TRACE ELEMENTS

NEWS UPDATES

2013

Case Of The Green Tongue

In some of my past lectures I have presented "The Case of The Green Tongue." This particular case involved a young child whose tongue was found to have a dark green discoloration. The child was also suffering from multiple health symptoms and recurring infections. The mother had an HTMA performed and the results found very high levels of vanadium. Excess vanadium is known to produce this particular type of discoloration on the tongue. Upon further investigation it was found that the child's bedroom was located just above the furnace located in the basement below. Apparently, the furnace was not vented properly and as a result, the products of combustion were entering the child's bedroom. It should be noted that one source of vanadium is from petrochemical combustion. Of course it is very fortunate that the source of vanadium was found in this case, but more importantly, it led to modification of the furnace that reduced exposure to deadly carbon monoxide. Subsequent nutritional therapy and reduced exposure from this source eventually resolved the tongue discoloration and amelioration of other health issues.

In the following case reported in The Lancet, a seventy year old male was admitted into the hospital with pain in his hip, as well as additional neurological symptoms. What was found, was a fistula on his thigh that exuded a blackish fluid, and a green staining of his tongue. It was determined that a hip replacement implant performed six years earlier was improperly fitted and had actually broken through the ceramic insert lining the acetabular cavity. It was noted that the prosthesis was markedly corroded and tests revealed elevated vanadium in the blood and urine, as well as aluminum. After revision of the hip prosthesis, a three month follow-up revealed a reduction in vanadium, aluminum and titanium levels, along with a reduction of the green staining of the tongue and improvement in neuropathy symptoms. Moretti, B, et el. Peripheral Neuropathy After Hip Replacement Failure: Is Vanadium The Culprit? Lancet, Vol.379 2012.

Comment: The value of physical examination cannot be over-emphasized. In the first case I discussed, one of our astute clients who attended one of my seminars remembered the relationship that I described between excess vanadium and its physical manifestation. This led to the suspicion of excess vanadium accumulation that led to the discovery of the source and ultimately prevented a potentially serious issue with carbon monoxide poisoning, perhaps saving a life. Excess of other heavy metals as well as nutrient minerals often present with physical findings. Plumbism for example, can cause a lead line along the gums, Mee's lines on the fingernails indicate excess arsenic. Mercury, copper, iron nickel and silver can present various skin manifestations, such as; discoloration, rashes, hives, etc.

Hair and Nail Mineral Patterns in Children With Autism

Minerals and nutrition in general are important for central nervous system (CNS) function and development. Therefore, it stands to reason that this study was performed to assess the levels of the trace and toxic elements in children diagnosed with autism. The study was also done to determine if the level of elements could be correlated with the severity of autism. The study included forty-five children who were graded for three groups, high functioning autistic group (HFA), medium functioning autism (MFA) and low functioning autism (LFA) and compared to a group of healthy children. Results showed the level of copper in the hair and nails of the autistic group were significantly elevated compared to the age and sex-matched controls. Copper was significantly more elevated in the LFA compared to the other grades and was also correlated

with the degree of severity. The LFA group also was found to have significantly lower zinc levels compared with normal controls. They also found lower levels of magnesium and selenium in the hair of the autistic children compared to the healthy control group. In addition, lead and mercury levels were also found to be high. The LFA group had higher levels of lead and mercury compared to the HFA group as well as lower concentrations of magnesium and selenium. Priya, MDL, Greeth, A. Level of trace Elements (Copper, Zinc, Magnesium and Selenium) and Toxic Elements (Lead and Mercury in the Hair and Nail of Children with Autism. Biol.trace Elem. Res. 142, 2, 2011.

