

Why Vitamin, Mineral and Nutritional Supplementation is Helpful for Patients With Down Syndrome

Peer Reviewed, Published Opinions of Physicians and Scientists

The use of supplemental vitamins and minerals in patients with Down syndrome has recently received a lot of media attention. This has inspired many parents and caregivers to seek advice from their physicians on the efficacy of nutritional supplementation for their loved ones. As a physician you are undoubtedly presented with these issues and are perhaps even skeptical that such intervention will be helpful to your patient.

Many physicians and parent groups have been opposed to such supplementation in the scientific press and areas even more accessible to the general public, like the World Wide Web. More often than not, these critiques focus on studies that find no basis for nutritional supplementation while ignoring other data suggesting that vitamin, mineral and other nutrient supplementation is beneficial to these patients. We have assembled a selection of quotations from scientific articles that DO indicate that nutritional supplementation is beneficial to persons with Down syndrome.

? What is the major weakness of claims that vitamin and mineral supplementation is of no value to patients with Down syndrome?

The critiques of nutritional supplementation of patients with Down syndrome have not, in the main, dealt with the **GENERAL HEALTH ISSUES** of these patients. Cognitive enhancement issues have generally overshadowed the fact that there are plenty of data supporting improved metabolic and immune function in patients with Down syndrome as a result of nutritional supplementation. Improvement in these can have profound effects on patient health.

Another criticism cites the lack of double-blind studies. However, LaPerchia (1987, *Adolescence*: 22:729) criticized previous use of double blind studies in assessing the efficacy of nutritional supplementation in cognitive disorders, including Down syndrome. She stated:

"They use the double-blind method of experimenting, a method which seems to ignore the complex diagnostic category, i.e., the heterogeneity of various language, learning and behavioral disorders that may be present in the treatment population. Thus, although some patients may respond positively to orbomolecular therapy, they may go undetected because so many of the other subjects did not demonstrate significant improvement. This method may be suitable for testing individual drugs, but it is virtually impossible for testing a treatment method."

In the early 80's, Harrell et al. (1981, *Proceedings of the National Academy of Sciences* 78:574) found that a vitamin/mineral supplement, of limited nutritional scope, enhanced IQ in a number of patients with Down syndrome. A flurry of later studies failed to replicate these initial findings. Despite this, one of the most widely cited studies claiming failure of nutritional supplements to be beneficial, made the following statements:

"While our attempt to replicate the Harrell et al. (2) research design did not confirm the promising results of that specific investigation, nutritional therapies cannot be dismissed out of hand. There are, for example, fourteen known metabolic diseases responsive to megavitamin regimes (18)"

"Although this goal remains elusive at this time, the utilization of such treatment approaches very early in life, below the age of three years, appears to be warranted because of potential developmental enhancement"

Menolascino et al. (1989). *Journal of Nutritional Science and Vitaminology*: 35:181

? What is the rationale that would lead one to believe that nutritional supplements may be beneficial to the general health of patients with Down syndrome?

First, Down syndrome is a genetic disorder involving an extra copy of chromosome 21. As such, patients with Down syndrome have a different *genotype* than other patients. Nutritional scientists have long recognized that persons with different genotypes have different nutritional needs. Indeed, Simopoulos (1999) in a recent article entitled "Genetic Variation and Nutrition" (*Nutrition Reviews*: 57:510) made the following observation:

"The most effective intervention or prevention of chronic diseases would occur through targeted changes in environmental factors, including diet, which are matched to an individual's genetic susceptibility."

Furthermore, nutritionists understand that nutrition can profoundly affect the health and development of persons afflicted with disorders such as Down syndrome. The American Dietetic Association made the following position statement regarding persons with developmental disabilities in a paper entitled "Position of the American Dietetic Association: Nutrition in comprehensive program planning for persons with developmental disabilities." Down syndrome was one of the examples given.

"Persons with developmental disabilities are at an increased nutritional risk because of feeding problems, drug/nutrient interactions, metabolic disorders, decreased mobility, and altered growth patterns."

