

AIDS Wasting Syndrome as an Entero-Metabolic Disorder: The Gut Hypothesis

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Abstract

There is an interesting relationship between the HIV virus, the health of the gastrointestinal tract, and AIDS wasting syndrome, involving Tumor Necrosis Factor alpha (TNF α), specific and non-specific immunity in the gut, gut permeability, and oxidative stress. It is hypothesized that the progression of HIV to full-blown AIDS may be impacted by maintaining a healthy gut. A therapeutic protocol which decreases oxidative stress, inhibits TNF α , enhances phase I and II liver detoxification, and improves specific and non-specific immunity in the gut should be part of a therapeutic protocol for HIV-infected individuals. Through a better understanding of the pathophysiology of HIV advancing to AIDS, the practitioner can develop a treatment strategy of nutritional and lifestyle changes which could theoretically prevent an HIV infection from advancing to full-blown AIDS.

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Introduction

HIV-infected individuals tend to progress toward AIDS and routinely develop severe nutritional deficiencies.¹⁻⁸ "Slim disease" is still commonly used as a synonym for AIDS in Africa.⁹ Some AIDS wasting research in the past decade has focused on defining the association between the HIV virus and the gastrointestinal tract.¹⁰⁻¹⁹ When reviewed as a whole, these reports reveal some interesting interrelationships between the HIV virus, Tumor Necrosis Factor alpha (TNF- α),^{20,21} secretory IgA (sIgA),²² the gastrointestinal tract including the liver, and related pathophysiologic changes at the cellular, subcellular, and molecular levels.^{10,23,24} More specifically, HIV replication requires activation of NF- κ B, a viral binding site.^{25,26} Activation of this site initiates viral replication and is signaled to proceed by TNF- α . In fact, HIV has been called a TNF- α disease.²⁷ However, NF- κ B transcription is also common to two other immunologic pathways; i.e., antigen/leukocyte induction of protein kinase C²⁸ and gut/liver pathways associated with oxidative stress.^{29,30} (Fig. 1) All three are interrelated and play a major role in the progression of HIV to full-blown AIDS. In turn, HIV directly promotes TNF- α production in the infected

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CD4 lymphocyte. As these cells die, there is an associated immunodeficiency which is most apparent in the intestine, where potential pathogens are normally present.³¹ In addition to pathogens, toxins and other antigens are ready to adhere to leukocyte binding sites and cause activation of protein kinase C dependent pathways. Protein kinase C also activates NF- κ B. The net result is HIV replication secondary to local mucosal inflammation.³² Inflammation also produces a leaky gut which is capable of overwhelming intestinal and hepatic detoxification pathways, resulting in oxidative stress. Oxidative stress then activates NF- κ B, which activates HIV viral replication. These three major HIV transcriptional factors deplete immunologic defenses and result in progression of HIV to AIDS.

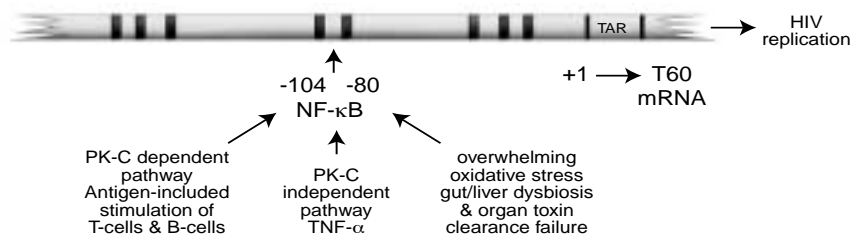
All three factors more or less center around the gut. The prevalence of pathologic flora in the gut lumen, as well as the competency of intestinal defenses to limit leaky gut and oxidative stress can be assessed.³³ The results of these assessments can then be used to guide therapeutic strategies.