Comment: This is an interesting study, even with its limitation of analyzing only a few elements. In drawing data from our own recent TEI database of fifty children diagnosed with autism, as a group we noted similar findings. Our study consisted of forty-three males and seven female children ranging in ages three to eleven years. These subjects however, were not classified into low, medium or a high functioning group, so our test subjects should be considered to likely represent all three functioning levels of autism. Our findings here at TEI however, did correlate well with the above study. The average HTMA copper levels were one-hundred and fifty-three percent above normal and zinc was fifty-five percent of normal. Average selenium values were sixty-two percent of normal, while magnesium levels were forty-seven percent. Lead and cadmium levels were not significantly elevated, but mercury was one-hundred and forty-five percent above normal and aluminum one-hundred and twenty-six percent above normal. Further, a significant imbalance between sodium and potassium was noted. Sodium was optimum but potassium was two-hundred and sixty-five percent of normal. The mineral pattern of the autistic group as a whole revealed a sympathetic mineral pattern. We should note that I am only presenting the general statistical pattern, which does not take into consideration individual variations of HTMA mineral patterns.

Excess Hair Mineral Accumulation, Oxidative Stress And Parkinsonism

Certain nutritive minerals in excess, as well as heavy metals are known to contribute to increased oxidative stress leading to neurological manifestations. Komatsu and colleagues reported their study of hair tissue mineral levels of manganese, iron, lead, cadmium and aluminum concentrations in a group of Mongolian people and the influence of these metals contributing to oxidative stress and Parkinson's disease-like symptoms that are prevalent in Mongolia. The study included two-hundred and ninety-nine subjects from several areas of Mongolia along with a healthy control group. Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) was measured to evaluate oxidative stress. Results showed that Mongolian subjects particularly those with Parkinsonism and arthritis had high accumulation of manganese, iron, lead, cadmium and aluminum in the hair compared to the controls. It was reported that the urinary 8-OHdG also correlated with the hair mineral results. Komatsu, F, et. al. A High Accumulation of Hair Minerals in Mongolian People: 2(nd) Report; Influence of Manganese, Iron, Lead, Cadmium and Aluminum to Oxidative Stress, Parkinsonism and Arthritis. Curr. Aging Sci. 1, 2011.

Comment: We have often noted hair mineral patterns of patients suffering from Parkinson's, ALS and other neurological conditions having elevations of a number of the minerals mentioned in this study. However, it is important to review the interrelationships of the minerals, i.e. ratios when evaluating patients with these conditions. The absolute levels of the minerals may not always be found to be in excess or in deficiency, but imbalances between the minerals can still contribute to increased oxidative stress and neurological manifestations. Hair mineral analysis can serve as an important adjunctive test in evaluating patients with neurological symptoms.

Magnesium and Stroke

Prospective studies were carried out on the effect of magnesium intake and stroke incidence. It was found that dietary magnesium intake was inversely associated with an increase in ischemic stroke. Low magnesium intake has been associated with a number of risk factors including, hypertension, diabetes, metabolic syndrome, insulin resistance, blood lipid peroxi-

dation, arrhythmia, inflammation, clotting and reduced vascular contractility. Magnesium supplementation may play a significant role in the prevention of ischemic stroke by impacting receptor blockades, glutamate release, antagonism of calcium influx, preventing ATP depletion and increasing cerebral vasodilation. Larsson, SC, et al. Dietary Magnesium Intake and Risk of Stroke: A Meta-Analysis of Prospective Studies. Am.J.Clin.Nutr. 95,2, 2012. Song, Y, Liu, S. Magnesium For Cardiovascular Health: Time For Intervention. Am.J.Clin.Nutr. 95,2, 2012.

Comment: Magnesium status has long been recognized to be associated with cardiac arrhythmia, coronary artery disease, hypertension, insulin and glucose regulation. Seelig, also noted that the stress response is enhanced when a magnesium deficiency is present, which can contribute to stress-related conditions, such as gastrointestinal and cardiovascular disturbances, arthritis, or emotional disturbances. The enhanced stress response may also aggravate other conditions such as arthritis and blood sugar disorders. Seelig, MS: Consequence of Magnesium Deficiency on the Enhancement of Stress Reactions: Prevention and Therapeutic Implications (A Review). J.Am.Col.Nutr. 13, 5, 1994.

