



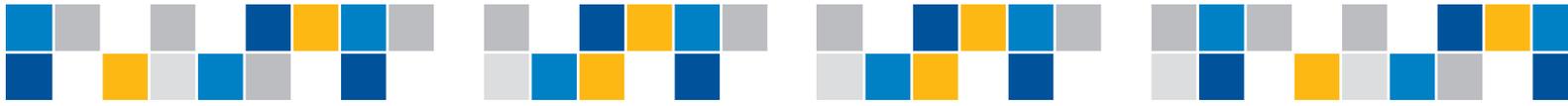
MicroNutrient Testing



Clinical Applications

Identifying Subclinical Nutrient Deficiencies in
Chronic Disease States – Why MicroNutrient Testing is Important in Your Practice





Medical research published in numerous peer-reviewed journals has scientifically documented the vital role that essential nutrients play in achieving and maintaining good health, and in preventing or treating many serious diseases. Some diseases that have been scientifically linked to nutrient imbalances include arthritis, Parkinson's, alcoholism/substance abuse, behavioral disorders, cancer, cardiovascular diseases, chronic fatigue, muscular degeneration, diabetes, immune disorders, multiple sclerosis, stroke and osteoporosis.

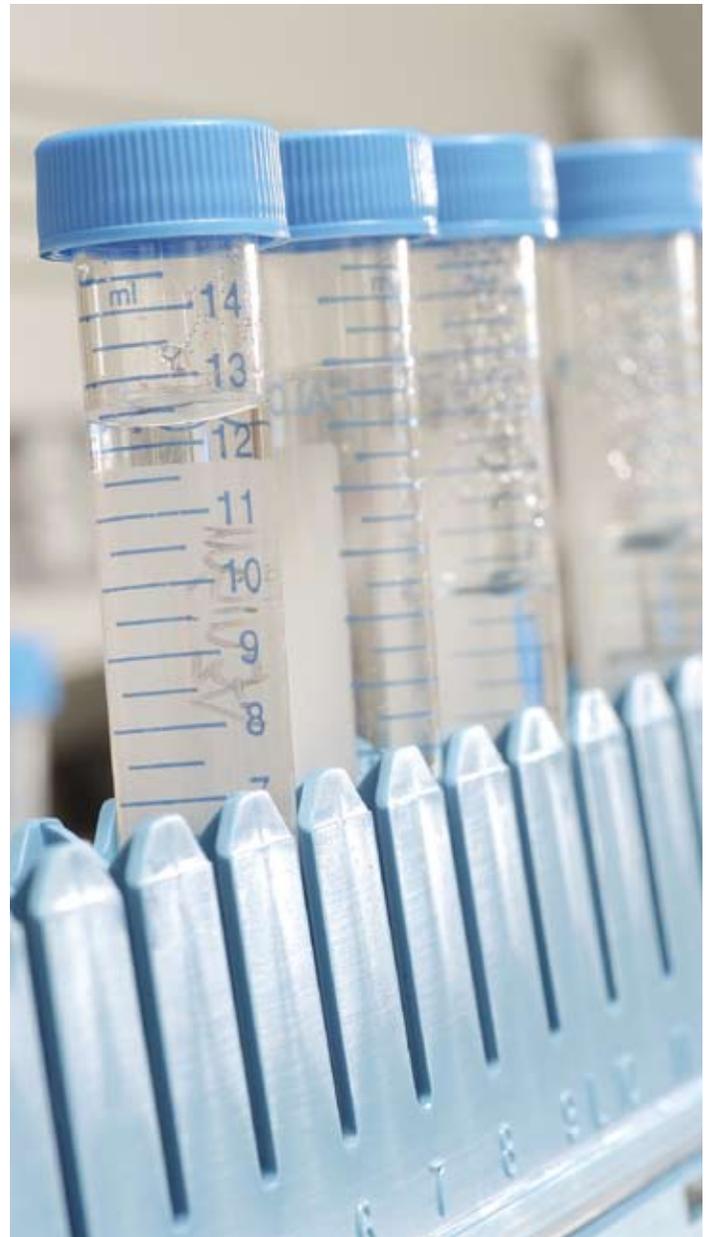
Established in 1993, SpectraCell Laboratories, Inc., has been a pioneer in the field of laboratory functional testing for micronutrients. Unlike traditional serum testing, SpectraCell's patented, ground-breaking technology, MicroNutrient Testing, offers the practitioner a true window to intracellular function with a long-term analysis of nutrient status. By supporting the practitioner in identifying subclinical nutritional deficiencies, MicroNutrient Testing aids the development of optimal interventions to assist patients in their quest for lasting health.

