THE Original Internist

C • O • N • T • E • N • T • S

CLINT PUBLICATIONS

VOL. 17, NO. 1 · ISSN 1529-4722 · MARCH 2010

Adrenal Support
from Biotics Research

BIOTICS RESEARCH CORPORATION
"The Best of Science and Nature"
www.bioticsresearch.com

Addressing **adrenal dysfunction** is frequently a difficult and frustrating process for the healthcare practitioner. The overwhelming prevalence of glucose dysregulation compounds the issue and must be addressed in order for resolution to occur. Biotics Research Corporation has developed several key innovative products that provide targeted, effective, nutritional support for those having these complex health challenges; **Bio-Glycozyme Forte**™ and **GlucoBalance**®. In addition, Biotics Research has developed **Cytozyme-PT/HPT**™ and **Cytozyme-AD**™, concentrated neonatal glandular support products. Also essential: two broad spectrum combination supplements that target the specific nutritional needs of the adrenal cotical hypofunctioning and hyperfunctioning patient, **ADB5-Plus**™ and the adaptogenic formula **ADHS**®.

BIOTICS RESEARCH CORPORATION
"The Best of Science and Nature"
www.bioticsresearch.com

For more information contact:

Biotics Research Corporation • (800) 231 - 5777
6801 Biotics Research Drive • Rosenberg TX 77471
Email: biotics@bioticsresearch.com

THE ORIGINAL INTERNIST

Clint Publications

720 Oak Knoll
Rolla, MO 65401
Telephone: (573) 341-8448
Fax: (573) 341-8494
E-mail: virginia@drkessinger.com

www.clintpublications.com

The Original Internist is published quarterly. Publication months are March, June, September and December, barring any unusual or unforeseen circumstances.

News items and/or letters pertaining to natural health care are welcome. The editorial staff reserves the right to edit and/or reject all material received. Letters to the editor may be condensed in order to fit the allotted space. An address and telephone number where the author may be reached during normal business hours should also be included for verification purposes. Deadline for article submission is the 5th of the month preceding publication.

SUBSCRIPTION & ADDRESS CHANGES

A subscription to *The Original Internist* is $50. A free one-year subscription will be given to anyone who submits a case study or scientific article which is accepted for publication. (This does not include letters to the editor.)

Please notify Clint Publications if you change your address or office name, or we cannot be responsible for proper delivery of your journal.

ADVERTISING

Advertising deadline is the 5th of the month preceding publication. For advertising rates or information, contact Clint Publications.

DISCLAIMER

The opinions expressed in *The Original Internist* are presented for the purpose of providing an open forum for unbiased case studies, contemporary ideas and discussion of matters relevant to natural health care. Its primary mission is to educate and inform those especially interested in promoting natural health care as a primary treatment. The opinions expressed in *The Original Internist* do not necessarily reflect the opinions and policies of Clint Publications or *The Original Internist.*

CALENDAR OF EVENTS

FOR ALL DABCI SEMINARS ….. VISIT OUR NEW WEBSITE www.drkessinger.com

March 13 - 14, 2010 Session # 24 (Dallas, TX)
Upper Gastrointestinal Disease
Instructor: Jack Kessinger, DC DABCI

March 20 - 21, 2010 Session #8 (Los Angeles, CA)
Blood Interpretation Workshop
Instructor: Jack Kessinger, DC DABCI

March 27 - 28, 2010 Session # 13 (Portland, OR)
Pediatrics
Instructor: Bill Kleber, DC DABCI

April 10 - 11, 2010 Session #25 (Dallas, TX)
Lower Gastrointestinal Disease
Instructor: Frank Strehl, DC DABCI

April 10 - 11, 2010 Session #3 (Hartford, CT)
The General Examination and Associated Pathology
Instructor: Ben Bowers, DC DABCI

April 17, 2010 Session 5 (NUHS CAMPUS Chicago)

April 17 - 18, 2010 Session # 4 (Kansas City, MO)
Diseases and Exam of the Pelvis & Associated Path
Instructor: Frank Strehl, DC DABCI

April 24 - 25, 2010 Session #9 (Los Angeles, CA)
Cardiovascular Disease: Prevention/Diag/Mgmt
Instructor: Jack Kessinger, DC DABCI

April 24 - 25, 2010 Session #14 (Portland, OR)
Spirometry & Pulmonary Disease
Instructor: Bill Kleber, DC DABCI

May 1 - 2, 2010 Session #26 (Dallas, TX)
Reports, Clinical Documentation & Drug Reactions
Instructor: Jack Kessinger, DC DABCI

May 1 - 2, 2010 Session #4 (Hartford, CT)
Diseases and Exam of the Male and Female Pelvis
Instructor: Frank Strehl, DC DABCI

May 15 - 16, 2010 Session #10 (Los Angeles, CA)
Electrocardiography & Phonocardiography
Instructor: Ben Bowers, DC DABCI

May 15 - 16, 2010 Session # 6 (Kansas City, MO)
Multi-Channel Blood Chem, CBC, Thyroid, TSH
Instructor: Jack Kessinger, DC DABCI

May 22 - 23, 2010 Session # 15 (Portland, OR)
Geriatrics
Instructor: Bill Kleber, DC DABCI

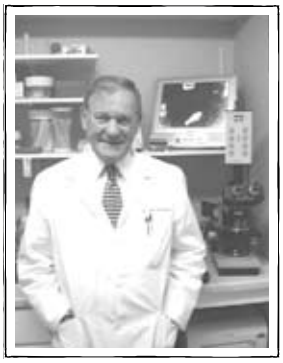
June 5 - 6, 2010 Session # 6 (Hartford, CT)
Multi-Channel Blood Chem, CBC, Thyroid, TSH
Instructor: Wayne Sodano, DC DABCI