Anonymous (1997). *Journal of the American Dietetic Association*: 97:189

Finally, since the 1980's, studies have consistently demonstrated that the biochemical differences within the bodies of persons with Down syndrome require supplementation of the diet with specific vitamins and nutrients. For instance, because of the over-expression of the enzyme, superoxide dismutase, it is now commonly accepted that the bodies of persons with Down syndrome are under more oxidative stress as a result of over production of free radicals in organs, especially in the brain.

"Recent developments in basic research have confirmed the relationship between etiopathogenesis and supplementation therapy with vitamins and trace elements. We have described the theoretical basis for antioxidant therapy in DS."
Antila and Westermark (1989). Journal of Developmental Biology. 33:183-188

"Our data support the notion that ROS (reactive oxygen species-editor) are involved in the premature aging of individuals with Down syndrome...Therefore fine-tuning of the antioxidant enzymes (e.g., vitamins and other small molecules that quench free radicals) become imperative if the cell is to function successfully in an oxygen-rich environment. Down syndrome is one situation where the antioxidant balance is affected due to gene dosage."
de Hann et al. (1997). Advances in Pharmacology. 38:379-402

More recently, Jovanovic et al. (1998) commented on the connection between Down syndrome, oxidative stress and Alzheimer's disease:

"The higher mean values of biomarkers of oxidative stress indicate an increased rate of oxidative damage in individual with DS.....Since oxidative DNA damage reflects increased degenerative processes, this data is in agreement with observed premature aging, increased incidence of cataracts and early Alzheimer's like changes in DS."
Free Radical Biology and Medicine: 25:1044

Similar observations have been made by others:

"There is now strong experimental evidence to support a prominent role for ROS and oxidative stress in the neuropathogenesis of DS."
Innello et al. (1999). Journal of Neural Transmission (suppl). 57:257-267

"There is an increasingly good body of evidence to suggest that increased oxidative stress may be involved in the pathology of DS. Therefore, it is theoretically possible that using antioxidant nutrients to scavenge oxygen-derived free radicals may ameliorate some of the complications of DS."
Ani et al. (2000). Developmental Medicine and Child Neurology. 42:207-213

"These observations could suggest that antioxidant supplementation in Down's syndrome has beneficial effects on the prevention of diabetes."
Ohyama et al. (2001). Diabetologia. 44:788-789



Is there any information that directly suggests that patients with Down syndrome are, in general, at increased risk for malnutrition?

Yes. There have been a number of studies demonstrating that persons with Down syndrome do not, as a population, have an adequate intake of many nutrients including vitamins and minerals. One of the first studies reporting this was published in the 1970's, Calvert et al. (1976) observed:

"More than half of the children ate less than the allowance for food energy..."

"...When thiamine intake was evaluated by age, 93 percent of children over six received less than the allowance."

"The nutritional quality of the diets for more than half of the children with Down syndrome was improved by the use of some form of vitamin mineral supplement."
Journal of the American Dietetic Association: 69:52

Later in the 1980's, Sylvester (1984) concluded:

"The evidence from the studies quoted demonstrates that patients with Down's syndrome are different from the mentally handicapped without Down's syndrome in several nutritional respects. They are prone to suffer multi-vitamin deficiencies and shortages of some trace metals; these shortages are life-long, since similar patterns of deficiencies have been found in Down's syndrome children. A significant reason for these deficiencies is malabsorption from the gut."
British Journal of Psychiatry: 145:115

Similarly, Reading (1984) stated:

"DS children should be investigated for the above and commence a food allergy free diet with relevant supplements to meet their needs as early as possible to allow maximum development."