In reviewing HTMA samples submitted to TEI that had been diagnosed with past strokes, we found that the male and female occurrence was quite similar. Of six-hundred cases, three-hundred and forty were females and two-hundred and sixty were males. Male stroke cases had a median magnesium level of 3.3 milligrams percent, approximately forty-seven percent of normal. Female median magnesium was 5.1 milligrams percent, or eight and one-half percent below normal. Both groups had calcium-to-magnesium ratios above eleven to one, indicating a relative and, or absolute magnesium deficit. This type of mineral relationship can lead to abnormal calcium transport, increasing susceptibility toward stroke. Even though serum magnesium is the most widely used test to determine magnesium deficiency, it does not represent total magnesium status or the intracellular magnesium pool. HTMA can be a tool not only to evaluate total magnesium status, but also the interrelationship between the calcium-to-magnesium ratio.

Drug Induced Changes in Mineral Concentration and Excretion In the Treatment of Non-Insulin-Dependent Diabetes – (Metformin)

Drugs are known to effect mineral concentrations in the body either by increasing excretion, enhancing retention, or by producing compartmental relocation and/or de-compartmentalize minerals. Metformin, also known commonly as Glucophage is the most widely prescribed oral anti-diabetic drug. It acts by suppressing glucose production by the liver. However, Dosa, et al recently published findings concerning the action of metformin on certain mineral concentrations in non-insulin-dependent diabetes mellitus patients (NIDDM). The study included a group of healthy adults and a group of NIIDM patients who had not taken anti-diabetic medication prior to the study. Plasma and urine levels of magnesium, copper and zinc were measured along with glucose, HDL, LDL, cholesterol, triglycerides, HbA1c and total red blood cell magnesium in both groups. There were major differences found in the NIIDM group for plasma and urine magnesium, zinc, copper and RBC magnesium compared to the control group. Following three months of therapy with metformin, these parameters were significantly modified. Urine magnesium loss was reduced and RBC magnesium concentration increased in the treatment group. The study suggests that these changes in mineral concentrations were due to the action of metformin therapy along with an improvement in glycemic control and reduction of HbA1c. *Dosa, MD, et al. Influence of Therapy with Metformin on the Concentration of Certain Divalent Cations in Patients with Non-Insulin-Dependent Diabetes Mellitus. Biol.Trace Elem.Res. 141, 1, 2011.*

Comment: We have often discussed the nutritional requirements of patients developing diabetes based upon HTMA studies. The authors in the above paper discuss the important contribution of mineral imbalances and their involvement in the development of NIDDM as well as other diseases. This study also demonstrates the impact of nutrient modification by metformin and may explain the mechanism for the effectiveness of metformin on NIDDM. If significant nutritional deficiencies and imbalances exist then the effectiveness of metformin may not be as significant and therefore, perhaps addressing nutritional imbalances can actually contribute to its effectiveness. This may be true for many other drugs as well.

Hair Mineral Concentrations and Insulin Resistance

A study by Chung, and Yum, investigated the relationship of hair mineral levels and insulin resistance in Korean adult males. Their study consisted of sixty-three patients with metabolic syndrome and sixty normal controls. Fasting glucose, total cholesterol, triglyceride, HDL, hair mineral levels and Homeostasis Model of Assessment - Insulin Resistance (HOMA-IR) were tested. They found a significant correlation between the hair calcium to magnesium ratio with HOMA-IR and insulin. Their findings concluded that insulin resistance was increased along with increased hair calcium to magnesium ratio and decreased concentrations of hair chromium. *Chung, J-H, Yum, K-S. Correlation of Hair Mineral Concentrations with Insulin Resistance in Korean Males. Biol.Trace Elem.Res. 150, 1-2, 2012.*

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"Low magnesium intakes and blood levels have been associated with type 2 diabetes, metabolic syndrome, elevated C-reactive protein, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer. Almost half (48%) of the US population consumed less than the required amount of magnesium from food in 2005-2006, and the figure was down from 56% in 2001-2002."