Normal Gastrointestinal Tract Immunity

In order to understand AIDS wasting syndrome and its effects on the GI tract, it may be helpful to briefly review the role which a normal GI tract, particularly the small intestine, plays in immunity. It is in the small intestine that the majority of exchanges occur between luminal contents, the mucosa, the lamina propria, and the gut-associated lymphoid tissue (GALT).³⁴⁻³⁶ The lamina propria houses plasma cells and other immune elements; in fact, the GALT is comprised of several times more

immune cell elements than the bone marrow, spleen, and lymph nodes combined.³⁷ Within and beneath the lamina propria rest the Peyer's patches. Luminal microbes are sampled in the Peyer's patch and inactivated by macrophages. Next, T-cell lymphocytes identify epitopes or protein-binding sites on the foreign organisms. This information is then passed to the B-cell lymphocytes. With this information for antibody production, the B-cells leave the Peyer's patch, become plasma cells, and migrate to various tissues throughout the body that have moist mucosal surfaces, including back to the lamina propria of the gut.^{34,35} From here sIgA is secreted onto the surface to protect the mucosa from adhesion by specific enteropathogens.³⁸ If there is no adhesion, then

Figure 1. The three major transcriptional factors regulating NF- κ B HIV induction/replication



HIV replication follows activation of NF- κ B in the viral genome. The three major transcriptional factors inducing activity are 1) protein kinase, 2) independent pathways (cytokines) and, 3) gut/liver detoxification failure causing overwhelming oxidative stress

there is no inflammation, and with no inflammation, there is no TNF production or subsequent leaky gut. The antibody-antigen complex is eventually expelled from the GI tract. Secretory IgA does not kill the organism; instead, it neutralizes the binding sites, preventing adhesion and subsequent disease. This precise immunologic activity is known as the specific immunity of the gut.

Table 1. Key elements in non-specific and specific gut immunity

Nonimmunologic Factors

- Indigenous intestinal flora
- Secretions
- Gastric barrier
- Peristaltic movement
- Liver filtration
- Miscellaneous
 - Pancreatic enzymes
 - Goblet cell mucus

Local Immunologic Defenses

- Secretory IgA
- Cell-mediated immunity
- Other immunoglobulins (IgG, IgM, IgE)

In addition to its role in specific gut immunity, sIgA is the cornerstone of passive immunity.³⁸ When a baby is born, it is incapable of defending itself from environmental bacteria and viruses. Yet, when breast fed, the baby acquires immunity against such organisms. This is because the baby's mother has a mature and ongoing system of autoimmunization described above, the GALT. Sooner or later, everything in the environment is eaten and then processed by the GALT. Just prior to parturition, plasma cells engorge the breast, and subsequently, the mother passes to the baby her immunity to pathogens ingested from her environment through plasma cell secretion of IgA into breast milk in the form of colostrum.

As the baby's GALT matures, it will sample its environment by placing items in its mouth. This will activate its own immune response to imprint lymphocytes and memory cells to defend against bacteria or viruses ingested. This is the same process in cows, providing a rationale for feeding bovine milk im-

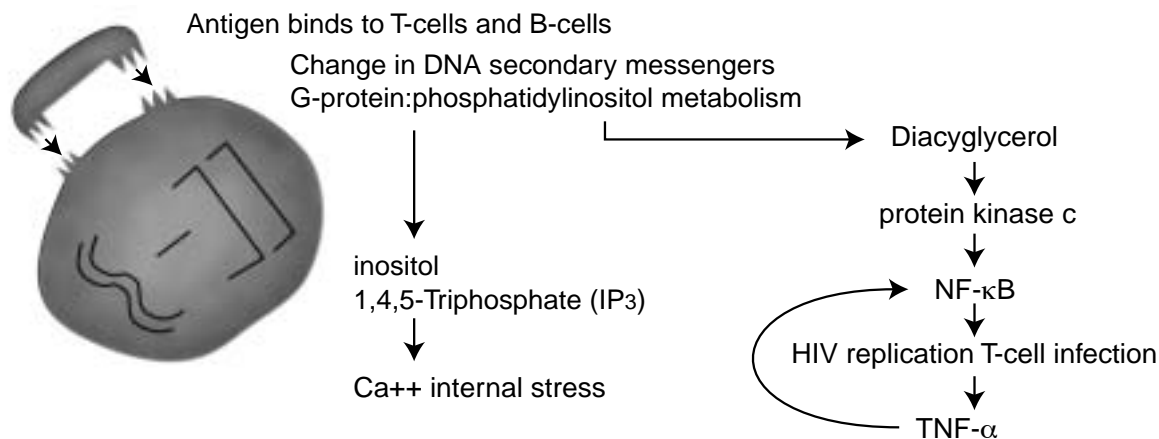
munoglobulin concentrate to immune-suppressed individuals.³⁹ Chickens also sample the environment and make antibodies against barnyard organisms.⁴⁰ Through different mechanisms, the chicken similarly passes its immunity through yolk antibodies (IgY).