June 5 - 6, 2010 Session # 7 (Kansas City, MO)
Additional Blood Tests, Tumor Markers for Internal Disorder Patient
Instructor: Ben Bowers, DC DABCI

June 12 - 13, 2010 Session # 11 (Los Angeles, CA)
Pharmacognosy (Herbal Therapy)
Instructor: Daniel Richardson, MSc, DN, PhD

For more information on our 2010-2011 seminars visit us online at
www.drkessinger.com
then click on ProHealth Seminars

From the Editor's Desk



Dr. Jack Kessinger

by: Jack Kessinger, DC, ND, DABCI
jack@drkessinger.com

Recent reports boast new protocols for prescribing statin (cholesterol lowering) drugs for healthy patients!!! Where's the science with an idea like that? The reasoning is presumed to prevent healthy people from developing cardiovascular disease. One of the statins (Baycol) was recently removed from the market because of at least 31 reports of fatal rhabdomyolysis. How many went unnoticed? We may never know.

Let me see? There is a well documented healthier approach for reducing cholesterol. This approach is commonly referred to as *natural health care*. Wouldn't it be a more responsible protocol to teach patients the importance of following a healthy diet, proper nutritional support, getting regular exercise and avoidance of tobacco smoke and excess alcohol for reducing cholesterol and obtaining optimum health? The natural approach seems like a more logical approach than the "band-aid" effect of a drug.

I've often wondered why the medical approach to counter the build-up of plaquing in the arteries continues to be concentrating on thinning the blood with medication (aspirin or coumadin), so it can more easily flow through smaller nutrient canals. What about the side effects of these medications?

As troubling as the statin drug for healthy patient theory is, I watched several interviews on television lately, debating whether pre-school children who have type II diabetes should be put on statins or not. Some medical experts say diet should be the first approach. Others think children are okay to take the drugs. The biggest debate was if they should have them before they become teenagers.

Wait a minute! Children should never have type II diabetes! Type II diabetes is completely avoidable, and curable with proper diet, nutrition and exercise. Parents must assess what their kids are consuming. Are they getting enough fruits and vegetables daily? Are they exercising? Or, are they sitting in front of the TV and computer in their extra time? Obesity among children has raised to over 30%. To further emphasize this, pull out some old photos of your grade school days, or better yet, your parents photos from grade school. Are there any obese children in these photos? Most likely not, maybe one or two at most. Now look at the children you see on the street, in the malls and in your office. How many of them are not at a healthy weight?

I am always shocked to see what today's average child eats. In our clinic we have parents fill out a food diary for one week of every food item their child consumes. It is not unusual to see NO FRUITS OR VEGETABLES on the list…. Unless you count french fries and catsup.

New studies show that the current generation of children will be the first generation who can expect a shorter lifespan than their parents. Up until recently, each generation's expected average lifespan has continued to exceed their predecessors. The reasons for this change are many, but can be attributed to the consumption of low nutrient processed foods, soft drinks (diet or not), a lack of physical activity and over use of prescription drugs, i.e., antibiotics and vaccines.

In my opinion, healthy people do not need drugs to stay healthy. What they need is education. Today's society is generally uneducated when it comes to preserving their own health. Not to mention preventing debilitating diseases such as type II diabetes and heart disease.

We teach our patients that type II diabetes and cardiovascular disease can be prevented, and in most cases reversed. We remind them that it takes dedication on the patient's or parent's part to maintain health. A nutritional diet and regular aerobic exercise are a must!

Regarding statin drugs for people with no signs of disease. Are we forgetting the side effects that these drugs proliferate? Putting a healthy person at risk by prescribing statin drugs at a young age, will no doubt lower the estimated life expectancy to be reduced even further.

What is happening to ethical care?

Dr. Kessinger has a local weekly radio program called "A Healthy Concept" every Tuesday morning from 9:30-10. The programs are available on his website www.drkessinger.com or go directly to www.drkessinger.com/radio.html ◆

100% All-Natural

GOT PAIN?

Experience Relief Like Never Before

Guaranteed Pain Free or It's Free!

Curamin enhances the body's natural defense mechanisms for the relief of PAIN due to overuse*

After suffering with severe knee pain, a friend of mine told me about this product. Within 45 minutes I was able to walk without a limp, also was able to bend my right knee while walking! I thought I was going to have to retire from working! This is amazing, I am almost 90% pain free after only 40 minutes, God Bless you for this!

—Tom H, Galveston, TX

WOW! Holy Camoly!!!!! I used other pain pills and nothing has helped as well as this Curamin, I just took it an hour ago! I was so impressed I had to write and tell you immediately. I definitely will be buying this as my new "best friend" when I have pain.

—Janine T, Grand Blanc, MI

"From my clinical experience, I have found Curamin to be highly effective. It is the #1 pain-relieving product that I recommend."

Duke and The Doctor

Duke Liberatore and Jan McBarron, M.D.
The #1 Health Talk Radio Show in the Nation

Samples Available

www.Curamin.com

Call: 866-598-5487

EuroPharma®

* THIS STATEMENT HAS NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE OR PREVENT DISEASE.

JC 34 91 + 3(5,6)EP

The Legacy Continues

Dr. Jay Kessinger

by: A. Jay Kessinger IV, DC, ND, DABCI
jay@drkessinger.com

When all else fails, return to basics. Before all else fails, get back to the fundamentals. While nothing else seems to work, go back to your "raisings." Review what you learned in the beginning. Take stock in the foundational truths you've found. Go forth with renewed vigor in your quest to serve with your best, allowing those you serve to pass their test, then with peace, shall you be enabled to find satisfactory rest.