"Surveys conducted over 30 years indicate rising calcium-to-magnesium food-intake ratios among adults and the elderly in the United States, excluding intake from supplements, which favor calcium over magnesium. The prevalence and incidence of type 2 diabetes in the United States increased sharply between 1994 and 2001 as the ratio of calcium-to-magnesium intake from food rose from <3.0 to >3.0. Dietary Reference Intakes determined by balance studies may be misleading if subjects have chronic latent magnesium deficiency but are assumed to be healthy. Cellular magnesium deficit, perhaps involving TRPM6/7 channels, elicits calcium-activated inflammatory cascades independent of injury or pathogens. Refining the magnesium requirements and understanding how low magnesium status and rising calcium-to-magnesium ratios influence the incidence of type 2 diabetes, metabolic syndrome, osteoporosis, and other inflammation-related disorders are research priorities."

Nutr Rev. 2012 Mar;70(3):153-64. doi: 10.1111/j.1753-4887.2011.00465.x. Epub 2012 Feb 15.Rosanoff A, Weaver CM, Rude RK. © 2012 International Life Sciences Institute. PMID: 22364157 [PubMed - indexed for MEDLINE] Center for Magnesium Education & Research, 13-1255 Malama Street, Pahoa, HI 96778, USA. ARosanoff@gmail.com

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This report was designed to investigate the relationship of magnesium intake with metabolic findings, depression and physical activity in elderly patients with type 2 diabetes. The study included two-hundred and ten patients that were sixty-five years of age and above who were diagnosed with type 2 diabetes. The patients were interviewed and lifestyle information and 24-hour dietary recall were obtained. Clinical variables were measured, including anthropometric measurements, blood pressure, and determination of blood and urine samples. Assessment of depression was based on DSM-IV criteria. Linear regression was used to determine the relationships of magnesium intake with nutritional variables and metabolic parameters. Results found that over eighty-eight percent of the group had magnesium intake less than the dietary reference intake, and thirty-seven percent were found to have hypomagnesaemia. Lower magnesium intake was associated with depression, metabolic syndrome, central adiposity, higher body fat and BMI. *http://www.nutritionj.com/content/11/1/41 Huang et al. Nutrition Journal 2012, 11:41*

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Insulin and Cancer Promotion

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In 2005, Andrew Morris and other researchers at the University of Dundee in the United Kingdom were studying therapy for patients with type 2 diabetes and found that a drug used for lowering insulin levels was associated with a significant decrease in cancer incidence. The drug was metformin an oral anti-diabetic agent. Diabetic patients treated with metformin were found to have twenty-five to forty percent less cancer incidence than patients who were on insulin therapy or taking other drugs that increase insulin secretion. Metformin activates an enzyme in the liver that reduces the production of glucose thereby reducing insulin and IGF levels. *Taubes, G. Unraveling the Obesity-Cancer Connection. Science 335, 2012.*

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Folic Acid and Reduced Risk of Autism

Folic acid not only aids in preventing neural tube birth defects, but researchers now feel it can also reduce the risk for autism spectrum disorder (ASD) in children. The study included over 85,000 children from a population-based prospective study in Norway and was from 2002 through 2008. The results concluded that the use of prenatal folic acid supplements near conception was associated with lower risk of autistic disorder and support the use of prenatal folic acid supplementation.
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Chromium and Diabetes Study

Chromium is known to be related to the normal function of insulin and is a constituent of cellular insulin receptors. A lack of chromium is related to insulin resistance. This study evaluated the effect of chromium supplementation on fasting plasma glucose, glycated hemoglobin (HbA1c), and lipid levels in type 2 diabetic patients who were also on insulin therapy. Patients were randomized and supplemented with 100 micrograms of chromium daily over a period of two weeks. The chromium dosage was then increased to 200 micrograms daily for the next six weeks. Fasting plasma glucose, HbA1c and serum lipids were measured after each phase and compared to baseline. Fasting plasma glucose showed a significant decrease after the first phase of chromium supplementation and tended to diminish even further during the second phase of supplementation. HbA1c also significantly decreased during both phases. *Effect of Chromium-Enriched Yeast on Fasting Plasma Glucose, Glycated Haemoglobin and Serum Lipid Levels in Patients with Type 2 Diabetes Mellitus Treated with Insluin. Jaroslav Racek, et al. Biol.Trace Elem. Res.155,1, 2013.*

