

Nutrients and HIV: Part 2—Vitamins A and E, Zinc, B-Vitamins, and Magnesium

by Lyn Patrick, ND

Abstract

There is compelling evidence that micronutrient deficiencies can profoundly affect immunity; micronutrient deficiencies are widely seen in HIV, even in asymptomatic patients. Direct relationships have been found between deficiencies of specific nutrients, such as vitamins A and B12, and a decline in CD4 counts. Deficiencies appear to influence vertical transmission (vitamin A) and may affect progression to AIDS (vitamin A, B12, zinc). Correction of deficiencies has been shown to affect symptoms and disease manifestation (AIDS dementia complex and B12; diarrhea, weight loss, and zinc), and certain micronutrients have demonstrated a direct anti-viral effect *in vitro* (vitamin E and zinc). The previous article in this series focused on selenium and beta carotene deficiencies in HIV/AIDS. This literature review elucidates how deficiencies of the micronutrients zinc, magnesium, vitamins A, E, and specific B vitamins relate to HIV symptomology and progression, and clearly illustrates the need for nutritional supplementation in HIV disease.

(*Altern Med Rev* 2000;5(1):39-51)

Vitamin A and HIV/AIDS

Vitamin A deficiency is a common occurrence in HIV infection, and serum levels appear to decrease as the disease progresses.¹ Low serum levels of vitamin A were found in 12-19 percent of HIV-positive, asymptomatic subjects in the United States.^{1,2} Vitamin A deficiency was found in an increasingly higher proportion of women than men ($p < .01$) in an HIV-infected, intravenous drug-using population.³

Low serum vitamin A levels were seen in 63 percent of 474 pregnant women in Malawi. Infant mortality was directly associated with maternal serum vitamin A levels.⁴ In a cohort of 133 HIV-infected mothers in the Baltimore area, the risk of perinatal transmission of HIV was associated with maternal vitamin A deficiency. Sixteen percent of transmitters and 5 percent of non-transmitters were severely vitamin A deficient. Vitamin A-deficient mothers were 3.69 times more likely to transmit the virus to their children.⁵ Research at Memorial Sloan Kettering Cancer Center in New York has confirmed maternal vitamin A deficiency as a risk factor for transmission of HIV. Seventy percent of children born to HIV+ mothers were vitamin A-deficient compared to age-matched controls as early as the first few months of life, regardless of the child's HIV status.⁶ Approximately 25 percent of this pediatric population was found to have growth or developmental delays.

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HIV-positive children also develop vitamin A deficiencies prior to AIDS diagnosis.⁷ The development of this deficiency does not appear to depend on dietary intake; in an HIV-positive population judged to have “adequate dietary intake” of vitamin A, 27 percent of the children had low retinol levels.⁸ Dietary and supplemental intake of 9,000-20,000 IU appears to delay progression to AIDS, reducing the relative risk of progression by approximately 50 percent.⁹

Trials with Vitamin A in HIV/AIDS

A randomized, double-blinded trial in Durban, South Africa, evaluated the effect of 5,000 IU retinyl palmitate and 30 mg beta carotene daily during the third trimester of pregnancy, and 200,000 IU at birth in HIV-positive mothers. Women receiving the supplements were less likely to have a pre-term birth (11.4% with vitamin A and 17.4% with placebo; $p=0.03$). Of the 80 pre-term deliveries, those who received vitamin A were less likely to transmit the virus (17.9% on vitamin A vs. 33.8% on placebo).¹⁰ A randomized, placebo-controlled trial of vitamin A in children of HIV-positive mothers in Durban evaluated the use of age-adjusted doses of vitamin A.¹¹ Children received a single dose at one and three months (50,000 IU), six and nine months (100,000 IU), and 12 and 15 months (200,000 IU). At follow-up (16 months), the supplemented group had 28 percent less diarrhea, 40 percent less prolonged bouts of diarrhea, and a 77-percent reduction in hospitalization for diarrhea. A multivariate analysis at the end of the trial suggested the therapeutic benefit was actually seen in the children who had contracted HIV and were later diagnosed HIV seropositive.

