

## Review Article

# Advances in nutrition support for quality of life in HIV<sup>+</sup>/AIDS

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Globally, acquired immunodeficiency syndrome (AIDS) is an epidemic, severe and fatal disease. Along with the etiological factors of human immunodeficiency virus infection (HIV+) and decreased immunity, there are a number of other risk factors including opportunistic infection, malnutrition, wasting syndrome, and oxidative stress. The nutritional problems have been shown to be significant and contribute to health and death in HIV<sup>+</sup>/AIDS patients. Weight loss, lean tissue depletion, lipoatrophy, loss of appetite, diarrhea, and the hypermetabolic state each increase risk of death. The role of nutrition and how oxidative stress is involved in the pathogenesis of HIV+ leading to AIDS is reviewed. Studies consistently show that serum antioxidant vitamins and minerals decrease while oxidative stress increases during AIDS progression. The optimization of nutritional status, intervention with foods and supplements, including nutrients and other bio-active food components, are needed to maintain the immune system. Various food components may be recommended to reduce the incidence and severity of infectious illnesses by forms of bio-protection which include reduced oxidative stress due to reactive oxygen species which stimulate HIV replication and AIDS progression. Probiotics or lactic acid bacteria and prebiotics are sometimes given on the presumed basis that they help maintain integrity of mucosal surfaces, improve antibody responses and increase white blood cell production. People with HIV<sup>+</sup>/AIDS can be informed about the basic concepts of optimal nutrition by identifying key foods and nutrients, along with lifestyle changes, that contribute to a strengthened immune system. Moreover, nutritional management, counseling and education should be beneficial to the quality and extension of life in AIDS.

**Key Words:** HIV infection, AIDS progression, oxidative stress, antioxidants, nutrition, diet supplements

## Introduction<sup>1-4, 9, 35</sup>

AIDS (acquired immunodeficiency syndrome) is a serious condition that comprises a deficiency of the immune system and other complex and severe diseases leading to death. It is the final stage in a progression of diseases resulting from human immunodeficiency virus infection (HIV+) which can be transmitted to other persons.<sup>1, 35</sup> In the early 1980s, the disease was first found in Africa and identified as "slim disease" and was later named AIDS in 1982 and, in 1986, reported to be an HIV infection.<sup>3</sup> Since then AIDS has become well known as an epidemic viral disease which has spread throughout the world.

In 2005, globally it was estimated that the people living with HIV/AIDS were 38.6 (33.4-46.0) million and that 2.8 (2.4-3.3) million died<sup>1</sup>. More than 25 million people have died of AIDS since 1981. The number of people living with HIV increased 3-4 times from 1990 to 2005, and is still rising. Young people (15-24 years old) account for half of all new HIV infections worldwide and about 6,000 become infected with HIV every day.<sup>1</sup>

More than a half of the people with HIV live in sub-Saharan Africa (24.5 million) and about one-fifth live in Asian countries (8.3 million). In China during 2005, it was estimated that 650,000 people were living with HIV, including about 75,000 AIDS patients while there were around 70,000 new HIV infections and 25,000 AIDS deaths.<sup>3</sup> In the USA, during the 1980s, there were rapid

increases in AIDS cases and deaths.<sup>1-4</sup> The number of AIDS cases annually rose to a peak in 1995 and then declined. Different from other regions, the most dramatic drops in both cases and deaths began in 1996, with the development and use of combination antiretroviral therapy and prevention programs.<sup>3</sup> The highest incidence of HIV+/AIDS is in Africa, but the lower risk of HIV infection and AIDS in America and other developed countries could be due to better nutritional status, education, and health hygiene.

The present review seeks to increase the understanding of the important role of nutrition on immunity and health status in HIV infection (HIV+) and in AIDS progression as well as of the inter-relationships between nutrients/non-nutrients and HIV+/AIDS. The review emphasizes the role of nutritional status and oxidative stress in influencing the progression of both asymptomatic and symptomatic AIDS. The potential use of antioxidants and of probiotic and prebiotic products to improve immune function and quality of life of AIDS patients is considered.