Comment: It has long been known that chromium deficiency is present in patients with diabetes and that supplementation aids in the improvement of insulin resistance and other complications associated with the progression of type 2 diabetes. The status of the body's chromium reserve is difficult to determine, however, hair tissue mineral concentrations can readily provide the tissue status of chromium. Additionally, is can also reflect chromium's relationship to other nutritional factors that may also contribute to the development and progression of type 2 diabetes. Unfortunately, even though the worldwide epidemic of diabetes is increasing, assessing and providing necessary nutritional support for treating and preventing the long-term complications caused by this disease is severely lacking.

Arsenic and Cardiovascular Disease Study

This study discusses the impact of long-term arsenic exposure and the incidence of cardiovascular disease. The study included over 3,500 Native American Indian men and women aged 45 to 74 years living in Arizona, Oklahoma, North and South Dakota. Arsenic was measured in urine at baseline and used as a biomarker of long-term arsenic exposure. Over 1,100 individuals developed fatal and nonfatal cardiovascular disease. The study concluded that long-term exposure to low to moderate arsenic levels was associated with the incidence of cardiovascular disease and mortality. *Association Between Exposure to Low to Moderate Arsenic Levels and Incident Cardiovascular Disease: A prospective Cohort Study. Moon, KA, et al. Ann. Intern. Med. Sept, 2013*

Comment: Sources of arsenic other than from industry can also be found in the environment. It can be found naturally occurring in water, and is present in foods, herbs, seafoods, seaweed, rodenticides, and insecticides as well and in weed control products. Hair tissue mineral analysis (HTMA) can be used to monitor arsenic exposure and has been correlated with intake as well as arsenic accumulation in internal organs with long-term intake.

Hair Mineral Patterns, Reproduction and Environmental Endocrine Disruptors

It is known that chemicals from the environment can impact fertility. It is also believed that heavy metals such as mercury as well as the status of some nutrient minerals can impact fertility and reproduction in humans. A report by Dickerson, et al, studied the hair mineral concentrations in women with fertility problems who underwent in vitro fertilization treatment and investigated treatment outcomes. Mercury, zinc and selenium were analyzed. Hair mercury revealed a negative correlation with oocyte yield and follicle number following ovarian stimulation. The hair zinc and selenium correlated positively with oocyte yield after ovarian stimulation. Their data found that mercury had a deleterious impact while zinc and selenium showed a positive impact in the ovarian response to gonadotropin therapy for in vitro fertilization. The researchers found that minerals such as zinc and selenium may be important for reproductive outcomes and are reflective of long-term environmental exposure and dietary status. Their study concluded that HTMA offers a method of investigating the impact of long term exposure to endocrine disruptors and nutritional status on reproductive outcomes. **E***ndocrine Disruptor and Nutritional Effects of Heavy Metals in Ovarian Hyperstimullation. Dickerson, EH, et al. J. Assist Reprod. Genet. 12, 2011.*

Comment: Nutritional status is very important in reproductive health and may involve many factors beyond those mentioned in this one article. For example not only are zinc and selenium important but also the metabolic type, thyroid status, hormonal status as well as other nutritional and heavy metals, such as manganese, copper and zinc relationship, iron, magnesium, lead and cadmium. The status of these factors can also be related to complications during pregnancy, such as; eclampsia, gestational diabetes and even postpartum depression. HTMA is a valuable tool for investigating and addressing the nutritional status in those women with reproductive problems and also during and following pregnancy.