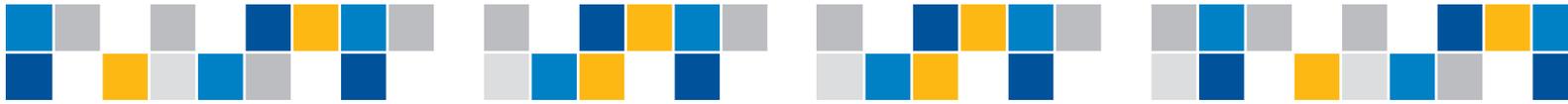
As medicine progresses in the pursuit of health and wellness, patient care is taking on a broader and deeper perspective. Our understanding of the importance of biochemical individuality and the role of subclinical deficiencies in chronic disease conditions continues to grow rapidly. It is the mission of SpectraCell Laboratories to provide the medical community with the information it needs to understand these developments and provide the diagnostic tools it requires to take full advantage of them.



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MicroNutrient Testing from Spectracell Laboratories

INTRACELLULAR FUNCTION OF ESSENTIAL NUTRIENTS

Nutrient deficiencies may be induced by a variety of conditions, in addition to inadequate intake. With a functional deficiency, a nutrient may be present, but it may not be properly activated, it may not be appropriately localized, or it may not have sufficient cofactors to function at a normal level of activity. Underlying reasons for a functional nutrient deficiency include inefficiencies or deficiencies in the following:

- absorption by the gastrointestinal tract
- transport to the appropriate tissue
- transport through the cell membrane into the cell
- intracellular activation storage
- concentration or activity of cofactors

ADDITIONAL CONTRIBUTING FACTORS

Other factors contributing to nutrient deficiencies include intracellular inhibitors that may be present, tissues that may have increased metabolic needs, or hyper-excretion, such as loss of zinc through sweat during intense physical exercise.

Thus, a functional deficiency includes anything that may reduce the concentration or the efficacy of a nutrient. No matter what the underlying cause, the result will be a defect in the biochemical pathways that depend upon the optimal function of that nutrient. A deficient or defective pathway may operate at a sub-optimal level for many months or even years before a clinical symptom may become apparent. Because SpectraCell's MicroNutrient Testing evaluates the function of a nutrient rather than just the concentration present in blood or tissue, the clinical consequences of any of the problems listed above will be more likely to be detected by SpectraCell's MicroNutrient Testing than by conventional serum concentration measurements.

RELEVANCE TO IMMUNOCOMPETENCE

Specific nutrients are essential cofactors for immune system function and nutritional balance is essential for the integration of immune system functions. Nutrient deficiencies impair immune responses and can lead to frequent infections and increased mortality.¹ Also, during aging, immune function is gradually lost as the thymus gland involutes and antigenic exposures accumulate.² Studies have suggested that this immune function decline may be slowed or even reversed through detection and correction of specific nutrient deficiencies.²

For example, zinc is critical to the maintenance of an effective immune response.³ This mineral performs catalytic, structural and regulatory roles within the immune system. Its deficiency negatively impacts peripheral T-cell proliferation, delayed type hypersensitivity reactions, T-helper cell, NK cell, and cytotoxic T-cell activities, macrophage and neutrophil functions and serum

thymulin levels. Even a slightly decreased zinc status can be associated with an increased number and severity of infections and/or autoimmune conditions.³ Zinc deficiencies are especially prevalent in the elderly,⁴ because of decreased consumption and reduced absorption of zinc, and are also frequently observed in hard-training athletes, who lose significant amounts of zinc as they sweat.⁵ Numerous studies have shown that once a deficiency has been identified, appropriate supplementation can lead to reduced episodes of infection, improved clinical state,^{1,4} and better recovery after strenuous athletic performance.⁵

B vitamins are also critical to optimal immune function. Vitamin B6 deficiency has been shown to depress both cell-mediated and humoral immune responses, whereas supplementation was found to improve immune function, especially in those most at risk for B6 deficiency, the elderly.⁶ Vitamin B12 deficiency has also been linked to poor immune function, especially in the elderly, and B12 therapy was also found to improve immune function in B12 deficient individuals.⁷ Finally, clinical and experimental evidence indicates that biotin also plays an essential role in the capacity of the immune system to respond to antigenic challenge.⁸

Specific amino acids have also been found to have beneficial immunomodulatory effects. Although arginine is regarded as a nonessential amino acid, it is needed at higher than normal levels during times of rapid cell division and can thus be considered 'conditionally' essential. This amino acid has a role in enhancing lymphocyte response to mitogens, and its use as a supplement during times of injury has proven beneficial to healing.⁹ A similar but even more pronounced role in immune function has been observed for the amino acid glutamine.¹⁰ Glutamine is an essential fuel for the proliferation and differentiation of human lymphocytes and has been observed to promote phagocytosis by macrophages. During inflammatory states and conditions of infection, injury or prolonged exercise, tissue glutamine consumption may outstrip production to create a deficiency. Under these conditions, supplementation with glutamine was found to reduce the frequency of infections in athletes during and after strenuous training.¹¹

Of all the nutrients obtainable from foodstuffs, antioxidants may be the most beneficial to the organism in general and to the immune system in particular. Tissue injury from oxidants is particularly hazardous because phagocytic cells produce reactive oxygen species in their defensive role against infection. Sufficient neutralizing antioxidants are therefore required to prevent injury to immune cells and to surrounding tissue. Much evidence suggests that antioxidant nutrients can improve immune function not only in the elderly, but also in younger individuals, and many studies have correlated antioxidant rich diets with a low incidence of cancer.¹² These findings suggest that boosting immune function with antioxidants results in greater protection against acute infections as well as chronic disease, such as cancer, throughout one's life.