Non-specific gut immunity includes hydrochloric acid, pancreatic enzymes, bile, lactoferrin, lactoperoxidase, dietary fiber, symbiotic organisms like Lactobacilli and Bifidobacteria, mucous, and motility. All of these mitigate adhesion in different ways (Table 1).

Immunocompromised Gut

In addition to the plasma cell, the HIV virus is also found in high concentrations in the lamina propria. Fox et al biopsied the intestines of 30 HIV patients and tested for HIV-RNA.⁴¹ They were able to demonstrate high concentrations of HIV-RNA in the crypt epithelium, macrophages, lymphocytes, and eosinophils. As the organism invades and replicates, it crosses into the portal circulation and is delivered to the liver, particularly the Kupffer cells. This represents an advance in disease and is associated with progressive global immune suppression secondary to ubiquitous depression of GALT function. With the gut compromised, there is adhesion of previously harmless but potentially enterotoxigenic organisms to the mucosa with ensuing inflammation.^{42,43} Common symptoms include diarrhea, weight loss, and fever. An immunocompromised individual does not need to ingest a foreign organism to have inflammatory diarrhea;^{14,15} an HIV-infected individual will get diarrhea because the normal balance of intestinal flora and other elements of the nonspecific immune defense system is altered, allowing antigens to cross the leaky gut. In this way, intestinal dysbiosis results in HIV replication by the protein kinase C/NFκB HIV replication pathway (Fig. 2).

Figure 2. Antigen induction of T-cells and subsequent induction of NF- κ B by Protein Kinase C.



Any antigen binding to a T or B-cell receptor initiates the cascade, ending in accelerating self-destruction. Therefore, an attempt to avoid exposure would be a wise part of the therapeutic plan in management of patients with HIV.

The Role of TNF- α in HIV Progression to AIDS

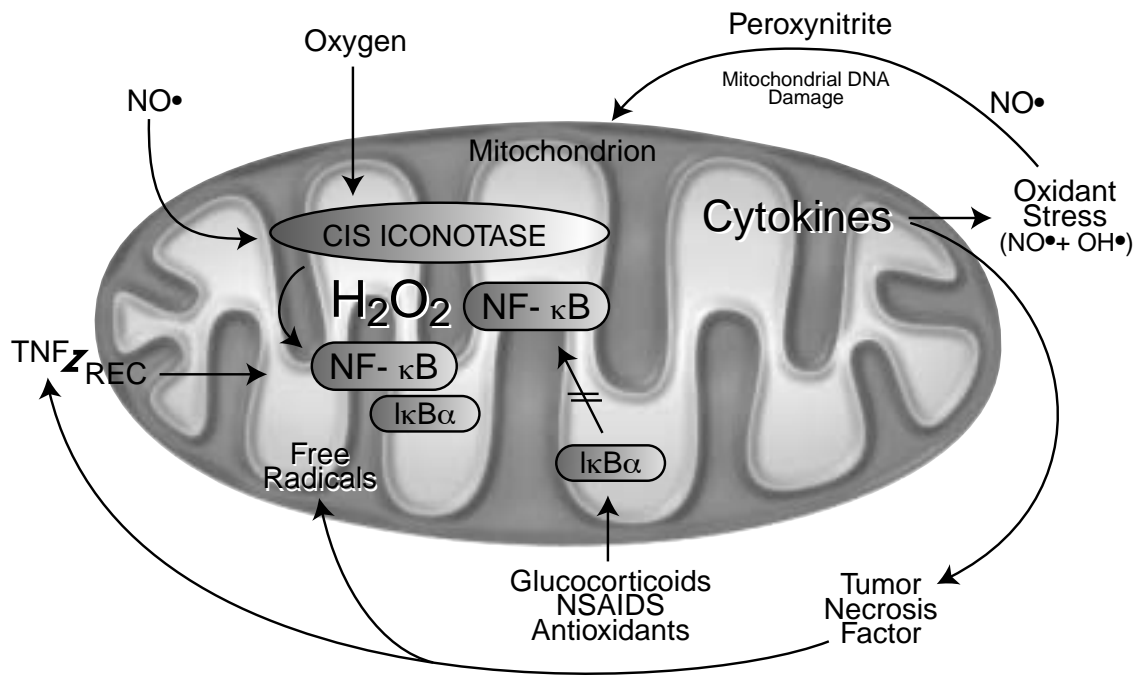
When the body is invaded by a foreign organism, an immune response is activated which, in turn, is mediated by cytokines. Common signs of cytokine activity include elevated white count, fever, anorexia, prostration, increased metabolic rate, negative nitrogen balance, hypoalbuminemia, and lymphopenia. TNF- α has a preeminent role in initiating the immune response. While it is normally beneficial to the host, in situations of overproduction, TNF- α itself can kill the host.⁴⁴ For example, excess acute levels of TNF- α have been associated with toxic shock syndrome, while chronic over-production is associated with inflammatory bowel disease,⁴⁵ rheumatoid arthritis,⁴⁶ and cirrhosis of the liver. TNF- α also induces oxidative stress by increasing the metabolic rate.²⁹ Patients under TNF- α influence exhibit an increase in glycolysis, glycogenolysis, lipolysis, proteolysis, and a negative nitrogen balance. This results in the typical weight loss and wasting seen in AIDS. The reverse may also occur, with oxidative stress inducing TNF- α , which should be considered when developing a therapeutic plan to prevent progression of HIV to AIDS.