Magnesium and Heart Disease

Over seven-thousand individuals without any known cardiovascular disease participated in a study to determine if urinary magnesium excretion and plasma magnesium were associated with ischemic heart disease risk. Urinary magnesium excretion was measured in two baseline twenty-four hour urine collections. The mean urinary magnesium excretion in males was 4.25 +- 1.65 mmol/24 hours and 3.54 +- 1.4 mmol/24 hours for women. A median follow-up at ten years found 462 fatal

and non-fatal ischemic heart disease events occurred. It was found that the lowest range of urinary magnesium excretion was associated with increased heart disease risk compared to higher excretion rates. There was no association found between plasma magnesium and heart disease. The study concluded that low urinary magnesium excretion was independently associated with higher ischemic heart disease incidence and suggests increasing dietary magnesium intake in those with the lowest urinary magnesium excretion could reduce the risk of ischemic heart disease. *Urinary and Plasma Magnesium and Risk of Ischemic Heart Disease. Joosten, MM, et al. The Am.J.Clin.Nutr. 97,6, 2013.*

Comment: Adequate magnesium intake would result in higher urinary magnesium excretion thus indicating a higher dietary intake compared to low urinary excretion. Therefore, it is logical that those with low urinary magnesium excretion had low dietary intake and have a higher risk of developing heart disease over time. Magnesium is an important intracellular mineral and is essential for many functions in the body and is especially important for normal cardiovascular function. Past studies have relied upon plasma magnesium levels to determine an association between heart disease and magnesium deficiency and most have been unable to show any relationship. The reason for this is that circulating magnesium levels are maintained within a narrow homeostatic range and additional magnesium reserves can be called upon as needed from storage areas, such as the muscle and bone. For this reason, circulating magnesium does not adequately indicate dietary intake or status. In addition, even though urinary magnesium excretion can somewhat provide information concerning dietary intake of magnesium, it cannot provide an indication of tissue status or the important interrelationships that magnesium shares with other minerals. Hair tissue mineral patterns however, can provide a reflection of dietary intake as well as the relationship of magnesium with calcium, sodium, potassium, etc. It has been reported that almost half the U.S. population consumed less than the required magnesium intake from the years 2005 and 2006. This dietary trend has subsequently lead to an increase in calcium intake relative to magnesium intake over the years from a ratio of less than three to one to greater than three to one, leading to a relative decrease in magnesium absorption from the diet and even reduced body reserves. When excess calcium develops in the tissues a relative magnesium deficit develops leading to chronic, calcium-activated inflammatory conditions throughout the body.

Stress and Hair Mineral Concentrations

The following discusses the hypothesis of stress and the impact upon mineral levels in the body based upon HTMA studies. Specifically, this study determined the hair tissue levels of calcium, copper, iron, magnesium, phosphorus and zinc levels in the hair of elementary school girls between the ages of five and ten years. Hair cortisone levels were also analyzed. Estimates of stress were obtained through the Coddington Life Events Scales for children. The questionnaire measures the frequency and timing of positive and negative life events relevant for the age group during the last year. The study found that higher levels of hair cortisone were associated with reduced hair levels of calcium, magnesium, zinc and calcium/phosphorus. The authors state, “This study demonstrates an independent association between chronic stress measures and hair mineral levels in young girls, indicating the importance of physiological stress-mineral pathways independently from individual or behavioral factors.” *Cross-Sectional Relationship Between Chronic Stress and Mineral Concentrations in Hair of Elementary School Girls. Vanaelst, B, et el. Biol.Trace Elem. Res. 153, 2013.*

Comment: Stress is known to affect not only physiological and psychological status but nutritional status as well. Changes in nutritional status in turn can lead to behavioral and biological changes leading to chronic activation of the stress response. Hair tissue mineral analysis (HTMA) can reflect the impact of long-term stress on nutritional status and thereby provide a specific approach to nutritional therapy.

Dietary Habits and Hair Mineral Patterns

Chojnacka, and colleagues investigated the diet of over one-hundred individuals while at the same time performing hair mineral analysis on the group. Evaluation of the data found that in those consuming highly processed foods there were statistically higher hair levels of sodium and phosphorus. Other findings from the study suggests that hair mineral content reflects the exposure or accumulation from the diet. *The Effect of Dietary Habits on Mineral Composition of Human Scalp Hair. Chojnmacka, K, et al. Environ. Toxicol.Pharmacol. 30,2, 2010.*