition to 25 – 30kcal/kg of body weight. Symptomatic patients require 1.5g – 2.0g of protein/kg of body weight as well as 35kcal/kg of body weight. One study using a whey protein enhanced supplement found that CD4 lymphocytes had increased significantly, in addition to mononuclear cell glutathione concentrations, compared to subjects who hadn't received additional protein.²²
2. **milk:** 200-400mL a day is recommended if animal foods are consumed, other wise 300-500mL per day is recommended⁵
3. **grains and legumes:** if the animal source food is not adequate high amounts of grains and legumes are recommended. The bioavailability of zinc can be increased through soaking.⁵
4. **vitamin A rich foods:** carrots, sweet potatoes, pumpkin, green leafy vegetables⁵
5. **vitamin C rich foods:** citrus fruit, cabbage, broccoli, and potatoes⁵
6. **vitamin B rich foods:** animal-source foods, dairy, green leafy vegetables⁵
7. **carbohydrates:** bread and other starch products which are fortified with micronutrients such as folate⁵ (although too much of this can lead to increased cardio vascular risk²²)
8. **fish oil:** contains omega-3 fatty acids which may have the potential to have anti-inflammatory effects²⁸ and reduce increased serum triglyceride levels which are common amongst PHAs on ART.³

Some have found that daily use of a multivitamin can be associated with a reduced risk of AIDS and a significantly reduced risk of a low CD4*⁺T cell count if used in conjunction with a nutritious and nutrient dense diet.^{4, 17}

A note on Muscle Tissue Preservation:

The nutritional substrates arginine (Arg), glutamine (Gln), and the leucine metabolite beta-hydroxy-beta methylbutyrate (HMB) have been found to reduce the loss of muscle and slow muscle protein turnover. Glutamine regulates muscle proteolysis, arginine (precursor of nitric oxide) aids in trauma wound healing and immune stimulation, and HMB exerts a protective effect on muscle, minimizing the processes that cause muscle damage. One study has shown that HMB/Arg/Gln increases the lean tissue of AIDS-wasted patients.²⁵

Table 1: Combination and dosage of nutrients that can slow the progression of HIV disease to AIDS, when taken for 52 weeks, even without anti-retroviral drugs²³

NUTRIENT	DOSAGE
Calcium	23 mg
Magnesium	23 mg
Boron	0.2 mg
Zinc	1.1 mg
Vanadium	2 mcg
Copper	100 mcg
Chromium	8 mcg
Manganese	620 mcg
Silica	770 mcg
AEP Iron (2-amino ethanol phosphate)	600 mcg
Iodine	2.9 mcg
Strontium	25.7 mcg
Molybdenum	0.3 mcg
Vitamin A	390 IU
Provitamin A	390 IU
Vitamin D3	31 IU
Vitamin B1	1.9 mg
Vitamin B2	1.9 mg
Vitamin B3	7.8 mg
D-Calcium Pantothenate	7.8 mg
Vitamin B6	1.9 mg
Vitamin B12	8 mcg
Vitamin C (calcium ascorbate)	23 mg
Vitamin E (D Alpha Tocopheryl Succinate)	5 IU
Vitamin K (Phytonadione)	23 mcg
Biotin	8 mcg
Folic Acid	31 mcg
Choline	4 mg
Inositol	4 mg
P.A.B.A. (Para Amino Benzoic Acid)	2 mg
Dessicated Beef Liver (undefatted)	400 mg
L-Glutamine	180 mg
Hydroxytryptophan L-S (5-HTP)	180 mg
N-Acetyl Cysteine	180 mg
Alpha Lipoic Acid	30 mg
Ascorbic Acid	40 mg
L-Selenomethionine	200 mcg
Organic sugar as a filler	No

Factors that May Impact Local Applicability

In this literature review it was found that there are some limitations to research on nutrition and HIV, which may affect impact local applicability. The first limitation being that the results of micronutrient treatment studies are difficult to interpret because of different study designs, doses, lengths of follow-up time, and study outcomes¹¹. Additionally, serum micronutrient levels are often used as a measure of micronutrient deficiencies, but they may not be an accurate proxy for nutritional status^{11,15}. This is because micronutrient levels are influenced by factors such as gender, time of day of measurement, acute infection, liver disease, technical parameters, and recent intake.¹¹ For instance, low plasma vitamin A and zinc concentrations can be depressed in the presence of an acute phase response, despite adequate body stores.¹⁰ There may also be interaction between micronutrients, and between micronutrients and antiretroviral drug treatment therapy, which makes generalization of findings to diverse populations difficult.¹¹ Measuring cellular levels of nutrients, e.g. liver stores of vitamin A or leukocyte levels of vitamin C, may be more accurate for measuring an individual's micronutrient stores¹⁷

The second limitation is that the body of research about micronutrient supplementation for HIV is inconclusive. Some studies have stated that is unclear if supplementation with micronutrients has any measurable impact on the progression of HIV disease.¹¹ Further research is needed to investigate the true clinical benefit of supplementation of various micronutrients in different clinical settings.¹¹ However, there is still considerable evidence which reveals that malnutrition can exacerbate the course of HIV disease.^{11,16} It has also been shown that micronutrient supplements can alleviate symptoms, delay progression to AIDS, reduce mortality, accelerate growth in children, improve birth outcomes, and reduce maternal mortality.^{2,10,11}

The third limitation is that the results from some of the studies in Sub-Saharan Africa, such as the clinical trial from Uganda²³, may not be applicable to the local Canadian context. This is because of the differences in diet and in general population health status, aside from the issue of HIV infection.

What We Did

We searched the Cochrane Library, Health-Evidence.ca, the Database of Abstracts of Reviews of Effects and Medline using a combination of text search terms [HIV AND (nutrition OR weight loss)]. For the Medline search, we used search filters that optimized the retrieval of systematic reviews and for HIV/AIDS related articles and limited the results to articles published since 1996.