Zinc

Zinc is a component of more than 200 mammalian metallo-enzymes.¹² In humans, zinc deficiency can manifest as T-cell lymphopenia, decreased lymphocyte response to

mitogens, depressed thymic hormone activity, a specific CD4+ T-cell population depression, decreased natural killer cell activity,¹³ and depressed serum concentrations of albumin, prealbumin, and transferrin.¹⁴ Zinc has a modulating role in blood sugar regulation, thyroid and gonadal function, adrenal hormone and prolactin production, and calcium/phosphorus metabolism, all of which are disturbed in a state of zinc deficiency.¹⁵ Zinc salts have been shown to have anti-viral activity, either directly or through immune-modulation, against more than 40 viruses.¹⁶

Zinc and HIV/AIDS

In HIV infection, zinc plays specific roles as an anti-oxidant, immune-modulator,¹⁷ and a possible direct anti-viral agent.^{18,19} Zinc, *in vitro*, has been found to inhibit cell death mediated by tumor necrosis factor (TNF), a cytokine linked to cellular apoptosis and wasting syndrome in HIV.²⁰

The HIV protease enzyme, currently the topic of much research and one of the central focuses of pharmaceutical HIV suppression, is necessary to potentiate the production of new HIV-1 viruses.²¹ The HIV virus binds to zinc ions in T-cells in order to produce proviral peptides which form the basis of new infectious viral particles. The HIV-1 protease enzyme then cuts the viral chains to form new infectious viral particles, which are released into the circulation and infect new immune cells. As with other proteases, including collagenase, angiotensin-converting enzyme (ACE), carboxypeptidase A, and neutral endopeptidases, zinc has both an enhancing and inhibiting activity, depending on the concentration of zinc in the surrounding tissues.²² Multiple studies have shown if sufficient zinc ions are bound to the protease it will remain inactive.²³

In HIV replication, viral RNA is transformed into viral DNA via the enzyme reverse transcriptase. Then the enzyme

integrase allows for the integration of viral DNA with host DNA. Zinc binds to the integrase enzyme via “zinc finger protein” structures and allows for optimal activity of the integrase enzyme. Inhibitors of zinc finger proteins are currently the subject of research in HIV pharmacology.^{24,25}

Although the net effect of *in vivo* tissue zinc concentrations on HIV replication has yet to be determined, there is evidence that adding zinc to antiviral medications enhances the medication’s effect. Comparable to the *in vitro* anti-viral activity of zidovudine (AZT), the peptide T22 is four-times stronger when bound to zinc ions via cysteine.²⁶

Baum demonstrated a need for zinc in an AZT-treated population in which 64 percent of the treated patients were zinc deficient, while only 24 percent of the untreated population had low zinc levels.²⁷ AZT metabolism necessitates a zinc-dependent thymidine kinase for conversion to its active form. The medication may contribute to zinc deficiency, which could lead to decreased effectiveness of the drug in a zinc-deficient patient. Baum also found AZT-treated patients with adequate zinc levels had a significantly greater mitogen response, which was not demonstrated in those who were zinc-deficient.²⁷

Zinc Deficiency in HIV/AIDS

The incidence of zinc deficiency in HIV infection has been documented in multiple studies.²⁸ In a survey of 228 in-patients with AIDS, 29 percent had low and 21 percent had marginally low serum zinc levels.²⁹ The presence of zinc deficiency in these patients significantly increased the chance of bacterial infection. While frank zinc deficiencies occur in AIDS patients as a result of malabsorption, medications, altered metabolic states, and fluid loss from nausea, vomiting, and diarrhea,³⁰ zinc deficiency in both plasma and serum has been observed in HIV+ patients in the asymptomatic state as well.^{2,31,32}

Low or marginally low plasma zinc levels were found in 50 percent of 100 healthy, asymptomatic HIV-1 seropositive patients without a history of alcoholism or clinical evidence of nutritional deficiencies.² Although some studies have not seen alterations in HIV patients’ serum zinc levels,³³⁻³⁵ others have documented declining plasma and serum levels as the disease progresses, and have found lower zinc levels in more advanced stages of the disease.^{32,36} Depressions in blood zinc levels in HIV/AIDS may reflect the presence of acute infections; serum zinc levels decrease as hepatic zinc uptake increases, reflecting zinc’s role as an acute-phase reactant.³⁷ Opportunistic infections have been shown to lower serum zinc levels, with depressed serum levels lasting long after the infection is resolved.³⁸