SpectraCell's SpectroX™ test will evaluate the functional antioxidant capacity of a patient's lymphocytes, thereby providing an estimate of the capacity of their immune system to protect against oxidative damage. The associated glutathione test will provide a functional estimate of the glutathione reserve of the cells as well. Glutathione, a sulfur-containing tri-peptide, functions as a major scavenger of reactive oxygen species, thereby protecting lymphocytes from oxidative damage and enhancing immune function.¹³ Glutathione and other sulfur-containing compounds appear to be severely depleted under certain conditions, such as HIV infection. Replenishment by N-acetyl-cysteine has been found to restore lost sulfur-containing nutrients and to improve immune function in HIV infected individuals.¹⁴

Thus, it is clear that the functional bioavailability of essential nutrients supports immunocompetence in many ways. MicroNutrient Testing measures the growth response of the individual's lymphocytes to mitogenic stimulation under a variety of nutrient depletion conditions. These results aid in identification of specific nutrient deficiencies that could impair the immune system's response to antigenic challenge, thereby potentially decreasing the frequency of infections and reducing the possibility of developing chronic disease.

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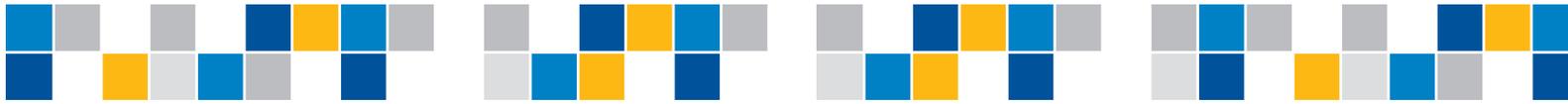
Specific Conditions & Clinical Applications

CARDIOVASCULAR DISEASE

In 1969 Kilmer McCully's pioneering research first associated elevated serum homocysteine (Hcy) with arteriosclerotic disease.¹ In the intervening 30 years, subsequent studies have associated mild-to-moderate elevations in homocysteine with coronary heart disease,² MI,³ cerebrovascular disease,⁴ carotid intima-media thickness,⁵ lower extremity arterial disease,⁶ and isolated systolic hypertension.^{7,8} Since homocysteine metabolism depends on B vitamins as cofactors, the relationship between B vitamin status, homocysteine levels and atherosclerosis has been the focus of many investigations. Epidemiological studies have found a negative correlation between homocysteine and plasma levels of folic acid, vitamin B6 and vitamin B12.^{2,9} Subsequent efforts at reducing plasma homocysteine levels have been promising,¹⁰ and suggest that therapy of elevated homocysteine with folic acid and vitamins B6 and B12 represents a reasonable addition to a cardiovascular disease prevention program.¹¹ SpectraCell's cardiovascular profile, which includes homocysteine, can detect functional deficiencies of vitamins B6, B12 and folic acid. Since numerous studies have documented a high prevalence of selected B vitamin deficiencies in the US population,¹² especially in the elderly, early detection of deficiencies is a critical step in disease prevention. SpectraCell's MicroNutrient Testing can detect functional deficiencies of vitamins B1, B2, B3, B6, B12, folic acid, biotin and pantothenic acid, no matter what the underlying reason for the deficiency may be.

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CANCER

Scientists continue to unravel the mechanisms of cancer induction and progression and to provide guidelines directed towards prevention of this disease.

It is now recognized that genetic mutations underlie cancer induction and it is becoming increasingly apparent that several classes of nutrients have prominent roles in the prevention of these mutations. A deficiency of any of the following micronutrients: folic acid, niacin, iron, zinc or vitamins B6, B12, C or E, can mimic radiation or chemical damage to DNA by causing chromosomal breaks and/or oxidative lesions.¹ Folic acid deficiency causes extensive incorporation of uracil into DNA, which leads to chromosome breaks.² There is also some evidence that vitamin B12 and B6 deficiencies can lead to chromosomal breakage by a similar mechanism.³ A level of folic acid deficiency associated with chromosomal breakage was found to be present in approximately 10% of the general US population and in a relatively much higher percentage of lower income individuals.⁴ Oxidative damage to DNA, secondary to deficiencies of dietary antioxidants, is another mechanism that may contribute to the development of malignancy.^{5,6} In addition to inhibiting mutational damage, antioxidants are also critical components of immune system surveillance. Once a malignancy has begun to grow, a healthy immune system can often hold it in check or eradicate it without the host ever realizing its presence. Deficiencies of micronutrients have been found to suppress lymphocyte mitogenesis, natural killer cell activity and cell-mediated and humoral immune responses (see above section for references). Thus, two prime goals of cancer prevention are to detect and reverse micronutrient deficiencies before cancer-causing mutations occur and to keep the immune system functioning at a high level, so that newly mutagenized cells are eradicated before they become a clinically detectable cancer.⁷ SpectraCell's MicroNutrient Testing, including tests for B vitamin and antioxidant deficiencies, can help to detect crucial micronutrient deficiencies before clinical symptoms appear and can contribute to the maintenance of an active, efficient immune system.