As stated above, TNF- α is responsible for an early essential step in the replication of the HIV virus; namely, NF- κ B induction. Further, TNF- α increases the toxic side-effects of the medications used to treat HIV, plays a role in AIDS dementia by its effect on the oligodendrocytes, and suppresses the function of B-cell lymphocytes.²⁷ In the GI tract, TNF- α has been found in the macrophages in the lamina propria, and is therefore strongly implicated in accelerating replication and dissemination of the HIV virus following inflammation from mucosal adhesion of opportunistic enteropathogens.

Cellular and Subcellular Events

At the cellular and subcellular levels, cytokines also increase nitric oxide (NO) production by polymorphoneucleocytes (PMNs) and macrophages.⁴⁷ NO, in turn, sets into motion cellular events resulting in mitochondrial production of H₂O₂, inducing NF- κ B, which leads to an increase in the production of cytokines (Fig. 3). These events, in turn, result in generation of reactive oxygen species which, if not quenched, increase oxidative stress. This self-potentiating cycle is completed as reactive oxygen species

Figure 3. Free radicals cause damage and apoptosis



NO• of oxidative stress uncouples oxidative phosphorylation causing mitochondrial damage and death. The resulting free electrons accumulate, causing cell damage.

themselves stimulate NF-κB. This self-inducing cycle causes more HIV replication; therefore, a therapeutic strategy must be aimed at down-regulating these events in every possible way.

Down-Regulation of the Cytokine/ NF-κB/Oxidative Stress Cycle

Since TNF-α is a principle player, it might be helpful to explore mechanisms to down-regulate TNF-α. The efficacy of glucocorticoids for therapeutic suppression of inflammation is well-known and has been used clinically for decades. However, the mechanism of this relationship remained unclear until recently.⁴⁸ Investigators have elucidated this mechanism and its components, which connect glucocorticoid action to decreased inflammation as shown in Figure 3. It has been suggested that a major effect of glucocorticoids, non-steroidal anti-inflammatory drugs, and antioxidants occurs

through stimulation of NF-κB inhibiting subunit IκBα.^{49,50} As elucidated by Schreck et al, a number of genes involved in early defense reactions of higher organisms can be activated by NF-κB.⁵⁰ NF-κB resides in the cytoplasm of nonstimulated cells in an inactive complex with the inhibitor IκBα. IκBα is released from cells in response to pathogenic stimuli; this allows NF-κB to enter the nucleus uninhibited, bind to elements which exert control over DNA, and induce the synthesis of mRNA. Activation of NF-κB is triggered by a variety of agents including cytokines, interleukin-1 and TNFα, viruses, double-stranded RNA, endotoxins, phorbol esters, UV light, and ionizing radiation. Low concentrations of H₂O₂ activate NF-κB. Subsequent analysis has revealed that antioxidants, as well as a number of other substances tested, suppressed the activation of NF-κB by H₂O₂⁵⁰ (Table 2).