Because of zinc’s role in acute infection and its subsequent altered metabolism in chronic infection, it has been argued that serum levels may not be an accurate reflection of immune impairment related to zinc body stores and zinc availability in HIV.³⁹ Thymulin, a thymic hormone which becomes biologically active only after binding with zinc ions, has been proposed as a more sensitive marker.⁴⁰ Zinc-binding by thymulin allows recognition by T-lymphocytes and enables T-lymphocyte differentiation; thymulin activity is decreased in cases of zinc deficiency. Low levels of thymulin are found in Down’s and Duchenne’s syndrome, type 1 diabetes, and HIV/AIDS.^{41,42} Thymulin levels in ARC (AIDS-Related Complex, an obsolete term which was used to describe AIDS at the beginning of symptom appearance) patients were demonstrated to be low, while serum zinc levels in the same subjects were within normal limits.⁴³

Trials With Zinc in HIV/AIDS

Regardless of the methodological issues of measuring zinc bioavailability, studies looking at zinc supplementation in HIV/AIDS have proven useful. Isa⁴⁴ evaluated 11 men

Table 1. Walter Reed Staging Classification of HIV Infection

	Positive antibody or viral isolation	Chronic lymphadenopathy	CD4/mm ³	DHS	Thrush	O.I.
WR0	-	-	>400	NL	-	-
WR1	+	-	>400	NL	-	-
WR2	+	+	>400	NL	-	-
WR3	+	±	<400	NL	-	-
WR4	+	±	<400	P	-	-
WR5	+	±	<400	C and/or +		-
WR6	+	±	<400	PC	±	+

DHS = Delayed hypersensitivity

NL = Normal

P = Partial cutaneous anergy (defined as intact cutaneous response to only one of four test antigens)

C = Complete cutaneous anergy to four test antigens

OI = Opportunistic infection

with AIDS who were classified as Stage 5 according to Walter Reed classification (see Table 1). Before zinc supplementation, serum and blood cell zinc levels did not differ significantly from controls. After 10 weeks' supplementation with oral zinc sulfate, providing 0.45mg/kg/day of elemental zinc, there was a significant ($p < 0.05$) increase in mean CD4+ cells (from 280 to 390/mm³). Absolute counts of CD3+ lymphocytes also rose significantly. During supplementation, all patients exhibited progressive weight gain, with a mean increase of seven pounds ($p < 0.001$), which could not be accounted for by increased calorie intake.

Mocchegiani⁴⁵ followed 18 HIV+ patients with CD4+ of 250-400/mm³ on anti-viral medication (AZT alone) who were supplemented with 12 mg elemental zinc daily for 30 days, and found the relative risk for opportunistic infection was significantly higher in the unsupplemented group on AZT. In 28 HIV+ patients on HAART (two nucleoside analogues and a protease inhibitor) who were supplemented with the same zinc protocol, no significant risk for opportunistic infections was found in the zinc-unsupplemented HAART group. There was an inverse correlation between serum zinc levels and HIV-RNA (viral load) in both groups. This researcher also observed that triple anti-viral therapy improved

zinc absorption and serum zinc levels. Theoretically, zinc absorption might have improved as a result of the anti-inflammatory effect on the gut of a lowered viral load.

Zinc supplementation has also been investigated in pediatric HIV. Thirteen stable HIV-infected children (mean, six years of age) were given oral zinc, 1.8-2.2 mg/kg/day.⁴⁶ Prior to supplementation, nine subjects had low serum zinc levels. After supplementation, six of the nine had normal serum zinc levels. After 3-4 weeks, two patients had significant increases in CD4+ count, and clinical scores improved in four patients. In another small trial of pediatric patients treated with 2 mg zinc/day for three weeks, significant increases were seen in total lymphocyte count, and a doubling of the CD4/CD8 ratio was observed, indicating a relative rise in CD4+ cell numbers.⁴⁷

