



Hypothesis

The oxidative stress-induced niacin sink (OSINS) model for HIV pathogenesis

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ABSTRACT

Although several specific micronutrient deficiencies are associated with disease progression and increased mortality risk in HIV/AIDS, and even a simple multivitamin/mineral supplement can prolong survival, this is typically viewed merely as nutritional support of the immune system, and only necessary if there are deficiencies to be rectified. However, the reality is more complex. Several striking nutrient-related metabolic abnormalities have been consistently documented in HIV infection. One is chronic oxidative stress, including a drastic depletion of cysteine from the glutathione pool, and a progressive decline of serum selenium that is correlated with disease progression and mortality. Another is decreased blood levels of tryptophan, with an associated intracellular niacin deficiency. Tryptophan depletion or "deletion" by induction of indoleamine-2,3-dioxygenase (IDO), the first step in oxidative tryptophan metabolism, is a known mechanism for immune suppression that is of critical importance in cancer and pregnancy, and, potentially, in HIV/AIDS. Existing evidence supports the hypothesis that these nutrient-related metabolic abnormalities in HIV infection regarding antioxidants, selenium, sulfur, tryptophan and niacin are interrelated, because HIV-associated oxidative stress can induce niacin/NAD⁺ depletion via activation of poly(ADP-ribose) polymerase (PARP), which could lead to tryptophan oxidation for compensatory *de novo* niacin synthesis, thereby contributing to immune tolerance and T-cell loss via tryptophan deletion and PARP-induced cell death. This "oxidative stress-induced niacin sink" (OSINS) model provides a mechanism whereby the oxidative stress associated with HIV infection can contribute to immunosuppression via tryptophan deletion. This model is directly supported by evidence that antioxidants can counteract indoleamine-2,3-dioxygenase (IDO), providing the critical link between oxidative stress and tryptophan metabolism proposed here. The OSINS model can be used to guide the design of nutraceutical regimens that can effectively complement antiretroviral therapy for HIV/AIDS.

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Il modello dello stress ossidativo indotto da deplezione di niacina per la patogenesi dell'HIV

[...] diverse importanti anomalie metaboliche sono state documentate in modo consistente nell'infezione da HIV. Una è lo stress ossidativo cronico, che comprende una drastica deplezione di acetilcisteina dal pool di glutathione, una progressiva diminuzione di selenio [...] un'altra è la deplezione di triptofano, con un'associata deficienza di niacina intracellulare.

Questo modello di "stress ossidativo indotto dalla perdita di niacina" (OSINS) può essere usato come guida per il disegno di regimi nutraceutici che possono efficacemente complementare la terapia per l'HIV/AIDS.