It is also known that glucocorticoids and antioxidants prevent transcription factor

Table 2. Agents which suppress activation of NF- κ B. From Schreck⁵⁰

N-Acetyl-L-cysteine	Scavenger (\bullet SH)	0.1-30 mM	++++ (30 mM)
L-Cysteine	Scavenger (-SH)	30-300 μ M	++++(0.3 mM)
2-Mercaptoethanol	Scavenger (-SH)	14 mM	++++
Glutathione	Scavenger (\bullet SH)	10 mM	++
Pyrrolidine dithiocarbamate	Scavenger ($>$ NCS ₂)	10 μ M - 5 mM	++++(100 μ M)
Diethyldithiocarbamate	Scavenger ($>$ NCS ₂)	100 μ M	++++
Disulfiram	Scavenger ($>$ NCS ₂)	100 μ M	++++
Butylated hydroxyanisol	Scavenger (non S)	10 - 400 μ M	+++ (400 μ M)
Orthaphenanthroline	Metal chelator (CU)	100 μ M	+++
Desferrioxamine	Metal chelator (FE)	100 μ M	+++
Ebselen (PZ 51)	Se peptide with GSH peroxidase activity	50 μ M	++
Diclofenac	cyclooxygenase inhibitor	1 - 50 μ M	-
Dyphenylene iodonium	NADPH oxidase inhibitor	1 - 20 μ M	-
Mannitol	OH-Scavenger	50 mM	-
Dimethylsulfoxide	OH-Scavenger	280 mM	-
Tetramethylurea	OH-Scavenger	10 mM	-
N-Nitro-L-arginine methylester	NO-synthesis inhibitor	5 - 10 mM	-
Quinacrine	PLA ₂ inhibitor	5 μ M	-
Aminobenzamide		10 mM	++
Sodium orthovanadate		1-1000 μ M	+++

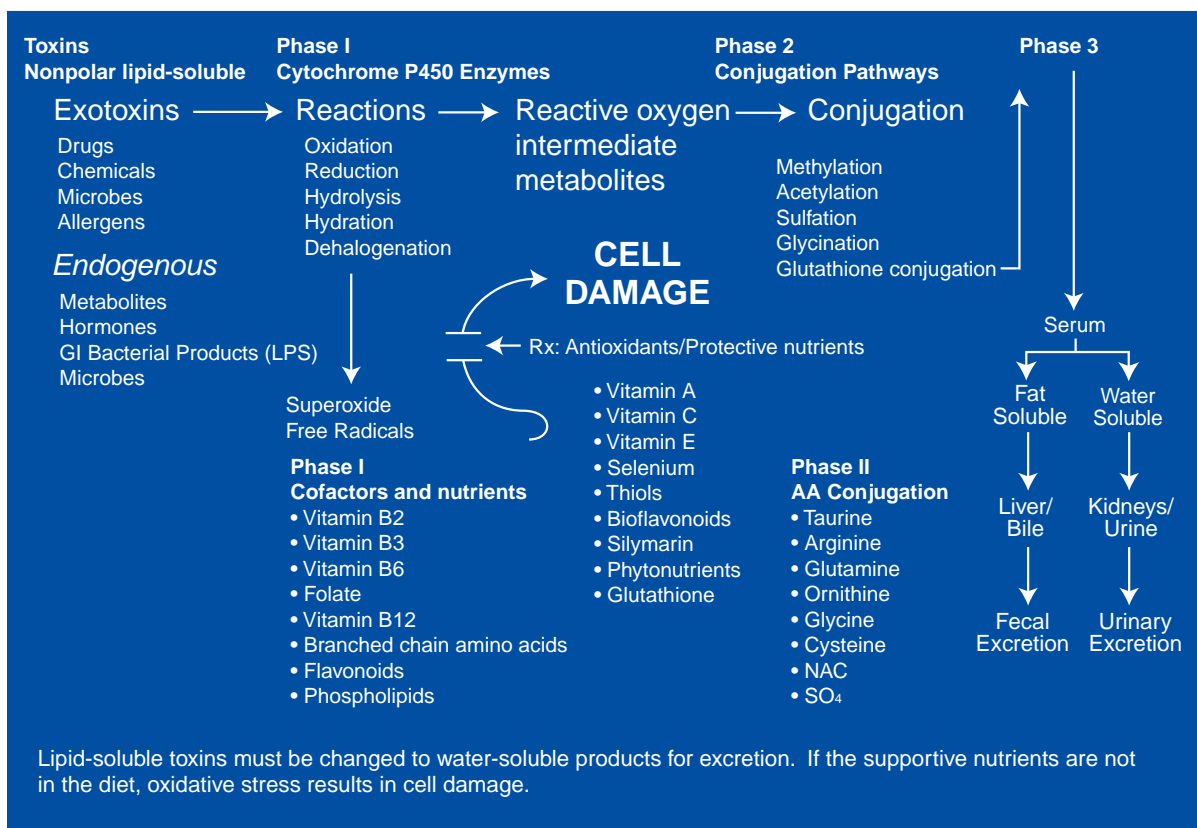
AP-1 from binding to target genes, and thus prevent their activation. This reduces the production of the enzyme collagenase, which is a contributor to tissue damage associated with inflammation.