Zinc Safety in HIV/AIDS

Tang followed a group of 281 HIV-1 positive men for a median 6.8 years in order to determine if dietary and supplemental zinc intake was associated with progression to AIDS.⁹ At any level above 11.6 mg/day, zinc was associated with an increased relative risk for progression, after controlling for age, symptoms, CD4+ count, energy intake, and medication use. With an intake over 20 mg daily, the relative risk increased to 2.06. Interpretation of this data is difficult, particularly since other findings in this study are confusing; intake of vitamin C between 157-254 mg or intake of niacin between 36.6-61.0 mg/day was associated with a higher risk of progression than either higher or lower levels of either nutrient. Other epidemiological and clinical studies of zinc intake, serum zinc levels, and their relationship to progression to AIDS found no evidence of increased risk of progression with increasing dietary/supplemental zinc intake.^{32,48}

Clearly, more studies looking at zinc regulation of viral replication and dosing

studies in HIV are needed, as zinc is clearly a key component of viral replication and inhibition of replication. In light of the adverse effects of zinc deficiency in HIV/AIDS, maintenance of normal physiological levels of zinc appears to be indicated.⁴⁹

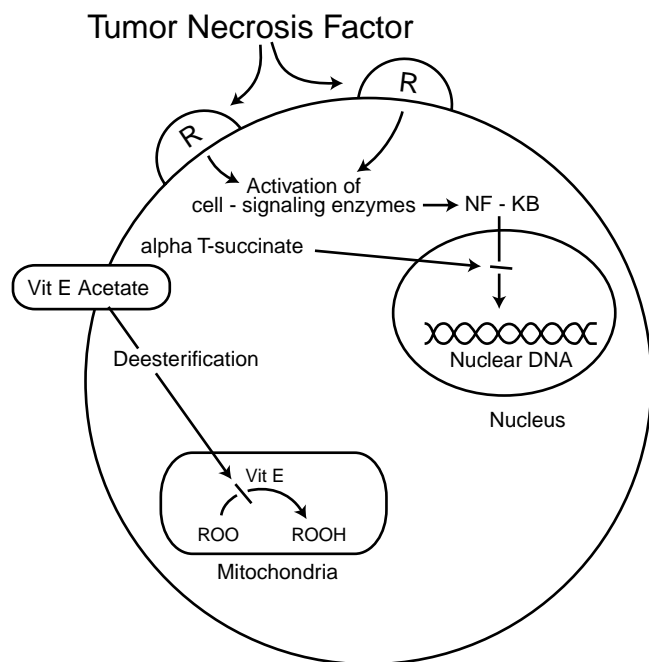
Vitamin E and HIV/AIDS

Vitamin E nutriture has been demonstrated to be significantly lower in HIV-positive patients than controls. In a dietary assessment study of 100 asymptomatic HIV+ men, 26 percent had a vitamin E intake of 50 percent or less of the RDA.² In this same patient population, 27 percent had marginal or overtly low serum levels of vitamin E. In a study of 18 AIDS, 12 ARC, and 13 HIV-positive patients, 50, 58, and 38 percent of patients had vitamin E intakes at least 50 percent below the RDA, respectively.⁵⁰ Even at RDA intakes, serum vitamin E deficiencies have been seen in HIV+ populations.⁵¹ A study of 296 HIV-positive men followed over six years showed a decreased risk of progression to AIDS with a doubling of vitamin E intake.⁴⁸

Vitamin E Trials in HIV/AIDS

The majority of research with vitamin E has been done in a murine model of AIDS and in cell cultures from patients with HIV/AIDS. Research in murine AIDS using a 15-fold increase in dietary vitamin E (160 IU/L liquid diet) demonstrated normalization of immune parameters that are altered in HIV/AIDS.⁵² These include: restoration of mitogen-induced splenic T-cell proliferation, elevation of natural killer cell activity, reduction of interleukin 6 (IL-6) and tumor necrosis factor, reduction of splenomegaly, and normalized cytokine secretion by thymocytes. An increase in mature T-helper cells, normalization of hepatic zinc, vitamin A and vitamin E levels, and a significant reduction of hepatic lipid peroxidation products were also noted.

Figure 1. Cell diagram showing vitamin E inhibition of tumor necrosis and NF-kB activity.