At the beginning of this year I started teaching a life science biology/anatomy/physiology class at a satellite college in our town. It is true that if you want to learn everything there is to know about a subject, prepare for, then instruct it. I knew, for instance, that NSAIDs slow healing and allow scar tissue formation in degenerative and other injurious conditions; however, I'm now renewed in my knowledge that the type of regeneration depends on whether the repair is from the original cells or if it is from fibrous connective tissue. In addition, I was aware of how the myocardium must maintain adequate energy reserves to last a lifetime. Henceforth, I am aware that the said myocardium is enabled to utilize lactic acid accumulation from skeletal muscle fatigue in the local production of ATP. This renewed understanding of subjects that I deal with every day in the health of my patients, reminded me of my child-hood, and the differences in which the children of today are brought up.

When I was a kid I had A.D.D., but they spelled it differently then. They spelled it BRAT, and they treated it differently too. They didn't give me any feel good drugs, but I got a clear picture of what my limits and expectations were. This tongue-in-cheek quip, serendipitously led me on a quest to research "brain chemical imbalance," the clinical reasoning of pre-scribing stimulant medications to treat ADHD, ADD, ODD, et.al. The science did not, to my satisfaction, support the standard medicinal treatment. Brain chemical imbalance was a lay-diagnosis in vogue, to satisfactorily describe objective findings of the abnormal inability to maintain mental focus and justify pharmaceutical intervention.

Brain chemical imbalance was, in the aforementioned cases, a clinical diagnosis with no laboratory procedures to qualify or quantify such an abnormality. It was this affirmation that led to the next question: why would children need a stimulant? The answer being that they haven't received enough sleep. The reasons enough sleep is not afforded are individual and multifaceted. Parental disciplinary practice is a major culprit; however, making sure the children adhere to an adequate bedtime is only a small area of concern. Also to be considered are dietary issues and lifestyle choices. Children, as well as their adult counterparts and mentors, need to eat a varied diet with fruits and vegetables as main-stay with artificial nonfood- "food" items being limited or avoided, as well as pro-inflammatory foods; i.e., pork, chips, lunch meats, and cow's milk. They also need to lead an active lifestyle with daily physical activities as common practice. In my opinion, too many times Ritalin, etc. are used as chemical baby sitters.

As a member of the DAN (defeat autism now) doctor team I've learned that ADHD et.al., autistic and trisomy-21 kids all have one of the following factors in common: IgG food allergies/sensitivities, sluggish bowel function, and/or an inability to get enough rest. The first step in treatment of an autistic child is to put them on a gluten free/casein free diet. This is the least that we can do for our hyperactive, dysfunctional younger patients, before they are succumbed to the world of pharmacology.

Of course, with a specific IgG food allergy panel and an individualized desensitizing rotation diet, each patient can be more specifically and better served with a quicker and more positive outcome, rather than just using a shotgun approach. Regardless, enough sleep, a varied diet, healthy bowel evacuation habits/functions, along with an active lifestyle is a prescription of help for these kids with ADHD, et.al. And it is a good prescription for people of all ages.

Dr. Jay Kessinger has a local weekly radio program called "A Healthy Concept" every Tuesday morning from 9:30-10. The programs are available on his website www.drkessinger.com or go directly to www.drkessinger.com/radio.html ◆

The Role of Andropause for the Practicing Internist

by: Datis Kharrazian, DC, DHSc, MS, MNeuroSci, FAACP, FACFN, DACBN, DABCN, DIBAK, CNS

INTRODUCTION

The human body orchestrates countless integrated physiological interactions every moment of its existence. These physiological responses occur due to cellular messengers such as hormones. When hormonal imbalances exist, physiology can be disrupted and disease may result. The perpetuation of disease promoted by hormone imbalances may be a consequence of polymorphic genetic-errors of metabolism or developed during one's lifespan. The human species appears to be susceptible to hormone dysregulation during the golden years as the body loses endocrine output, diminishes ATP production, and loses efficient intracellular communication.

Medical society is quick to identify these symptoms in women as menopause develops. As women age and develop dysregulation of their hypothalamic-pituitary-ovarian feedback loop, many symptoms and risks arise. Conditions such as osteoporosis, cardiovascular disease, obesity, depression, and cancer may be promoted when hormones are not balanced in normal senescence. Medical practice in the 21st century has developed numerous guidelines and standard of care protocols to identify and manage menopause presentations in women, but these medical practices do not have practice guidelines and models to manage *male* hormone disorders.

As men age, they too are susceptible to hormone dysregulation and loss of orchestration of their hypothalamic-pituitary-gonad feedback loop. Andropause is the appropriate term for what many would call "male menopause." Male menopause is a misnomer because men do not menstruate. Instead, men go through a gradual decline in their ability to produce an androgen-dominant phase. Therefore, the term andropause is more appropriate and refers to a physiological state in which the production of androgen dominant hormones such as testosterone decline.

Despite years of evidence that andropause can have severe impacts on men's health, its treatment and identification has not evolved into standard health evaluations. The average health care professional is not well trained in the identification of symptoms associated with andropause. Instead, the manifestations of andropause such as obesity or elevated cholesterol levels are being treated individually. In addition, the managed-care health system does not look favorably into routinely measuring hormone levels in men who do not have serious endocrinological dysfunction. Clear guidelines for male hormone disorders have not been established.[1]

The level of androgen production can be the reason why some men will age with vitality, vigor, and virility, and others will not. The identification of andropause is commonly overlooked because there is a slow and gradual drop of testosterone compared to female menopause, in which there is an abrupt drop in estrogen and immediate symptoms of decreased hormones.[2]

The practice of medicine today does not account for male hormone imbalances. Physicians trained in traditional medicine are not routinely instructed in the skills necessary to evaluate male hormone disorders.[3]

PREVALENCE OF ANDROPAUSE

Andropause is becoming a serious health problem in industrialized countries. This problem may be due to the increased levels of xenoestrogens and exotoxins in the environment. Andropause may be genetic expressions of male physiology created by the chemical, physical, and environmental factors that industrialization has created in the past century.[4] Andropause was first identified in the scientific literature in 1944 in a study published in the *Journal of the American Medical Association*.[5] The study subjects complained of fatigue, loss of morning erections, depression, irritability, reduced libido, aching and stiff joints, and classic hot flashes. The study demonstrated that these symptoms were corrected when testosterone levels were restored.