"These assessments indicate that patients with DS are likely to be: -1. Low in certain vitamins-despite supplementation. 2. Low in certain minerals/trace elements-despite supplementation."
Nutrition and Health: 3:91

"The absorption of zinc seems to be decreased in DS, mean retention of zinc being 30% (n=9[n represents the number of patients-editor]) compared with 58% in healthy adults (n=4)."
Antila and Westermark. (1989). International Journal of Developmental Biology. 33:183-188

In the 90's, Unonu and Johnson (1992) offered this opinion:

"First, a nutrition component should be part of every intervention program for young children with Down Syndrome."
Journal of the American Dietetic Association: 92:856

Luke et al. (1996) observed:

"The macronutrient distribution of the diets conformed well to recommended levels, but micronutrient intakes did not consistently meet the RDA's. Vitamin and mineral intakes were lower overall in subjects with Down Syndrome than in control subjects, except for vitamin C."
Journal of the American Dietetic Association: 96:1262

It is not a huge leap in logic to realize that patients with Down syndrome may need dietary modification and supplemental minerals and vitamins, especially, antioxidants, in a manner similar to the aged as outlined by Ortega (1997):

"In conclusion, the results appear to suggest that a lower intake of fat, saturated fat, and cholesterol, and a higher intake of carbohydrate, fiber, vitamins (especially folate, vitamins C and E and b carotenes), and minerals (iron and zinc) might be advisable to improve not only the nutritive status and general health of the elderly but also their cognitive ability."
Journal of Clinical Nutrition: 66:803

Very recently Angelopoulou et al. (2000) made this observation:

"Our study provides evidence that young male adults with Down syndrome have lower BMD (bone mineral density - editor) of the spine as well as inferior muscle leg strength than otherwise mentally retarded people, with the same age and IQ range...almost all of the DS people have feeding problems during their infancy which may contribute to low calcium intake and inadequate bone mineralization."
Calcified Tissue International. 66:176-180

Similarly, Congiz et al. (2000) states:

"In general, fat soluble vitamins A and E were found to be less in DS children...When the age categories are compared, Zn was seen less in both younger and older children of the DS group.."
Trace Elements and Electrolytes. 17:156-160

Finally, Seven et al. (2001) just reported:

"Carnitine is responsible for several chemical processes, including lipid metabolism, nerve cell conduction, reduction in muscle hypotonia, and limitation in oxidative damage to cells...In conclusion, this study shows that plasma total and free carnitine levels in DS patients are significantly lower than in normal children of the same age.."
American Journal of Human Biology. 13:721-725

Is there information suggesting that supplementation is needed for specific vitamins, minerals and other nutrients?

Yes. Through the years, many scientists and physicians have offered evidence for the need of specific vitamin and mineral supplementation for patients with Down syndrome in peer-reviewed scientific journals. The following is a selection of some of the opinions offered by researchers and health-care professionals in those publications:

"Separately, the parameters of vitamin B₆ metabolism studied to date in mongoloid (old term for Down syndrome patients—editor) subjects are not strong proof of a derangement of metabolism of this vitamin in these subjects. However, when taken together, they constitute suggestive evidence of an abnormality of vitamin B₆ in mongolism."
McCoy et al. (1969). Annals of the New York Academy of Sciences: 166:116

"Therefore, these data provide additional evidence of abnormal B₆ metabolism in Down's syndrome."
Coburn et al. (1983). The American Journal of Clinical Nutrition: 38:352

"Plasma Se was significantly lower in Down's patients than in normal subjects."
Sinet et al. (1984). Acta Paediatrica Scandanavia: 73:275

"The authors conclude that there may be an interaction between the inherent risk of Alzheimer's disease in Down syndrome and the possible protective action of vitamin E in slowing down this process."
Jackson et al. (1988). Journal of Mental Deficiency Research: 32:479

"The present study revealed ascorbic acid deficiency in the blood of many children with Down's syndrome. It also revealed a fairly definite connection between vitamin C deficiency and diet in these patients and a similar link between ascorbic acid deficiency and this incidence of infections."
Columbo et al. (1989). Minerva Pediatrica: 41:189

"The present study revealed a degree of carnitine deficiency in a large percentage of Down's syndrome children.....On the basis of these data, supplementary carnitine is recommended in cases of deficiency, particularly in view of the value of carnitine in the prevention of cell aging."