(Adapted from Packer L, Suzuki, Y). Vitamin E and Alpha-Lipoate: Role In Antioxidant Recycling and Activation of the NF-KB Transcription Factor. *Molec Aspects Med* 1993;14: 229-239.

Vitamin E has been shown to protect against bone marrow toxicity, a well established side-effect of AZT.⁵³ In murine bone marrow cell cultures, and in mice given AZT, d-alpha-tocopheryl succinate (ATS) protected against the bone marrow toxicity otherwise seen with AZT. Mice were given ATS orally, 50 IU/kg/day for five days. In cell cultures, ATS inhibited HIV replication and increased the anti-viral effect of AZT 800 percent.⁵⁴

A study of the effects of d-alpha-tocopherol on bone marrow cultures from stage IV (CDC) AIDS patients revealed similar findings.⁵⁵ At a concentration of 1 to 100 micromol/L, d-a-tocopherol was able to significantly increase the growth of bone marrow cells in culture. When added to erythropoietin, the medication used to partially reverse AZT-induced anemia, AZT-suppression of bone marrow cell growth was

significantly reversed. Although AZT is no longer the main medication used to reduce viral levels of HIV-1, bone marrow failure with anemia, leukopenia, and/or thrombocytopenia is still a feature of progressed stages of HIV infection.⁵⁶ The suppression of hematopoietic progenitor cells is not directly due to HIV infection, since only a minority of these cells become infected.⁵⁷ It has been suggested this effect is instead mediated indirectly by cytokine-induced toxicity via oxidative damage.⁵⁵

Anti-viral Mechanisms of Vitamin E

The main cause of CD4+ T-lymphocyte death in HIV is not due to direct viral invasion, but the process of apoptosis, a cell-autonomous "suicide" initiated by several different mechanisms.⁵⁸ One of the main mechanisms which appears to trigger CD4+ cell death is oxidative stress.⁵⁹ Reactive oxygen species (ROS) are involved in cell signaling mechanisms which cause cellular apoptosis and activate HIV-1 replication. Both of these processes can be initiated by inflammatory cytokines, particularly tumor necrosis factor-alpha (TNF- α).⁶⁰ TNF- α is produced as a result of macrophage stimulation and functions as part of the normal immune response, mediating inflammation and producing anti-tumor factors. Overproduction of TNF- α is associated with rheumatoid arthritis, inflammatory bowel disease, liver cirrhosis, and AIDS wasting syndrome, in addition to other aspects of AIDS pathology (see Kaminski et al⁶¹ for a review of TNF- α regulation in HIV). As a result of increased production of TNF- α and other cytokines, immune cells release free radicals which cause cellular damage, initiate apoptosis, and further activate viral replication through the induction of a signaling messenger, nuclear factor kappa B (NF-kB).⁶² Antioxidants, including vitamin E, reduced NF-kB levels in HIV-1-infected lymphocyte cell cultures and decreased production of oxidant

compounds in lymphocytes, which would otherwise lead to viral activation or cell death.^{63,64}

Vitamin E is a lipophilic antioxidant which protects cell membranes from lipid peroxidation.⁶⁵ Packer has demonstrated that α -tocopheryl acetate (E acetate) almost completely blocked NF-kB activation in HIV-1-infected cell cultures, whereas α -tocopherol at the same concentration had a minimal effect.⁶⁶ Alpha-tocopheryl succinate (ATS) completely inhibited NF-kB binding, which was more effective than E acetate, alpha tocopherol, alpha lipoic acid, and N-acetylcysteine.⁶⁶ The authors attribute the NF-kB inhibition effect of E acetate to its ability to pass through the cytosol and inhibit free radical production in the mitochondria (see Figure 1). ATS inhibited DNA binding of NF-kB, resulting in complete inhibition of NF-kB. Human trials of alpha tocopheryl acetate and succinate are necessary to determine if these compounds can successfully halt viral replication *in vivo*.