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### HIV infection, immunity and other cofactors in AIDS<sup>4-5, 9, 33</sup>

People who become infected with HIV may be asymptomatic for years. Meanwhile, their immune system becomes gradually weakened until they have symptoms. Generally, acute HIV infection progresses, either slowly or rapidly, to early symptomatic HIV infection and finally to advanced HIV infection<sup>5, 33</sup> or AIDS.<sup>2</sup> Most of HIV+ persons will progress to AIDS if not well treated, however, there is a small number of patients, the so-called "long-term non-progressors", who develop AIDS very slowly, or never at all. The immune system in AIDS patients is depleted by HIV infection and they are very susceptible to opportunistic infections which do not normally occur in healthy persons. Common major symptoms are fevers, chills, sweats (especially at night), swollen glands, weakness and weight loss.

With HIV infection, CD4+ T lymphocytes in various organs are the main HIV target and subsequently inactivated or killed by the virus. The immune system in HIV-infected persons and AIDS patients is thereby compromised. The main reason for CD4+ T-lymphocyte depletion is apoptosis. Different biological and chemical agents have been found able to trigger apoptosis in CD4+ T cells, namely gp120 and Tat (some viral proteins), TNF- $\alpha$  (tumor necrosis factor-alpha), a cytokine secreted by activated macrophages and toxins produced by opportunistic microorganisms. The so-called cofactors of AIDS pathogenesis can include alcohol and oxidative stress which can also induce apoptosis of CD4+ T lymphocytes.

The immunodeficiency disorder found is a setting for harmful infectious microorganisms such as bacteria, viruses, parasites and fungi. During the late stages of HIV infection, opportunistic diseases are generally seen. The HIV virus cannot be destroyed and lives in the body undetected for months or years before any sign of illness appears. AIDS patients suffer from many opportunistic microorganisms. These include several severe pathological conditions such as *pneumocystis carinii* pneumonia, tuberculosis, *cytomegalovirus retinitis* and Kaposi's sarcoma. These opportunistic infections accentuate malnutrition and wasting syndromes.<sup>4</sup>

### Oxidative stress in HIV+/AIDS patients<sup>6, 8, 9, 11-12, 16-18, 21-22, 28, 34, 36-37, 39-40</sup>

Oxidation is a critical factor in the pathogenesis of AIDS and HIV expression. Numerous studies have shown that AIDS patients have oxidative stress which is a condition caused by increasing ROS (reactive oxygen species) and

decreasing antioxidants. Some asymptomatic HIV-infected individuals and AIDS patients have decreased levels of antioxidant vitamins, sulfhydryl (SH) potential and total glutathione (GSH). These reducing equivalents are required by microorganisms for division and survival.<sup>19</sup> A decrease in the level of vitamins, and SH-containing compounds, may also result from malnutrition and diarrhea. However, opportunistic infections, diarrhea and malnutrition cannot fully account for the low level of GSH and cysteine (acid-soluble SH) found in HIV-positive, but symptom-free and well-nourished patients. In the AIDS risk groups, exposure to oxidizing agents such as tobacco smoke, drugs (paracetamol), paraquat, ethanol, would also lead to the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG). GSSG is efficiently excreted from cells.<sup>34</sup>

Thus, the systemic decrease of glutathione concentration in HIV+ may result from both, decrease in synthesis and increased degradation. The oxidative stress to which the AIDS patients are subject would lead to anomalies in many cells, including lymphocytes, resulting in opportunistic infection, immunological abnormalities and neoplasia.

Several studies<sup>10, 19, 21</sup>, have observed that the blood levels of vitamin A, beta-carotene, vitamin E and the antioxidative status in HIV+/AIDS persons significantly decreased compared to apparently healthy persons (Table 1). This indicates that there is a lack of antioxidants (i.e. superoxide dismutase-Mn, vitamin E, selenium and glutathione) in AIDS patients which is most likely due to poor nutrition with lowered dietary antioxidants.