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IMMUNOSENESCENCE

Immunosenescence is a treatable, age-related result of cellular degeneration. Aging has been described as a series of processes that result in vulnerability to challenge, thereby increasing the rate at which we approach death. Scientific evidence indicates that depressed immunity can increase this rate, and it is likely that diminishing immune function with age is a key factor in the aging process.

There are a number of theories of aging, including free radical, programmed senescence and immunological theories.^{1,2} Understanding the complex aging process requires the interrelationships of numerous theories. For example, evidence demonstrates that antioxidant nutrients reduce free radical damage and improve cell-mediated immune function in older people, suggesting an overlap of the free radical and immunological theories.³

Studies show that changes in immunity with aging include altered lymphocyte subpopulation percentages, decreased thymic hormone concentrations, decreased suppressor activity of T-cells, reduced interleukin-2 (IL-2) secretion, decreased in-vitro lymphocyte proliferative responses to mitogens, reduced antibody production and increased soluble-serum IL-2 receptors.⁴ Depressed T-cell function is the most common change, and delaying the initiation of this process may play a key role in slowing the aging process. An important element in achieving such a delay is the maintenance of functionally adequate cellular levels of essential vitamins, minerals, amino acids and antioxidants.

A compromised immune function often precedes infection. Infections, no matter how mild, adversely affect nutritional status, which in turn can further compromise immunity and further exacerbate the effects of infection.⁵ Various micronutrients have been implicated and include: pyridoxine (B6), folic acid, pantothenate, vitamins B12, C, E and the trace elements iron, zinc and copper.^{6,7}

Dietary deficiencies of specific nutrients profoundly alter cell-mediated immune responses in humans. Diets deficient in calories, protein, vitamins A, B6, B12, folate, biotin and zinc can result in depressed production of thymic hormones critical for T-lymphocyte differentiation and function⁸ and premature aging of the immune system, immunosenescence.

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NEURODEGENERATION

Among the fears of growing old is deterioration of mental capacity. Seven percent of adults over the age of 65 have Alzheimer's Disease (AD). By age 85, the average person has a 50% possibility of developing dementia. Once the condition has become symptomatic, little but palliative care can be offered. Prevention, as part of any anti-aging program, is essential. Increased free radical generation is associated with aging. Normal oxidative metabolism promotes accumulated damage to macromolecules, especially when endogenous antioxidant defenses are not balanced against oxidant forces.¹ Brain tissue is more susceptible than other tissues to oxidative stress. Its high rate of metabolic activity produces superoxide radicals at a high rate, and it has a relative deficit of defense mechanisms. Also, neural tissue has a high concentration of polyunsaturated fatty acids as components of its membrane lipids, which are especially susceptible to free radical attack. Finally, neural tissue forms a complex network, which has little capacity for regeneration following damage.² A common feature in the brains of these patients is the deposit of beta-amyloid, which can directly promote free radical formation.³ Finally, clinical investigations have correlated low plasma levels of antioxidants, especially vitamins C and E, with a higher incidence of AD.^{4,5}

The elderly are especially prone to deficiencies of vitamins B12, B6 and folic acid. Vitamin B12 deficiency can occur secondary to decreased acid production by stomach mucosal parietal cells. The prevalence of atrophic gastritis in this population is estimated to be 20-50% and is a greater cause of B12 deficiency than decreased secretion of intrinsic factor. The decreased secretion of HCl leads to impaired release of B12 from proteins and peptides with consequent decreased B12 absorption.⁶ The Framingham Health Study Cohort found that an elderly population was 30% deficient in folate, 20-25% deficient in B12, and 20% deficient in B6.⁶ Studies have related low plasma levels of these vitamins in elderly individuals with loss of cognitive function and AD.⁷

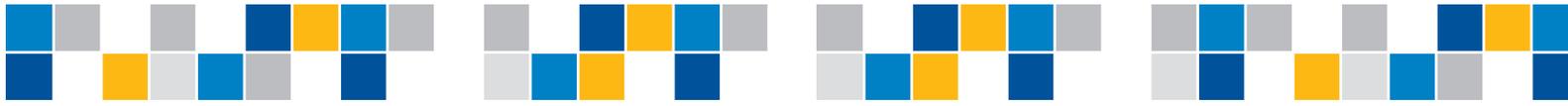
Loss of cognitive function secondary to vitamin deficiency is thought to progress by two independent mechanisms. Decreased availability of folic acid and B12 leads to decreased synthesis of methionine and S-adenosyl methionine (SAM). The result is a decreased availability of methyl groups that are essential for the synthesis of myelin, neurotransmitters and membrane lipids. A chronic state of hypomethylation is thought to slowly disrupt brain metabolism and, over time, significantly contribute to cognitive impairment.^{8,9} A second major mechanism of neurodisruption involves the elevation of serum homocysteine from the decreased level of its conversion to methionine in the absence of sufficient intracellular folic acid and B12.