Andropause is abundant in society. A tool that has been designed to evaluate for symptoms of andropause worldwide is the Aging Males' Symptoms (AMS) scale. A study conducted to evaluate the prevalence of andropause in the Japanese population found approximately 50% of men in their forties who were screened at the Kurashiki Central Hospital had moderate or severe

(Continued on next page)

symptoms in the sexual subscore.[6] In a recent study, andropause symptoms and erectile dysfunction were found to be common among infertile men, affecting approximately 38% of this population. This finding suggests individuals who suffer from infertility and erectile dysfunction must be screened for andropause.[7]

An epidemiological study was conducted on 1,408 healthy white males, 20 to 60 years of age in Paris, France, who were recruited on an occupational basis and underwent physical examinations and measurements of plasma sex hormones. Many of the subjects were found to demonstrate early testosterone deficiency even when adjustments for body mass index, subscapular skinfold, tobacco consumption, and alcohol consumption were modified.[8]

IDENTIFICATION OF ANDROPAUSE LITERATURE REVIEW

Different forms of low-testosterone syndromes exist, including genetic disorders, primary andropause, secondary andropause, and functional andropause (which is the most common cause). Functional andropause takes place when the ratios shift between testosterone and other hormones. The most common cause of functional andropause is a difference in the ratio between serum levels of testosterone and estrogen. For example, a normal serum testosterone to estrogen ratio may be 50:1. Some men with andropause appear to have an 8:1 ratio. These men may have normal lab ranges of testosterone but their state of estrogen dominance is expressing a low testosterone state.[9]

Hormones can be evaluated in the serum in either a free-fraction form or bound to protein. Once a gland, such as the testes, produces a hormone, it is bound to proteins. Testosterone is primarily bound to the sex-hormone binding globulin. Hormones in a protein-bound state are unable to bind to receptor sites to influence a ligand transcriptional response, but the protein-bound state of the hormone allows for the hormone to be peripherally transported to other tissues. Hormones such as testosterone are only able to bind to receptor sites when they lose their protein-bound state and become free-fraction hormones. It is only the free-fraction hormone that has the potential to bind to receptor sites and produce a transcriptional and proteomic response. Hence, the term *bioavailable* is also given to free-fraction hormones since it is only these hormones that are available to influence gene expression. Laboratory analysis of testosterone includes both protein-bound and free-fraction. The total testosterone can also be measured as an evaluation of the combined total free-fraction and protein-bound testosterone.

In andropause, it appears that the evaluation of both protein-bound and free-fraction hormones should be considered, especially the latter, because decreased free-fraction states appear to be related to the symptoms of andropause.[10] The ratio between free-fraction and protein-bound hormones is strongly influenced by the amount of sex hormone-binding protein production. As the levels of sex hormone-binding protein levels are elevated, the percentage of free-fraction hormones may be reduced. The analysis of total serum testosterone or protein-bound testosterone solely is not adequate to identify changes of free-fraction levels that are present with increased sex hormone-binding proteins.[11]

Andropause is classified as primary or secondary based on the levels of luteinizing hormone (LH) and testosterone. The pituitary-testicular feedback loop is a negative feedback loop: As the levels of testosterone decline due to Leydig cell failure, LH output is increased and this is classified as primary andropause. In secondary andropause, the pituitary is unable to produce adequate LH and therefore the testicular Leydig cells are not stimulated to produce testosterone. Both primary and secondary andropause may exhibit as depressed testosterone levels and, based on current models of testosterone replacement therapy, the treatment is unchanged. The point to remember however is that not all cases of primary hypogonadism present with depressed testosterone levels. Therefore, the measurement of LH should always be considered when andropause is screened. Elevated LH indicates failure of the Leydig cells, although testosterone levels may be normal due to increased LH output to compensate, and primary andropause is present.

The evaluation of andropause can be compared to the evaluation of thyroid hypofunction. In primary hypothyroidism the diagnosis is made based on TSH, not thyroxine. If the TSH is elevated it indicates that the thyroid cells are unable to meet the demands of producing hormones, and thyroid-replacement therapy is initiated despite normal thyroxine levels. It is proposed that the same evaluation and management must be considered with elevated LH and primary andropause. If the LH levels are elevated despite normal testosterone levels, it indicates that the testicular cells are unable to meet the demands of producing androgens and therefore testosterone replacement therapy may be required.[12]

It has been estimated that circulating testosterone declines longitudinally from age 19 at an average rate of 1% per year. The free, or dialyzable, fraction of serum testosterone and the bioavailable (the sum of free-fraction and loosely-bound to albumin fraction) testos-

(Continued on next page)

IODORAL®

Lugol solution in tablet form

Available in tablets of 12.5 mg packaged in bottles of 90 tablets and 180 tablets

Now available also in tablets of 50 mg packaged in bottles of 30 and 90 tablets

Based on the collective experience of U.S. physicians who used Lugol solution extensively in their practice for iodine supplementation over the past century, the recommended daily intake for iodine supplementation was 0.1 to 0.3 ml containing 12.5 to 37.5 mg elemental iodine [1-3]. We recently confirmed the keen observation of our medical predecessors: this is exactly the range of iodine/iodide intake required for whole body sufficiency, based on a recently developed iodine/iodide loading test [3]. For non obese subjects, whole body sufficiency for iodine can be achieved within 3 months with daily intake of 12.5 to 50 mg [4,5].