AIDS progression could be contributed to by some toxic foods and drinks as well as toxic chemicals, herbicides, alcohol and tobacco.<sup>2-5</sup> All of these cytotoxic and oxidant chemicals could cause cell apoptosis and oxidative stress.<sup>2-3, 7, 13-16, 20, 22</sup> Therefore, anti-apoptotic and antioxidant strategies might be considered, alongside antiviral strategies, in order to design more efficient therapies for AIDS in the near future.<sup>8, 16, 21, 36</sup>

### Nutritional problems in HIV+/AIDS<sup>7, 9-10, 13-14, 19, 25, 30, 32, 42</sup>

Nutrition plays an important role in maintaining the immune system.<sup>1-4</sup> Imbalance of nutritional status is a main cofactor in HIV infection and can contribute to death during AIDS progression. Conversely, asymptomatic and symptomatic HIV infection can also affect nutritional status and play a role at each AIDS step.<sup>6</sup> Several nutritional deficiencies and diet-related effects are frequently

**Table 1.** Blood levels of beta-carotene, vitamins (A and E) and malondialdehyde in Thai HIV+/AIDS patients (Suttajit, M., Unpublished data)

Determinants	Blood Levels		p values
	Normal (N =32)	HIV+ (N =60)	
Beta-carotene (mcg %)	147 $\pm$ 37.1	100.4 $\pm$ 48.8	< 0.001
Vitamin A ((mcg %)	60.1 $\pm$ 11.4	59.1 $\pm$ 33.6	NS
Vitamin E (mg %)	1.21 $\pm$ 0.21	0.90 $\pm$ 0.48	<0.001
Malondialdehyde (mcg %)	20.31 $\pm$ 2.69	25.08 $\pm$ 9.06	<0.005
Plasma antioxidant capacity	0.16 $\pm$ 0.01	2.69 $\pm$ 0.08	<0.005

and evidently found in AIDS patients. Malnutrition and wasting syndromes in HIV<sup>+</sup>/AIDS sufferers are difficult to avoid when there is nausea, vomiting, diarrhea, thrush, esophageal and oral lesions, decreased appetite, lower absorption and lipodystrophy.<sup>6</sup> Hypermetabolic states and drug-treatment side effects also contribute to body weight loss, a decrease in lean body mass<sup>1-3, 6, 8-12, 15, 17-25</sup> These nutritional situations create a high risk of death for HIV<sup>+</sup>/AIDS patients.<sup>6</sup>

Malnutrition should be detected early, treated and monitored, in order to improve the ability to respond to therapies as well as survival and quality of life.<sup>7</sup> Medical nutrition treatment and intervention improve the immune system, slow HIV<sup>+</sup>/AIDS progression and lower the risk of early death.<sup>8</sup>

Nutrition interventions have a wide range of benefits for HIV-related outcomes.<sup>6</sup> The nutritional needs of AIDS patients are weight gain, lean tissue repletion<sup>9</sup> and life extension. The impact depends on the type of intervention, duration, underlying severity and nutrition status<sup>6</sup>. An oral diet intake of a wide variety of nutrient-dense foods combined with oral supplementation and nutritional counseling should help to meet increased needs. However, less than two thirds of nutritional needs may be met by oral feeding, so that other nutritional supports, such as enteral or parenteral feeding, may be required.<sup>10</sup> The supplementation of vitamins and minerals at optimal doses may be also required to maintain optimal nutritional. Judicious and cost efficient use of laboratory markers of nutritional status needs consideration.

As of now, there is no cure for HIV infection or AIDS, nor is there any effective vaccine to prevent HIV infection. Newer medications may slow down the progression of the opportunistic infections and reduce the progression from HIV infection to full-blown AIDS. However, despite extensive improvements in antimicrobial and anti-

retroviral drugs, the incidence of HIV infection is still rising and about three millions are still dying annually from malnutrition, opportunistic diseases and oxidative stress during AIDS progression<sup>4</sup>. AIDS persons often seek alternative approaches using medicinal herbs, and supplements for symptoms as separate treatment or in combination with their conventional medications.