Adverse effects of glucocorticoid therapies occur because of their generalized alteration of the cell transcription process. These adverse side-effects have not been seen

with concomitant administration of antioxidants.⁴²

There are a number of non-toxic substances of nutritional or botanical origin which inhibit TNF- α and NF- κ B expression. These substances include curcumin from *Curcuma longa*,⁵¹⁻⁵³ N-acetylcysteine,⁵⁴⁻⁵⁶ α -lipoic acid,⁵⁷ omega-3 fatty acids,⁵⁸ L-carnitine,⁵⁹ and the vitamin E ester, α tocopheryl succinate.⁶⁰

Figure 4. Detoxification pathways and supportive nutrients



The Gut/Liver Oxidative Stress-NF-κB Connection

Luminal toxins, whether ingested or locally produced, are detoxified by the Phase I (cytochrome p450) pathways and Phase II conjugating enzymes within the mucosa of the gut and the liver (Kupffer cells)⁶¹ (Fig. 4). In brief, Phase I and Phase II prepares a lipid soluble toxin for excretion in the urine or bile. Phase I alters the molecule by hydrolysis, reduction, oxidation or dehalogenation, producing oxygen free radicals as a by-product, which are harmful if not quenched⁶² by antioxidants including vitamins A, C, E, the trace minerals selenium, copper, zinc, and manganese, and other nutrients like coenzyme Q10, thiols, bioflavonoids, and a host of other phytonutrients. The cytochrome p450 pathway's function requires an ample supply of other common nutrients such as the B vitamins, branched chain amino acids, and phospholipids.

Phase II is responsible for further processing the toxin to an almost completely water-soluble molecule for excretion. This is accomplished via methylation, acetylation, sulfination, glucuronidation, glutathione conjugation, or conjugation with the amino acids glycine, taurine, glutamine, ornithine, arginine, and sulfur derived from cysteine, N-acetylcysteine, and methionine precursors.⁶³ Under conditions of stress or disease, glutamine becomes a conditionally essential amino acid.

Glutathione is a tripeptide composed of glycine, glutamic acid and cysteine, and plays a major role in Phase II detoxification. The processing of glutathione conjugates to water-soluble end-products comprises a major part of Phase II detoxification. Failure of Phase II detoxification results in a build-up of free radicals and toxic biotransformed intermediates generated during Phase I processes. This has special significance in HIV since oxidative stress related to intestinal dysbiosis

by itself is as capable of induction of NF- κ B/HIV replication as is the antigen/protein kinase pathway and TNF- α . A more global view of these events can guide therapy.

Effect of Oxidative Stress on Mitochondria and Cell Death

Death from AIDS is related to HIV infection but more directly related to nutritional aberrancies at the whole body, cellular, and subcellular levels. The tissues that are affected in HIV by TNF- α /oxidative stress are the same tissues that have the highest mitochondrial number and activity – the brain, the heart, the liver, the kidney, the muscles, the adrenals, the GI mucosa, and the cellular elements of the immune system. These are all mitochondrially active, oxidative phosphorylation rich tissues. The mitochondria produces energy which is derived from food, and also normally generates superoxide, hydrogen peroxide, and hydroxyl radicals as a normal consequence of metabolic activity. If not quenched, superoxide can cross membranes and interact with iron and sulfur, or inactivate enzyme systems like cytochrome p450.⁶⁴ That change in intracellular reduction-oxidation potential can have an immediate effect on the function of that cell by altering enzyme activity through the change of metalo-enzyme function. Two to four percent of the oxygen used in the mitochondria generates hydrogen peroxide, which is a very important modulator of the expression of NF- κ B, which then binds to the nuclear DNA, causing the expression of cytokines to be up-regulated, and resulting in oxidative stress. There is increased calcium uptake by the mitochondria, which changes intramitochondrial pH, leading to an increase in nitric oxide and superoxide production, and to mitochondrial death. As this process continues, it eventually causes cell death by apoptosis.