High serum homocysteine is believed to be a critical link between reduced levels of certain B vitamins and the severity of cognitive dysfunction, through its toxicity to vascular endothelium and to neuronal cells. The high prevalence of hyperhomocysteinemia in the elderly is strongly associated with an increased risk of occlusive vascular disease, stroke and thrombosis.¹⁰ Thus, damage to neural tissue from elevated levels of homocysteine can occur directly, from toxic effects on neurons, and indirectly, from a chronic decrease in blood flow and oxygenation, secondary to endothelial damage. Case- and population-based studies of dietary backgrounds and brain tissue analysis have led investigators to conclude that chronic folate deficiency induces cerebral atrophy.^{11,12}

Thus, it is becoming clear that various nutrient deficiencies throughout our lives can lead to dementia by more than one mechanism and that prevention of dementia must begin well before old age is reached. A prime method of prevention is avoidance of nutritional deficiencies, especially of B vitamins, and maintenance of a positive balance of antioxidants. Many victims of dementia did not consider themselves malnourished and most people are unaware of the state of their antioxidant/oxidant balance. SpectraCell's functional nutrient evaluation, including B vitamin and antioxidant analysis, may contribute to a better understanding of your patients' specialized nutrient needs before deficiencies become irreversible symptoms of dementia.

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DIABETES MELLITUS

This widespread metabolic disease has been associated with several nutrient deficiencies, some of which have been linked to progression of clinical disorders that can occur secondary to chronic diabetes. Magnesium deficiency, in particular, has been associated with type 1 and type 2 diabetes as well as with gestational diabetes. Patients with diabetes were found to have a lower mean plasma magnesium concentration than non-diabetic control subjects.¹ Plasma magnesium levels were also related to insulin sensitivity. Supplementation of type 2 diabetics with magnesium was found to improve both insulin secretion and insulin sensitivity.² Experimental studies in animals and cross-sectional studies in humans have suggested that low serum magnesium levels might actually contribute to the development of diabetes. A recent prospective study revealed a graded inverse relationship between serum magnesium levels and the development of diabetes,³ and yet another study suggested that high levels of magnesium in drinking water lowered the risk of dying from diabetes.⁴ Magnesium deficiency has also been linked to progression of clinical disorders related to chronic diabetes. One prospective study found an inverse relationship between plasma magnesium levels and the occurrence or progression of diabetic retinopathy.² In another study, EMG polyneuropathy signs were more frequent in diabetic patients having low red blood cell magnesium. Magnesium supplementation improved nerve conduction in these patients even though their metabolic status remained unchanged.⁵

Deficiencies of several vitamins have also been identified in diabetic individuals. Vitamin B6 levels were found to be lower in diabetic animals than in normal controls⁶, and sub-clinical vitamin B1 deficiency was prevalent in pregnant women with gestational diabetes.⁷ Deficiencies of antioxidant vitamins have also been associated with diabetes. Several studies have found that diabetic patients had at least a 30% lower level of plasma ascorbic acid than non-diabetic subjects,⁸ and a strong independent association was found between low plasma vitamin E levels and an increased risk of developing diabetes.⁹ Subjects with clinical nephropathy had lower mean plasma ascorbic acid levels and higher mean renal clearance of ascorbic acid than patients having only microalbuminuria. It was proposed that the higher ascorbic acid clearance in diabetic patients with renal disease can lead to a decreased systemic level of antioxidant protection, which in turn can contribute to increased development of atherosclerosis and to the increased degree of cardiovascular morbidity and mortality observed in diabetic patients.¹⁰ Thus, SpectraCell's antioxidant panel and functional determinations of B vitamins and minerals can help to detect diabetes-related nutrient deficiencies before they contribute to the progression of the disease or to the development and progression of its complications.

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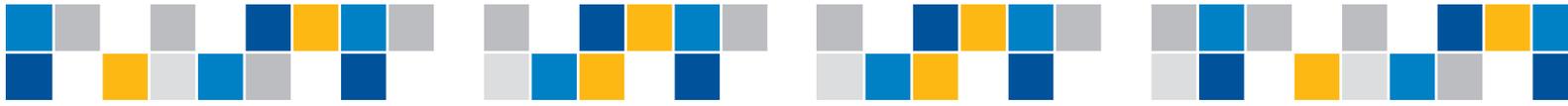