1) Abraham, G.E., Flechas, J.D., Hakala, J.C., *Orthoiodosupplementation: Iodine sufficiency of the whole human body.* The Original Internist, 9:30-41, 2002.
2) Gennaro, A.R., Remington: *The Science and Practice of Pharmacy, 19th Edition, 1995,* Mack Publishing Co., 976 & 1267.
3) Abraham, G.E., *The safe and effective implementation of orthoiodosupplementation in medical practice.* The Original Internist, 11:17-33, 2004.
4) Abraham, G.E., *The concept of orthoiodosupplementation and its clinical implications.* The Original Internist, 11:29-38, 2004.
5) Abraham, G.E., *The historical background of the iodine project.* The Original Internist, 12(2):57-66, 2005.

For further information on:

- **IODORAL®**
- **Reprints of relevant articles**
- **How to implement orthoiodosupplementation in your practice**
- **How to request kits for the iodine/iodide loading test**

Vist our website at www.optimox.com

Or contact us at: **OPTIMOX CORPORATION P.O. Box 3378 Torrance, CA 90510-3378**
or Call Toll Free: (800) 223-1601 or Fax: (310) 618-8748 or Email: optimox@earthlink.net

terone decline more rapidly with age.[13] The identification of andropause cannot be isolated only to serum testosterone levels. The influence of estrogens and sex hormone-binding globulins can influence the ratios between total protein-bound testosterone and free, bioavailable testosterone.[14] The progressive decline in testosterone levels has been demonstrated in both cross-sectional and longitudinal studies, and overall at least 25% of men over the age of 70 years meet laboratory criteria for hypogonadism.[15]

In summary, the identification of andropause cannot be limited to an isolated serum protein-bound testosterone test. Serum protein-bound testosterone does not account for disorders of andropause related to hypothalamic-pituitary-testicular dysfunction, abnormal ratios with estradiol, and altered ratios of bioavailable versus protein-bound androgens. A complete evaluation of andropause should include total serum testosterone, serum protein-bound testosterone, serum free-free fraction testosterone, serum sex hormone-binding globulin, serum LH, and serum estradiol. LH is necessary to differentiate primary and secondary hypogonadism. It will also identify primary hypogonadal patterns that do not exhibit low testosterone due to pituitary compensation. The serum free-fraction hormones and sex hormone-binding globulin will identify patterns associated with andropause-related disorders that are specific to decreased production of bioavailable testosterone. The serum estradiol levels can be used to identify abnormal testosterone: estradiol ratios that can antagonize the androgenic response.

INFLUENCE OF ANDROPAUSE ON MALE PHYSIOLOGY

Andropause, as identified with low testosterone levels, has numerous adverse impacts on male physiology. Low testosterone levels correlate with increased obesity, an increased waist-to-hip ratio, insulin insensitivity with higher concentrations of glucose and insulin, an increase in cardiovascular risk factors, including an increase in low-density lipoproteins, a decrease in high-density lipoproteins, increased fibrinogen levels, and an increase in apolipoprotein B.[16] The impact of androgen imbalance appears to cross several medical specialties, which include cardiology, urology, proctology, endocrinology, psychology, and general medicine. Many common diseases that are treated today may be a consequence or influenced by andropause, yet it is not common practice for healthcare professionals to screen for andropause in everyday practice.

Coronary heart disease is the second leading cause of death (after cancer) in the United States and in most other industrialized countries. The role of andropause and the impact androgens contribute to cardiovascular function has not received the attention it deserves. This is partly due to the negative associations of androgens on cardiovascular function in females. Many physicians have assumed that the negative impact of androgens on female physiology is the same for men, but this is incorrect. In men, testosterone appears to have a positive impact on cardiovascular risk.[17] It appears that testosterone and estrogen have opposite impacts on cardiovascular health in men and women. In women, estradiol exhibits protective influences and testosterone promotes cardiovascular risk. On the other hand, in men, testosterone appears to exhibit protective influences and estradiol promotes cardiovascular risk. Therefore, in men, as their testosterone becomes depressed and/or estrogen elevates, cardiovascular risk rises.[18] Administration of exogenous testosterone therapy in middle-aged obese men improved body compensation and cardiovascular risk factors. Plasminogen activator inhibitor-1 (PAI-1) is an enzyme that promotes fibrinolysis. Increased levels of PAI-1 increase coagulation of the arterial system due to diminished ability to degrade arterial clots. Hypotestosteronemia in men has been shown to negatively correlate with PAI-1.[20]

As men age and develop insulin resistance and obesity, the aromatase enzyme found in men's body fat may upregulate and convert testosterone to estrogen. As the incidence of obesity, insulin resistance and diabetes reach staggering numbers within the United States, there is great potential for many men to develop an andropause pattern of hyperestrogenemia.[21] These men may develop the symptoms of androgen deficiency despite their testosterone levels dropping due the antagonistic impact of estrogens on testosterone. Hyperestrogenemia has been associated as an independent risk factor for the onset of myocardial infarction (MI).[22] Studies correlating hormone findings after MI have noted elevations of estrogen in men in acute MI and months following MI.[23, 24]

Testosterone has impacts on numerous cardiovascular risk factors. For example, the following changes take place as testosterone levels decline: cholesterol and triglycerides increase, arterial plaque increases, coronary artery dilation decreases, lipoprotein A increases, fibrinogen levels increase, insulin levels increase, obesity increases, and estrogen levels increase.[25] Therefore, the identification and treatment of andropause can have a significant influence on decreasing the risk factors associated with cardiovascular disease.