B Vitamins and HIV/AIDS

B-vitamin deficiencies have been well documented in HIV-positive patients, even in early asymptomatic states.¹ Beach found low riboflavin levels in 26 percent, low B6 levels in 53 percent, and low B12 levels in 23 percent of CDC stage III men.² Boudes et al found low erythrocyte and serum folate levels in 64 percent of 74 HIV-infected individuals at all stages of infection.⁶⁷ Low mean circulating levels of choline have also been found in HIV-infected men and women.⁶⁸ Abrams found an association with increased intake of thiamine and niacin and decreased progression to AIDS.⁴⁸

HIV-infected patients require levels of B vitamins in multiples of the RDA in order to achieve normal plasma levels (see Table 2). Low plasma levels of vitamin B12 and B6 appear to be widespread in HIV infection.⁶⁹ A significant decrease in risk of progression to AIDS was also observed with B-vitamin intakes in multiples of the RDA⁹ (see Table 3).

Table 2. Inadequate plasma levels in relation to dietary intake.⁶⁹

Nutrient	RDA		2-5 X RDA		6-10 X RDA		11-25 X RDA		>25 X RDA	
	HIV ⁺	HIV ⁻	HIV ⁺	HIV ⁻	HIV ⁺	HIV ⁻	HIV ⁺	HIV ⁻	HIV ⁺	HIV ⁻
Vitamin B6 (2mg/day)	18/32	6/15	10/48	2/12	3/6	1/2	0/2		0/10	0/1
Vitamin B12 (2µg/day)	1/4	0/3	6/31	0/12	2/32	1/14	4/26	0/4	0/13	0/3
Vitamin A (3300 IU/day)	1/3	0/4	9/43	0/21	1/32	0/10	3/18	0/3	1/3	
VitaminE (10mg/day)	8/19	1/12	3/29	1/11	1/2	1/3	0/3		2/30	0/2
Zinc (15mg/day)	10/36	2/14	6/24	0/8	1/13	0/1	1/1			

Proportion of HIV⁺ and HIV⁻ subjects with inadequate biochemical status of vitamins and zinc. HIV⁺, HIV⁻, human immunodeficiency virus 1 – seropositive or – seronegative subjects, respectively. RDA, recommended dietary allowance.

Table 3. B-vitamin intake in HIV patients and risk of progression to AIDS⁹

Nutrient and quartile of intake	No. of AIDS events/total no. of subjects in intake stratum	Relative hazard	95% confidence interval
Vitamin B1 (mg/day)			
<1.4	30/71	1.00	
1.4 - 2.4	29/70	1.13	0.67 - 1.90
2.4 - 4.9	28/70	0.80	0.47 - 1.36
>4.9	21/70	0.63	0.36 - 1.11
Vitamin B2 (mg/day)			
<2.0	29/71	1.00	
2.0 - 3.0	27/70	0.99	0.59 - 1.68
3.0 - 5.9	32/70	0.98	0.58 - 1.66
>5.9	20/70	0.61	0.34 - 1.08
Vitamin B6 (mg/day)			
<2.0	31/71	1.00	
2.0 - 3.2	27/70	0.87	0.51 - 1.47
3.2 - 5.7	28/70	0.81	0.48 - 1.38
>5.7	22/70	0.60	0.35 - 1.05

Vitamin B6

Vitamin B6 deficiency appears to be prevalent in CDC stage III individuals, despite an adequate dietary intake of B6.⁷⁰ Thirty-four percent of 44 asymptomatic HIV-positive subjects in the study were B6 deficient, as evidenced by assessment of red cell aspartate aminotransferase stimulation. Another 30 percent had marginal B6 status, despite dietary intake over RDA levels in most of the subjects in the study. Vitamin B6 status in these patients was significantly associated with immune function; deficient patients showed a decreased lymphocyte mitogen responsiveness and reduced natural killer cell cytotoxicity when compared to those who were B6 replete/HIV-positive ($p < .04$). Vitamin B6 deficiencies have

been linked to lowered immunologic function as well as increased risk for certain malignancies.^{71,72}

Vitamin B12

Vitamin B12 deficiency, defined as a low serum B12 level, occurs commonly in HIV/AIDS; the incidence varies from 10-35 percent, depending on the population size and stage of progression.^{67,73-77} Even in studies of asymptomatic HIV-positive patients, seven percent have been found to have frank B12 deficit.⁷⁸ B12 malabsorption is common in HIV; mechanisms include production of gastric parietal cell antibodies, intrinsic factor antibodies, duodenal and colonic inflammation,⁷⁹ and gastric acid hyposecretion.⁸⁰