CHRONIC FATIGUE SYNDROME AND FIBROMYALGIA

Very little is known with certainty about the cause and stubborn persistence of fatigue in Chronic Fatigue Syndrome (CFS). There are, however, reports of nutrient deficiencies associated with CFS as well as reports of specific nutrient supplementation providing partial relief of symptoms. B vitamins appear to be especially relevant. Fifty percent of a group of 60 patients diagnosed with CFS were deficient in serum folate, while another 13% showed borderline folate deficiency.¹ In another study of more than 100 CFS patients, 30% had elevated methylmalonic acid in their urine,² a test considered to be more sensitive than serum vitamin B12 for diagnosis of cobalamin deficiency. Heap et al.³ found preliminary evidence for a reduced functional status of vitamins B1, B2, and, especially, B6, in CFS patients compared to healthy controls. Another study found that all the patients tested, who fulfilled the criteria for CFS and fibromyalgia, had elevated levels of homocysteine (Hcy) in their cerebrospinal fluid. Moreover, there was a correlation between high Hcy and low vitamin B12 in the cerebrospinal fluid and reported fatigue levels.⁴ The minerals magnesium and zinc may also have clinical relevance to CFS. Several studies have revealed lower erythrocyte magnesium levels in CFS patients than in controls,^{5,6} although not all studies have confirmed these findings.⁷ In a study of 28 women with CFS, mean red blood cell zinc levels, although within the normal range, were significantly lower than the levels measured for a group of healthy control women.⁵ Recent studies are beginning to find that antioxidant status may be compromised in patients with CFS. One study found that LDL and VLDL from CFS patients were more susceptible to lipoprotein peroxidation than matched, non-CFS individuals⁸ and another study found oxidative damage to DNA and to lipids in muscle specimens of CFS patients compared to age-matched controls.⁹ Yet another study identified increased protein peroxidation in fibromyalgia patients compared to age-matched controls.¹⁰ This oxidative stress in muscle may not only lead to oxidative damage but could also deplete systemic antioxidant reserves. SpectraCell's MicroNutrient Testing, including tests for functional B vitamins, magnesium, zinc and antioxidant reserves, combined with our serum homocysteine assay, may help to determine if these functional deficiencies could be part of the clinical picture of CFS and fibromyalgia patients.

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ARTHRITIS AND MUSCULOSKELETAL DISORDERS

Numerous studies have documented reduced levels of B vitamins, minerals and antioxidants in rheumatoid arthritis (RA) patients¹⁻⁵ and juvenile RA patients.^{6,7} These deficiencies may be secondary to the disease process, to medications, or to poor dietary intake. Even marginal deficiencies may have clinical consequences in these patients, since the relatively limited blood supply to joints may increase susceptibility of these tissues to systemic nutrient deficiencies. Several studies have demonstrated increased oxidative stress in RA patients and have suggested that this stress might play a role in the tissue damage and inflammation associated with RA. In particular, Hawkins and Davies³ found that oxidants caused site-specific, rather than non-specific, damage to collagen. And, several studies have suggested that low antioxidant levels may be a risk factor for RA.^{4,5} Some evidence indicates that an antioxidant deficiency may also be involved in the progression of osteoarthritis (OA),⁸ and a high intake of antioxidant nutrients, especially vitamin C, seemed to reduce the risk of cartilage loss and disease progression in osteoarthritis patients.⁹

B vitamin deficiencies also appear to be prevalent in RA, especially in association with elevated serum homocysteine (Hcy) levels. RA patients were found to have significantly higher levels of Hcy than healthy controls,¹⁰ and serum folic acid and vitamin B12 were found to be correspondingly low.¹¹ It was suggested that the elevated Hcy associated with folic acid, vitamin B6 and B12 deficiencies may have a role in the high cardiovascular mortality seen in RA patients.¹¹ Serum Hcy elevation seems especially prevalent in patients treated with either methotrexate or sulfasalazine,¹² and supplementation with folic acid was found to reduce side effects of MTX therapy.¹³ Zinc and magnesium deficiencies have also been documented in RA patient populations, relative to healthy controls.^{1,14} Finally, it has been suggested that vitamin B6 and, possibly, vitamin B2 deficiencies may be etiologic factors in carpal tunnel syndrome,^{15,16} and these vitamins have been used in the therapy of this condition.¹⁶

Thus, SpectraCell's wide range of tests for specific B vitamins, minerals, glutathione, antioxidant function and plasma homocysteine may be helpful in the therapy and prevention of progression of RA as well as for several other musculoskeletal disorders.

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INFECTIOUS DISEASES AND AIDS

It has long been thought that the nutritional status can influence an individual's susceptibility to infection as well as the severity of the infection. In support of this contention, numerous investigations have found that diets deficient in one or more nutrients could exacerbate an infection.¹ The basis for this increased susceptibility and virulence was originally thought to be a reduced level of immune function secondary to the underlying nutritional deficiency. However, in a very elegant series of investigations using both an animal model and humans, Beck and coworkers² found that an antioxidant deficiency not only decreased specific immune functions, but also led to specific mutational changes in the viral genome such that a normally avirulent virus became virulent.³ It was also shown that once these mutations occurred, even mice with normal nutrition developed disease when exposed to the mutated virus.³ In the human population studied, patients who developed clinical sequelae from viral exposure had lower serum levels of several nutrients, including vitamin B2, selenium, carotenes and lycopene,⁴ than a control, non-infected group. Furthermore, investigations of influenza virus have found that oxidative stress influenced both the infectivity as well as the severity of the infection.⁵ One study found that infected mice supplemented with vitamin E had reduced viral titers, less appetite loss and one-third less weight loss compared with infected, non-supplemented mice.⁶