(Continued on next page)

Middle-aged men with symptoms of andropause, together with absolute or compensated testosterone deficiency, have demonstrated increased carotid intimal-media thickness when compared to data of men with normal testosterone levels. Therefore, testosterone may offer protection against the development of atherosclerosis in middle-aged men.[26] Research clearly indicates the associated increased risk of cardiovascular markers with low testosterone levels. Evaluations of male hormone physiology should be investigated in all men who have increased risk factors for cardiovascular disease.

A study conducted in men undergoing coronary angiography found correlations between testosterone and coronary artery disease. The study performed femoral artery angiograms and blood tests for fibrinogen, plasminogen activator inhibitor-1, estradiol, total testosterone, free testosterone, HDL, LDL, and total cholesterol. The study concluded that hypotestosteronemia may be a cardiovascular risk factor in men. The study also found that the negative correlation was stronger with free testosterone due to its bioactivity.[27] Increased levels of high density lipoprotein (HDL) is a protective marker for cardiovascular disease due to its action of carrying lipids away from the peripheral arterial system to the liver. Testosterone levels have correlated positively with HDL levels. Men with depressed testosterone appear to produce less amounts of HDL.[28]

Despite all the advances made in cardiovascular pharmacology in the past decade, the rate of death from cardiovascular disease in men appears to be increasing. Although the increased rate of morbidity from cardiovascular disease in men cannot be attributed to any single factor, one overlooked risk that is clearly not being identified in men today is the influence of androgen balance on cardiovascular disease. In addition, recent research has demonstrated that statin medications appear to decrease total testosterone levels in men. In 2005, Lipitor alone was the second most commonly prescribed medication in the United States. It may not make sense to use a drug for cardiovascular disease if it lowers one risk to increase several other risks. In addition, current research is questioning the efficacy of statin drugs in lowering long-term cardiovascular risk.

The incidence of hip factures in the United States is growing every year and with the progression of the baby bombers into the elderly population it will continue to rise. Most studies on osteoporosis in the past two decades have focused exclusively on women, however research conducted on men has found an association between low testosterone and bone density loss. Osteoporosis is an issue of great concern in the elderly male population. A fracture of the hip can lead to serious complications in the elderly. Androgen balance has great influences on bone density, yet men with osteopenia or osteoporosis are not routinely evaluated for andropause. Androgen hormones induce activity of osteoblasts and improve bone density, while lack of these steroids result in osteoporosis. More specifically, estrogens decrease osteoclast activity while testosterone stimulates osteoblast activity, leading to increase bone density with androgen balanced males and decreased bone mass with estrogen dominant or androgen deficient males.

The influence of androgens can be understood from analyzing bone development from as early as puberty. At the beginning of puberty the increase in linear growth of bones is directly correlated with increasing testosterone concentrations. At the end of puberty, depending on the presence of testosterone, epiphyseal closure occurs, an event that can be consistently delayed in the presence of low testosterone concentrations.[29]

A control study of men who presented with hip fractures after simple falls over a ten-month period were matched with a control group of subjects, with a mean age of 73 years. The study measured and compared the total and free testosterone of these subjects. The study found that 71% of the hip-fractured men were testosterone-deficient versus 32% of the control subjects. They concluded that gonadal deficiency appears to be an important and heretofore understudied risk factor for hip fractures in men and that prevention of hip fractures may involve early recognition and treatment of testosterone deficiency.[30] A similar case-controlled study conducted with nonmatched subjects also found that reduced free testosterone levels in the elderly men increased risk for minor trauma hip fractures.[31] Clear predisposition of spinal osteoporosis and testosterone deficiency has also been determined.[32]

Osteoporosis is a serious condition that can lead to life-threatening risk in the elderly. Women that are menopausal are routinely screened for bone density health and managed by addressing hormone influences. This same practice must be incorporated with males. If a male develops decreased bone density, evaluation and management for andropause should be standard.

Obesity and the complications associated with obesity are a growing concern in the United States. Americans

(Continued on next page)

A Daily Dietary Supplement for the Whole Family!

Lauricidin®

Dr. Jon J. Kabara
Discoverer of Monolaurin

"The Original Monolaurin"

Add to your protocol for the following reasons and benefits:

- An active ingredient found in Mother's milk, Saw Palmetto and Bitter Melon
- Helps support the immune system
- Inactivates laboratory bacteria, viruses and fungi/yeast
- A non-toxic USFDA-approved food additive
- Helps regulate bowel function
- Can be taken with other medications
- Does not destroy friendly bacteria
- Biochemically balances the body to health

A Essential Nutrient for Good Health and Self-Healing.
Safe for Children, Adults, and Pets

Mention CDID2010
10% Discount

toll-Free 877-770-7270

sales@lauricidin.com | www.lauricidin.com

are fatter today than any other time in American history, and America is the fattest country in the world. Androgen balance in males appears to have major influences on obesity and the maintenance of lean muscle mass. As the levels of testosterone, an anabolic hormone, decline, it appears that it is harder to maintain lean body mass and muscle tone, while it is easier to store abdominal fat. Research has demonstrated that when men with low testosterone concentrations are placed on exogenous testosterone, they increase lean body mass and decrease abdominal fat even without any changes to diet and exercise. Many men notice as they go into andropause that their body changes. They notice that their body fat increases and that their lean body mass decreases. Testosterone appears to have a tremendous influence on male metabolism.[33] As a man's level of testosterone declines he becomes more prone to the development of insulin resistance, which promotes obesity.[34]

Record-breaking sales of erectile dysfunction drugs such as Viagra suggest that androgen insufficiency may be more common than we currently recognize. Testosterone is the hormone that stimulates the desire for sexual activity and it contributes to healthy erectile function in men. Researchers suspect that testosterone insufficiency may be a leading cause in low libido and erectile dysfunction.[35] Despite growing development of diagnosable erectile dysfunction and loss of libido, the current health care model does not routinely evaluate men's androgen levels when they present with these disorders.