Therapeutic Strategies

A recent study examined selenium deficiency and the rate of HIV progression to AIDS. The researchers discovered that selenium deficiency in HIV-infected persons was associated with nearly a 20 times greater likelihood of death due to AIDS when compared to persons infected with the virus who had adequate selenium levels.⁶⁵ Look et al reported that serum selenium levels were inversely correlated with serum concentration of the cytokines, interleukin 8, and TNF- α receptors.⁶⁶ A selenium deficiency has also been implicated in enhanced virulism of other viral infections, such as the coxsackie enterovirus.⁶⁷ Selenium is required for superoxide dismutase, which is involved with quenching free radicals in the mitochondria, and plays a role in maintaining reduced glutathione levels in the cell.^{68,69}

Alcohol has been shown to increase gut permeability, which is proinflammatory and thus should be avoided.⁷⁰ Since intestinal dysbiosis,⁴ increased gut permeability,^{10,71,72} and impaired hepatic detoxification⁷³ contribute to HIV virulence, tests such as the Comprehensive Digestive Stool Analysis, Gut Permeability, and Comprehensive Hepatic Detoxification (Great Smokies Laboratory, Asheville, NC) may be used to assess status of the gut. Other tests such as membrane fatty acid analysis,⁷⁴ hair trace mineral analysis, and vitamin analysis^{5,6} may provide useful information to tailor a complementary supplement program aimed at down-regulating factors causing NF- κ B release or otherwise limiting proinflammatory mediators or events. A number of anti-TNF- α prescription drugs are available. Some of these, however, have significant side-effects so should be avoided in favor of non-prescription supplements with similar activity including NAC,⁵⁴⁻⁵⁶ curcumin,⁵¹⁻⁵³ L-carnitine,⁵⁹ omega-3 fatty acids,⁵⁸ α -lipoic acid,⁵⁷ and α tocopheryl succinate.⁶⁰

Table 3. Nutrients for consideration in HIV.

Hepatic Phase I and Phase II Support	Intestinal Lumen
<p><i>Phase I</i></p> <ul style="list-style-type: none"> branch chain amino acids B vitamins glutathione flavonoids phospholipids <p><i>Phase II</i></p> <p><i>conjugating amino acids</i></p> <ul style="list-style-type: none"> glycine taurine glutamine ornithine arginine cysteine methionine <p><i>Antioxidants</i></p> <ul style="list-style-type: none"> carotenoids ascorbic acid tocopherols selenium copper zinc manganese coenzyme Q10 thiols bioflavonoids silymarin oligomeric proanthocyanidins lipoic acid <p><i>Favorable prostaglandin precursors</i></p> <ul style="list-style-type: none"> EPA DHA CLA GLA <p><i>Hormones promoting normalization of cytokines</i></p> <ul style="list-style-type: none"> DHEA* 	<p><i>Non-specific immunity</i></p> <ul style="list-style-type: none"> pre- and probiotics soluble and insoluble fibers bismuth salts glutamine <p><i>Specific immunity</i></p> <ul style="list-style-type: none"> hyperimmune bovine colostrum or egg yolk antibody <p>Anti - TNFα</p> <ul style="list-style-type: none"> N - acetylcysteine curcumin lipoic acid α - tocopheryl succinate L - carnitine omega - 3 fatty acids <p>* Mulder JW, Firssen J, Krijnen PH, et al. DHEA as a predictor for progression to AIDS in asymptomatic human immunodeficiency virus-infected men. <i>J Inf Dis</i> 1992;165: 413-418</p>

acids by facultative anaerobes, which serve as the primary fuel for the colonocyte.⁷⁸ Since the enterocytes' (in the small intestine) primary fuel is glutamine,⁷⁸ during times of stress it can become a conditionally essential amino acid and liberal supplementation is recommended.

Prebiotics such as fiber, and probiotics such as Lactobacillus to correct dysbiosis are of value.⁷⁹ In addition to insoluble fiber, watery stools can be bulked up and bound by bismuth-containing agents. Although sIgA may decrease, globulins from dairy cows

such as hyperimmune bovine milk or the egg yolk from the common store-bought egg provide billions of antibody units that can act as surrogate sIgA. If the eggs are poached, quick scrambled, or cooked over easy, there will be no salmonella problem and the antibodies are heat stable.