### Dietary supplementation of vitamins, probiotics and prebiotics<sup>23-24, 26, 41</sup>

There is a complex and synergistic relationship between malnutrition and HIV<sup>+</sup>/AIDS. Several studies indicate that there is decreased serum vitamins and minerals and increased oxidative stress during HIV infection and AIDS progression. HIV infection also affects nutritional status and its impact begins early during asymptomatic infection and continues throughout disease progression. Increased reactive oxygen species (ROS) have been shown to stimulate HIV replication and AIDS progression.<sup>5-6, 38</sup> Food and nutrient interventions could help optimise nutritional status and maintain immune system as shown in Table 2. High and specific doses of vitamins (A, B<sub>1</sub>, B<sub>2</sub>, and folic acid, C, E and D), synthetic antioxidants and minerals are proposed by some workers to reduce the incidence and severity of infectious illnesses, and to protect or reduce oxidative stress induced by reactive oxygen species.<sup>8, 13</sup>

The presence of opportunistic microorganisms such as *E. coli*, salmonella and clostridium in the intestinal tract in HIV<sup>+</sup>/AIDS may be managed or prevented by routine use of some products containing lactic-acid producing probiotics. The lactobacillus bacteria can support and maintain the integrity of the mucosal surfaces, improving antibody responses and increasing white blood cell proliferation.<sup>15</sup> The addition of prebiotics which are indigestible polymeric carbohydrates or oligosaccharides (m and

**Table 2.** Recommended supplements of nutrients and non-nutrients for HIV<sup>+</sup>/AIDS

Recommended supplements	Preventive Functions	References
Nutrients:		
- Vitamins and precursors (A and beta-carotene)	-Maintaining and protecting skin and epithelium and increasing immune function	- Fabio <i>et al.</i> <sup>19</sup>
- Vitamins B plus other essentials	-Co-enzymes for energy metabolism and increase of lean body mass	- Carol <sup>10</sup> , Davidhizar <sup>14</sup> , Hosein <sup>23</sup> , Kaiser <sup>24</sup> , Lands <sup>26</sup>
- Vitamins C and E	-Antioxidants, anti-apoptosis and preventing oxidative stress	- Upton <sup>41</sup>
Minerals (Se, Fe and Zn)	-Cofactors for antioxidant enzymes	- Chandra <sup>13</sup>
	-Healing skin irritations	- Davidhizar <sup>14</sup>
Non-nutrients:		
-Antioxidants		
- CoQ <sub>10</sub>	- Increases T4/T8 ratios	- Droge <sup>17</sup> , Folkers <sup>19</sup>
-N-Acetylcystein	- Precursor of glutathione, reduction of HIV replication and induction of apoptosis by TNF- $\alpha$	- Raju <sup>34</sup> , Roederer <sup>35</sup> , Talley <sup>40</sup>
-Prebiotics and probiotics	-Increase immune functions	- De Simone <sup>15</sup>

even simple sugars) in food and beverages can stimulate the growth of probiotic flora.

To prevent malnutrition and loss of lean body mass, HIV+/AIDS patients should be well fed with the spectrum of macro- and micro-nutrients. There is controversy about supplementation with high doses of vitamins and antioxidants in HIV+ patients. In view of the high urinary loss of some nutrients, and questions about what constitutes toxicity, there is a need to redefine ideal dose in the treatment of HIV-infected individuals.

In the prevention of potentially pathogenic infections such as *salmonellosis*, *listeriosis*, *cryptosporidiosis*, *mycrosporidiosis*, *mycobacterium avium* complex (MAC) and candidiasis, nutrition-related toxicity, food safety and hygienicity must be considered. To prevent the growth of such microorganisms, diet supplements need to be evaluated for their pre-biotic role for healthy intestinal microflora and those substrates which may promote pathogenic organism growth.

In conclusion, it is evident that HIV infection and AIDS progression are closely associated with dietary factors and inappropriate nutritional. The goal of nutritional intervention in HIV+/ AIDS is to maintain or replete lean body mass to improve the quality of life. Nutrition counseling, intervention and total parenteral nutrition can help patients gain weight in a relatively healthy fashion. Supplementation with foods, traditional or formulated, and where necessary and science-based, energy, macro and micro-nutrients, essential and favourably bio-active, some with antioxidative properties, and prebiotics plus probiotics, improve disease resistance and health status with less severe HIV infection and risk of AIDS progression.

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