Columbo et al. (1989). *Minerva Pediatrica*: 41:173

"In conclusion, we believe that, in spite of the heterogeneity of the population, our DS patients have benefited from the selenite supplementation through optimization of their antioxidant protection by GSHPx."

Antila et al. (1990). *Advances in Experimental Medicine and Biology*: 264:183

"Treated Down Syndrome patients showed statistically significant improvements of visual memory and attention both in absolute terms and in comparison with other groups" (regarding L-acetyl carnitine supplementation—editor).

De Falco et al. (1994). *La Clinica Terapeutica*: 144:123

"To avoid lowering already inadequate intakes of several vitamins and minerals, we suggest that treatment of obesity in children with Down syndrome combine a balanced diet without energy restriction, vitamin and mineral supplementation (riboflavin, pyridoxine, iron and calcium, zinc and copper—editor), and increased physical activity."

Luke et al. (1996). *Journal of the American Dietetic Association*: 96:1262

And so the data continue to accumulate that persons with Down syndrome have special dietary needs that need to be addressed by specific nutritional supplementation. A number of recent studies vividly underscore this point:

"Our data suggest that zinc deficiency is a conceivable cause of subclinical hypothyroidism and support the usefulness of periodic zinc supplementation which improves thyroid function in hypozincemic Down Syndrome..."

Bucci et al. (1999). *Biological Trace Element Research*. 67:257-267

"The protective effect against basal chromosomal damage provided by vitamin E in DS lymphocytes suggests that the decrease of oxidative damage by this vitamin may also improve the efficiency of DNA lesions in these cells."

Pincheira et al. (1999). *Clinical Genetics*. 55:192-197

"Moreover, active lifestyle early in childhood and adolescence when peak bone mass is achieved, increased physical exercise that improves muscular strength and adequate calcium and vitamin D intake should be instituted to avoid or postpone the development of osteoporosis in DS patients."

Angelopoulou et al. (2000). *Calcified Tissue International*. 66:176-180

"Because individuals with DS have low homocysteine levels and a high probability of a folate trap, intervention with folinic acid (5-formyltetrahydrofolate) has several advantages over intervention with folic acid. This form of folate is more efficiently absorbed as the reduced metabolite, is rapidly polyglutamated, and is more readily available for folate-dependent reactions."

Pogribna et al. (2001). *American Journal of Human Genetics*. 69:88-95

Down syndrome is an extremely complex disease. In the words of Lejeune (1990):

"Short of discovering how to silence selectively one of the 3 chromosomes 21, no rational medication can be envisaged before pathogenesis has been unraveled, at least partially."

American Journal of Medical Genetics. Supplement. 7:20

We agree. This, however, does not preclude sensible and prudent attention to the nutritional needs of persons with Down syndrome until molecular biology provides the ultimate cure. As stated above, many times and in many different ways, the very genotype that makes these patients different phenotypically imposes upon them the added burden of different nutritional requirements. This is indisputable. Clearly, the present debate has been spawned by our lack of a more complete understanding of the metabolism of patients with Down syndrome. Your decision to supplement your patient or child with nutrients should be made with the full realization that scientific evidence does exist to support your point of view.

"Surely, we are not yet able to restore the destiny, but we are possibly just in the situation of being able to prevent its worsening."

Lejeune (1990). *American Journal of Medical Genetics Supplement*: 7:20

In closing, regardless of whether you agree that nutritional supplementation is right for your child, we at International Nutrition Inc., share your feelings that persons with DS are very special as so eloquently stated by David Nicklin, MD about his daughter:

"In accepting her fully, I have slowly come to accept myself more fully, with all my human flaws and struggles. I lose track of this still, sometimes daily, in our culture that so much judges and values people by their beauty, wealth and ability. Kate is there every day reminding me, making me smile, a living contradiction to my confusions."

Journal American Board of Family Practice (2000). 13:160



1-800-899-3413

11436 Cronridge Drive, Suite W

Owings Mills, MD 21117 USA

Phone (410) 902-1760 Fax (410) 902-1767

www.nutrivene.com ask@nutrivene.com