Other dietary factors such as isoflavones from soy foods have been shown to directly down-regulate tyrosine protein kinase C. Thus, inclusion of foods containing such phytonutrients might be appropriate.⁸⁰

If there is no inflammation, there is no TNF- α . If the intestine is controlled to prevent TNF- α enhancement, then attention can be directed toward simple behavioral modification to include hand-washing and

Therapy should also involve identification and elimination of antigens which induce protein kinase C, particularly in the gut lumen; without antigen there can be no induction. Therefore, an effort must be made to identify ingestion or exposures to antigens, and the patient advised to take steps to eliminate them. The intestine naturally contains bacteria and other organisms, as well as inert antigen. To protect the mucosa from enteropathogen adhesion, recommendations should be made to protect and replete innate and specific gut immune factors. This begins with the anaerobic paste, beneficial bacteria adhering to the intestinal lumen.⁷⁵⁻⁷⁷ Insoluble fiber plays a role in sweeping pathogens off the mucosa, while soluble fiber provides substrate for the production of short chain fatty

other defense measures to avoid contracting an upper respiratory tract infection (URI). When episodic surges of TNF- α related to URIs are controlled and eubiosis in the gut protected, a major step has been taken to retard progression of HIV.

If testing shows hepatic Phase I and Phase II detoxification problems,⁸¹⁻⁸³ they should be corrected. Oral supplements take on the role of medicinal foods. Where the protein kinase C pathway focused on reducing antigen/GALT induction, here the focus is on enhancing cellular and subcellular activity related to the cytochrome p450 activity of Phase I and conjugation activity of Phase II^{84,85} to limit oxidative stress and eliminate toxic intermediates. Phase I requires the B vitamins, flavonoids, branched chain amino acids, and other phytonutrients.⁸⁶ Phase II requires glutathione, methionine, cysteine, taurine, and glycine to support conjugation and solubilization of noxious Phase I intermediate molecules in preparation for excretion.⁸⁷ The length of oral supplementation will depend on retesting during the course of illness, usually every 3-6 months.

Since reactive oxygen species (ROS) result in disassociation of NF- κ B from I κ B α , oxidative stress must be controlled. Thus, the practitioner might consider recommending an antioxidant like vitamin C for coverage of circulating ROS, vitamin E for membrane ROS quenching, and nutrients such as arginine, N-acetylcysteine, selenium, manganese, zinc, and copper to support production of glutathione and superoxide dismutase for intracellular activity. Other single nutrients in the lipid category such as CoQ10,⁸⁸ conjugated linolenic acid,⁸⁹ gamma linolenic acid,⁹⁰ docosahexaenoic acid,^{91,92} and lipoic acid⁹³ work at different sites but contribute to the goal of decreasing oxidative stress or damage secondary to destructive inflammatory intermediary molecules and should be considered as components of treatment. For a summary of nutrients see Table 3.

Summary

Patients infected by the HIV virus do not die from the virus but rather from a pathophysiological process associated with the virus and a compromised immune system. This process is becoming clearer and seems to center in part around the gut, involving antigen/leukocyte receptor interaction which initiates protein kinase C, TNF- α , and/or oxidative stress, all of which may promote HIV replication. The intestine becomes a focal point for NF- κ B induction, which directly initiates HIV replication. Protein kinase C and TNF- α share a common denominator in that they increase the metabolic rate, resulting in the production of oxygen free radicals. Local inflammation due to mucosal adhesion of resident luminal pathogens leads to opportunistic infections and a leaky gut, which itself is capable of producing extreme oxidative stress. Oxidative stress results in cellular and subcellular injury and death, and also feeds back to accelerate NF- κ B release and stimulate HIV replication. Unchecked, it becomes a self-fueling cycle with a predictable outcome.

What the patient ingests will determine the qualitative and quantitative response to illness in both a positive and negative way. Antioxidants and anti-TNF- α supplements may decrease NF- κ B, while behaviors such as excess alcohol ingestion produce a leaky gut, inflammation, and may activate HIV replication. The diet and nutrients ingested by the HIV patient are, therefore, of great importance. Through a better understanding of the pathophysiology of HIV advancing to AIDS, the practitioner can develop a treatment strategy of nutritional and lifestyle changes which could theoretically prevent an HIV infection from advancing to full-blown AIDS.

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