Research by Herbert et al has detailed some of the mechanisms involved in B12 malabsorption and metabolism in HIV infection.⁸¹ By assessing levels of holotranscobalamin II (a cobalamin-binding protein) they found evidence of negative B12 balance and B12 deficits in 52 of 95 HIV-positive patients, 79 of whom had normal serum B12 levels (above 250 pg/ml). Negative B12 balance (excretion exceeding absorption) was found in patients with serum levels as high as 500-749 pg/ml, evidenced by low levels of cobalamin-binding (less than 40pg/ml cobalamin on holotranscobalamin II). The authors theorize nerve tissue may be damaged by metabolic changes, such as increased homocysteine and methylmalonate, which are secondary to B12 deficit but are not necessarily correlated with low serum levels of B12.

In 108 HIV-positive men who were followed for 18 months, the development of B12 deficiency was associated with a declining CD4 count ($p=0.0377$), while normalization of B12 levels was associated with higher CD4 counts ($p=0.0061$).¹ In this study, low baseline B12 significantly predicted progression to AIDS, as reflected by CD4 count ($P=0.041$) and an AIDS index—a composite measurement of CD4 cell count and beta 2-microglobulin levels.

Cognitive changes in HIV and AIDS, commonly referred to as AIDS dementia complex, is evidenced by cognitive, behavioral, and motor function abnormalities.⁸² While AIDS dementia is most commonly seen in end-stage AIDS, neurological symptoms are the first evidence of AIDS in 10 percent of patients.⁸³ Vitamin B12 levels were assayed in 64 asymptomatic HIV+ patients, and a significant association was found between low serum B12 levels and cognitive deficits in information processing speed and visuo-spatial problem-solving skills.⁸⁴ Low B12 levels in 64 HIV+ patients referred to a neurology clinic correlated with presence of both peripheral neuropathy and myelopathy.⁷⁷ Twenty percent had either

low serum B12 levels or positive Schilling test. Five of eight symptomatic patients who received parenteral B12 repletion therapy had a therapeutic response within one week of treatment. Reversal of a case of advanced AIDS dementia complex has been achieved by parenteral B12 therapy.⁸⁵

Vitamin B12 repletion may have a direct effect on immunity in HIV+ patients. A study of HIV-negative B12-deficient patients receiving B12 injections of 500 mcg every other day for two weeks resulted in improved lymphocyte counts, CD8+ counts, and improved NK cell activity.⁸⁶

Magnesium

In a study of 64 HIV-positive patients across the spectrum of infection, (27 asymptomatic, 18 symptomatic, and 19 confirmed AIDS), 59 percent were magnesium deficient, which was unrelated to the stage of disease, compared to nine percent of HIV-negative controls.⁶⁸ Magnesium was the most significant mineral deficiency compared to uninfected controls, and low magnesium levels were not attributable to alcohol intake, weight loss, or diarrhea. The only correlation appeared to be serum glutathione concentrations. The authors speculate low magnesium levels might be related to fatigue, lethargy, and impaired mentation in HIV. While not all studies of serum nutrient levels in HIV have seen hypomagnesemia,³⁴ studies reporting low magnesium levels found deficiencies in 30-65 percent of patients.^{87,88} In one study, low magnesium levels in HIV infection were directly related to CD4+ counts.⁸⁷

Conclusion

Surveys of supplement use among HIV+ patients have revealed consistently fewer deficiencies in micronutrients among those taking supplements, particularly antioxidants.⁶⁸ This decreased incidence of deficiency occurred across all stages of the infection;

however, even in those taking supplements, 29 percent still had subnormal levels of one or more antioxidants. In another study, daily multivitamin use was associated with a 30-percent reduced risk of progression to AIDS and a 40-percent reduced risk of low CD4 counts at baseline.⁴⁸ The basis for the use of supplemental micronutrients in the treatment of HIV/AIDS is well established in the literature. Levels of supplementation must be sufficient to normalize serum and tissue levels and to prevent viral replication, which ensues as a result of free radical-induced cytokine proliferation.

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