In addition to acute infections, chronic viral infection has been associated with increased oxidative stress and subsequent increased probability of progression to viral-associated carcinoma. Yu et al.⁷ followed over 7000 chronic hepatitis C men for an average of 5.3 years. Those patients who progressed to hepatocellular carcinoma (HCC) had lower mean plasma selenium levels and decreased levels of carotenoids than patients who did not develop HCC. Subsequently, Emerit et al.⁸ found that 19 of 20 patients chronically infected with hepatitis C virus had higher than normal levels of lipid peroxidation products and other oxidants that had chromosome-damaging properties. Finally, Ho et al.⁹ examined nutrition as a potential, independent risk factor in the progression of genital human papillomavirus (HPV) to cervical intraepithelial neoplasia (CIN). In a case control study they found an inverse correlation between plasma alpha-tocopherol levels and the risk of CIN. They also observed that high levels of ascorbic acid were protective.

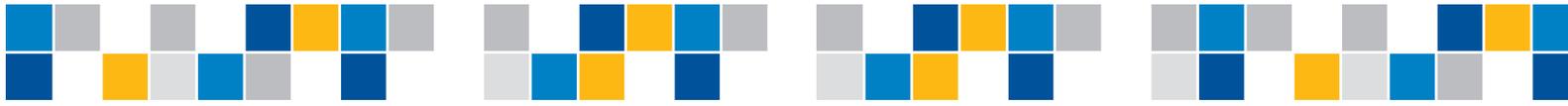
Human immunodeficiency viral (HIV) infection represents another example where the progression of HIV infection to AIDS appears to be influenced by nutritional factors, especially by antioxidants and vitamin B12. Insufficient intake, malabsorption, diarrhea, impaired storage, altered metabolism and increased usage can all contribute to the nutritional deficiencies observed in HIV infected individuals. Deficiencies of vitamins A, E, B6, B12 and C, carotenoids, selenium, glutathione, zinc and total thiol (cysteine) levels are prevalent in HIV infected populations.¹⁰⁻¹² It is now believed by many investigators that the major pathologic feature of HIV infection is the generation of oxidative stress, secondary to overproduction of reactive oxygen species and depletion of antioxidants.¹³ This process in turn leads to apoptosis (programmed cell death) and consequent depletion of CD4 cells.¹⁴ Combinations

of the nutrient deficiencies listed above are believed to contribute to the generation of the free radical overload that promotes the apoptosis of CD4 T lymphocytes.¹⁵ In addition to antioxidants, deficiencies of vitamin B12 and glutamine appear to be especially relevant to HIV disease progression. In a non-concurrent prospective cohort study of 310 HIV seropositive subjects, Tang et al.¹⁶ found that those participants with low serum B12 had significantly shorter AIDS-free time than those with adequate B12 levels. And, HIV infection appears to induce glutamine deficiency, possibly secondary to the rapid turnover of immune cells that occurs in most stages of the infection.¹⁷ A double-blind, placebo-controlled study found that administration of 40 grams of glutamine/day in combination with a mixture of antioxidants caused an average gain of 1.8 kg of lean body mass over 12 weeks, compared to a gain of 0.4 kg by the control group.¹⁸

SpectraCell's antioxidant panel, the SpectroX™ + glutathione tests, can be used to estimate antioxidant defenses in either acute or chronic infections, especially hepatitis C virus and HIV. MicroNutrient Testing for functional deficiencies of B vitamins, zinc, magnesium and glutamine can also be valuable in designing individual combinations of supplements that may help your patients avoid, delay or slow the progression of viral disease.

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WOMEN'S HEALTH ISSUES

PREMENSTRUAL SYNDROME (PMS)

Several nutrients have been found associated with PMS and found useful for its relief. Thys-Jacobs noted the similarity between the symptoms of PMS and hypocalcemia and described several clinical trials that found calcium supplementation effectively alleviated the majority of symptoms associated with PMS.¹ Both magnesium² and vitamin B6³ also appear to be associated with the symptoms of PMS. The success of therapy with these nutrients may be related to the prevalence of their reduced availability in modern diets and consequent deficiencies.^{4,5} In a random sampling of patients admitted to an ER, the B6 deficiency was estimated to be as high as 32%.⁵

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PREGNANCY

It has not been especially well recognized that the rapid cell division characteristic of a growing fetus represents a nutritional drain, especially of B vitamins, minerals and antioxidants, on a pregnant woman. One study demonstrated that the levels of retinal, thiamin, vitamin B6, folic acid and vitamin B12 decreased significantly as pregnancy advanced. Another study found that mean intakes of iron, zinc, calcium, magnesium, folic acid, vitamin D and vitamin E were below recommended standards for pregnant women.² Yet another series of studies found that a marginal degree of biotin deficiency developed in a substantial number of women during normal pregnancy, and that this deficiency was severe enough to produce metabolic derangements capable of causing fetal malformations.³ It has also been noted that approximately 50% of women develop a biochemical thiamin deficiency during pregnancy, which could contribute to low birth weight.⁴ The rate of folate catabolism progressively increases during pregnancy, reaching a peak in the third trimester, at the time of maximal fetal growth. The increased need for folate appears to be due to its increased usage for fetal nucleic acid synthesis and cell division. Folic acid supplementation is especially critical if the mother is taking any of the common drugs which act as folic acid antagonists, such as trimethoprim, triampteren, carbamazapine, phenytoin, phenobarbitol or primidone.⁶ Thus, because of the strenuous nutritional demands of a growing fetus, pregnancy represents a nutritionally perilous state for every pregnant woman, as she provides nutrients to support her child's rapid growth in addition to supplying her own metabolic needs.