Andropause has not only demonstrated to impact male physiology and disease promotion, but it also appears to influence men's mental health and psychological status.[36] Testosterone levels appear to impact a man's sense of well-being, vitality, and mood. It is not uncommon for men who are going into andropause to have feelings of depression and a lack of motivation, only to be resolved as their hormone physiology is improved.[37] Research using the Aging Male's Symptom (AMS) questionnaire has found a higher prevalence of major depressive disorders in males who scored higher on the AMS questionnaire scale.[38] Males who demonstrate laboratory findings of andropause are also more at risk for cognitive decline and the development of neurodegenerative diseases such as Alzheimer's.[39]

SUMMARY OF BASIC ANDROPAUSE CONCEPTS

In summary, many associations have been published between andropause and cardiovascular disease, depression, infertility, erectile dysfunction, neurodegeneration, obesity, insulin resistance, etc. Despite the growing evidence of andropause prevalence and risk, little has been done in the healthcare model to establish guidelines for screening and management. Andropause must be taken as seriously as menopause to avoid endless suffering and the inappropriate management of conditions that are secondary to andropause.

Male hormone disorders are probably one of the most overlooked and ignored dysfunctions in health care today. Health care practitioners have dismissed the far-reaching impact these disorders may have on functional physiology. Men's health has been compromised, marriages have been broken, careers have failed, and disease prevention has not reached its full potential due to its significance not being acknowledged by health practitioners. Men who present with conditions associated with andropause should be properly screened. Based on the evidence, the identification and management of andropause must be incorporated into the practice of healthcare providers to avoid suffering and to prevent disease.

1) Basaria S. (2005). Andropause: need for concrete guidelines until more evidence becomes available. J Endocrinol Invest, 28, 667-670.
2) Gray A, Berlin JA, McKinley JB & Longcope C. (1991). An examination of research design effects on the association of testosterone and male aging: results of meta-analysis. J Clin Epidemiol, 44, 671-684.
3) Darby E. & Anawalt B.D. (2005). Male hypogonadism: an update on diagnosis and treatment. Treat Endocrinol, 4, 293-309.
4) Vermeulen A. (1993). Environment, human reproduction, menopause and andropause. Environmental Health Prospective Supplements, 101, 91-100.
5) Heller CG & Meyers GB. (1944) The male climacteric, its symptomatology , diagnosis and treatment. JAMA, 126, 472-477.
6) Ichioka K., Nishiyama H, Yoshimaura K. Itoh N., Okubo K, Terai A. (2006). Urology, 67, 689-593.
7) O'Brein J.H., Lazarou D., Deane L., Jarvi K, Zini A. (2005). Erectile dysfunction and andropause symptoms in infertile men. Journal of Urology, 174, 1932-1934.
8) (1992). The influence of aging on plasma sex hormones in Men. The telcom study. Am J Epidemiol, 135, 783-791.
9) Vermeulen A, Deslypere JP. (1985). Testicular endocrine function in the aging male. Maturitas, 7, 273-279.
10) Mooradian A.D. & Korenman S.G. (2006) Management of the cardinal features of andropause. Am J Ther. 13, 145-160.

(Continued on next page)