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MENOPAUSE

Post-menopausal women become increasingly subject to higher rates of bone loss, cardiovascular disease and cancer, especially breast cancer, than they were before menopause. This increase often coincides with reduced intake of nutrients through decreased absorptive efficiency, decreased appetite and reduced levels of activity. Thus, risk reduction programs encompassing diet, appropriate nutrient supplementation and exercise are essential for post-menopausal women to maintain good health into old age. A major component of any risk reduction program is maintaining optimal levels of antioxidants, minerals and B vitamins. The role of antioxidant vitamins in preventing cardiovascular diseases, especially stroke, has achieved substantial importance with the knowledge that oxidative modification of low-density lipoprotein can promote atherosclerosis and that vitamin E consumption is inversely related to the risk of death from coronary heart disease.¹ Epidemiological studies have also provided substantial evidence that diets rich in antioxidants significantly reduce the risk of premature death from cardiovascular disease and cancer, and that levels of intake 25-35% below the optimal threshold predict a minimal 2-fold increased risk of disease.² The role of B vitamin intake, especially of folic acid, vitamin B2 and vitamin B6, has evolved from the prevention of anemia to the prevention of heart disease and stroke, and, more recently, to the prevention of cancer.³ Impressive evidence has been compiled targeting B vitamin and, especially, folic acid deficiency as key culprits in the occurrence of human mutations and subsequent carcinogenesis.⁴ Since vitamin deficiencies, especially those that occur with aging, are so prevalent,⁵ a postmenopausal health maintenance program should include measurement of functional levels of B vitamins, minerals and antioxidants.

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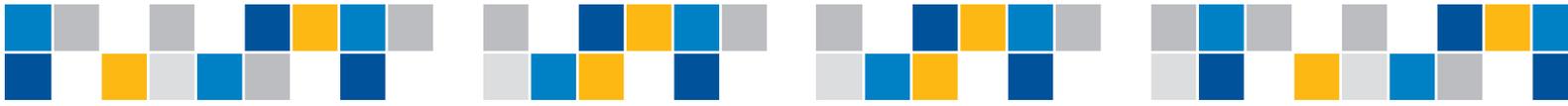
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OSTEOPOROSIS

Healthcare providers and the general public have long been aware of the importance of calcium and vitamin D for maintenance of bone density after menopause. Less well known is the accumulating evidence that a predisposition for osteoporosis begins in childhood and adolescence.¹ In fact, some evidence indicates that a woman's diet while pregnant can influence her child's later bone mass.² Thus, monitoring functional calcium levels may be as important early in a woman's life as it is after menopause, especially for strenuously athletic adolescents and young adults.³ Certain medical conditions, such as irritable bowel syndrome and renal disease, can also predispose women to osteoporosis.^{4,5} In addition to a need for calcium, a sufficient supply of magnesium and zinc in the diet have also been found to be critical for preventing loss of bone mass,⁶ and aging itself constitutes an independent risk factor for magnesium deficiency.⁷ Thus, osteoporosis prevention is a lifelong process of assuring women have sufficient levels of magnesium and zinc, as well as adequate amounts of calcium and vitamin D.

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Conclusion

Extensive scientific and clinical studies spanning over 50 years have repeatedly demonstrated that vitamin, mineral and antioxidant deficiencies can have adverse effects upon health, from acute infections to chronic disease, at all stages of our lives.

SpectraCell offers you a window to the cell to scientifically assess your patients' intracellular requirements and to provide targeted recommendations to correct the functional deficits that exist. MicroNutrient Testing is a unique and important part of a clinically driven, physician prescribed wellness plan.

Standard serum tests measure the quantities of vitamins and minerals present in serum, providing limited information on intracellular levels.

At SpectraCell, we grow your patients' lymphocytes in tissue culture to determine functional intracellular deficiencies that can limit mitogenic responses and cell-mediated functions essential to our health and well being.

SpectraCell's MicroNutrient Testing measures functional levels of a broad range of vitamins, minerals, amino acids and antioxidants, as well as other essential nutrients. These tests offer the clinician a scientific basis for repletion of specific nutrient deficiencies by targeting the specific genetic, metabolic, biochemical and physiological requirements of each patient.

You are uniquely qualified to guide your patients' nutritional care. By using MicroNutrient Testing to identify your patients' specific needs, you can provide scientifically based therapy that aids the development of optimal interventions and assists patients in their quest for lasting health.



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