11) Tremblay R.R. & Gagne J.M. (2005). Can we get away from serum total testosterone in the diagnosis of andropause? Aging Male, 8, 147-150.
12) Vermeulen A, Deslypere JP. (1985). Testicular endocrine function in the aging male. Maturitas, 7, 273-279.
13) Mooradian A.D. & Korenman S.G. (2006) Management of the cardinal features of andropause. Am J Ther. 13, 145-160.
14) Tremblay R.R. & Gagne J.M. (2005). Can we get away from serum total testosterone in the diagnosis of andropause? Aging Male, 8, 147-150.
15) Seidman S.N., Normative hypogonadism and depression: does 'andropause' exist? Int J Impot Res, Epub ahead of print.
16) Phillips G. (1993). Relationships between serum sex hormones and glucose-insulin-lipid defect in men with obesity. Metabolism, 42, 116-120.
17) Philips G. (1996). The association of hyperestrogenemia with coronary thrombosis in men. Arterioscler Thromb Vasc Biol, 16, 1383-1387.
18) Phillips G. (1993). Relationship of serum sex hormones to coronary heart disease. Steroids, 58, 286-290.
19) Marin P, Holmang S, Honsson L, et al. (1992). The effects of testosterone treatments on body composition and metabolism in middle-aged obese men. Int J Obes. 16, 991-997.
20) Caron P, Bennet A, Camare R, et al (1989). Plasminogen activator inhibitor in plasma is related to testosterone in men. Metabolism, 38, 1010-1015.
21) Philips G. (1993). Sex hormones and hemostatic risk factors for coronary heart disease in men with hypertension. J of Hypertension, 11, 699-702.
22) Phillips GB. (1976). Evidence for hyperestrogenemia as a risk factor for myocardial infarction in men. Lancet. 2, 14-18.
23) Klaiber El, Broverman DM, Haffajee CI, Hochman JS, Sacks GM, Dalen JE. (1982). Serum estrogen levels in men with acute myocardial infarction. Am J Med. 73, 872-881.
24) Phillips GB, Casteilli WP, Abbott RD, McNamara PM. (1983). Association of hypestrogenemia and coronary heart disease in men in the Framingham cohort. Am J Med. 74, 863-869.
25) Phillips G, Pinkernell BH, Jing TY. (1994). The association of Hypotestosteronemia with coronary artery disease in men. Arterioscler Thromb, 14, 701-706.
26) Makinen J., Jarvisalo M.J., Pollanen P., Perheentupa A., Irjala K, Koskenvuo M.,Makiner J., Huhtaniemi I, Raitakari O.T. (2005). Increased carotid atherosclerosis in andropausal middle-aged men. J Am Coll Cardiol, 45, 1603-1608.
27) Gerald BP, Pinkernell BH, Jing TY. (1994). The association of hypotestosteronemia with coronary artery disease in men. Arteriosclerosis and Thrombosis, 14, 701-706.
28) Gutai J, LaPorte R, Kuller L, et al. (1981). Plasma testosterone, high-density lipoprotein cholesterol and other lipoprotein fractions. Am J Cardiol, 48, 897-902.
29) Finkelstein JS. (1998). Androgens and bone metabolism. Testosterone action, deficiency, substitution. Berlin: Springer-Verlag, 1998:187-207.
30) Jackson JA, Riggs MW, Speikerman AM. (1992). Testosterone deficiency as a risk factor for hip fractures in men: a case-control study. American Journal of Medical Sciences, 304, 4-8.
31) Stanley HL, Schmitt BP, Poses RM, Deiss WP. Does hypogonadism contribute to the occurrence of minimal trauma hip fracture in elderly men? J Am Geriatr Soc, 39, 776-791.
32) Jackson JA & Kleerekoper. (1990). Osteoporosis in men: Diagnosis, pathophysiology, and prevention. Medicine, 69, 139-152.
33) Bhasin S, Storest TW, Berman N, Yarasheshi, et al. (1997). Testosterone replacement increases fat-free mass and muscle size in hypogonadal men. J Clin Endocrinol Metab, 82, 407-413.
34) Harman S.M. (2005). Testosterone in older men after the institute of medicine report: where do we go from here? Climacteric, 8, 124-135.
35) Bates & Betsy. (1997). Libido decline may signal low testosterone. Family Practice, 11, 40.
36) Seidman S.N., Normative hypogonadism and depression: does 'andropause' exist? Int J Impot Res, Epub ahead of print.
37) Barret-Conner E, Von Muhlen D, Krits-Silverstein D. (1999) Bioavailable testosterone and depressed mood in older men: the Ranch Bernardo Study. J Clin Endocrinol Metab, 1999; 84: 573-577.
38) Yoshida N.M., Kumano H., Kubobki T. (2006). Does the aging males' symptoms scale assess major depressive disorder?: a pilot study. Maturitas, 53, 171-175.
39) Meethal S.V., Smith M.A., Bowmen R.L. Atwod C.S.(2005). The gonadotropin connection in Alzheimer's disease. Endocrine, 26, 317-326.◆

Adrenal Hormones and Adaptation to Stress

by: Rachel Olivier, MS, ND, PhD
Submitted by: Biotics Research Corporation

The phenomenon of *stress*, a now dominant constituent of our daily vocabulary, was coined over seventy years ago by Hans Selye.[1] Selye described the occurrence as nonspecific bodily changes that transpired in response to physically harmful stimuli.[2] In his reporting, Selye also indicated that although the adrenal glands are the first glands to respond to stress, they are also the first glands to fail under stressful conditions. The body possesses a complex system for adapting to stressful conditions, due primarily to the fact that the ability of an organism to adjust homeostasis, and in turn increase the chance of survival is dependent upon the activation of the stress system. This activation in turn leads to both behavioral and peripheral changes.[3]

The adrenal glands, a pair of triangular structures located atop each kidney, play a key role in stress adaptation and regulation. Not only are they necessary for life, but they also play an essential role in energy production, and in controlling the conversion of carbohydrate, protein and fat into glucose, as a source of fuel for the body. Moreover, they partake in the fluid and electrolyte balance of cells in both the interstitial fluids and in the blood stream, and are an important component in the production of sex hormones, especially following menopause. By virtue of the cortisol effect, the adrenals also play a role in the storage of fat, as cortisol has a direct effect on fat storage and weight gain in stressed individuals.

The adrenal glands are made up of two discrete parts, the inner adrenal cortex and the outer adrenal medulla. The adrenal cortex secretes four major groups of hormones, classified as the glucocorticoids, the mineralcorticoids, androgens and estrogens. The adrenal medulla is responsible for the secretion of the catecholamines, particularly epinephrine and norepinephrine. The secretion of all adrenal steroids, including the glucocorticord cortisol, is under the control of the pituitary adrenocorticotropic hormone (ACTH), which functions by a negative feedback mechanism. Consequently, a high level of circulating cortisol will suppress the secretion of ACTH, while a drop in cortisol will result in an increased ACTH secretion.[4] The action of the glucocorticoids is catabolic, stimulating the breakdown of protein and the inhibition of protein synthesis. Increased cortisol in the circulation initiates fat deposition in adipose tissue, and consequently weight gain is common with cortisol excess. Blood glucose homeostasis is also affected by cortisol, and its action is two-fold, via the stimulation of hepatic gluconeogenesis and via the inhibition of glucose uptake by tissues. Additionally, both the inflammatory and immune responses are suppressed by glucocorticoids. Thymic and lymph atrophy are known to develop in the presence of excess cortisol.[4]

Cortisol, the prototype of the glucocorticoids, is the hormone synthesized in the greatest quantity by the adrenal glands; approximately two hundred fold that of aldosterone. It exerts numerous physiologic actions on the body, including maintenance of normal blood pressure, regulation of fluid and electrolyte balance, protein metabolism, body fat distribution, glucose metabolism, and normal muscle formation. It also exerts action on both the hematopoietic system (blood cell formation) and on the lymphatic tissues.[4] The secretion of cortisol is executed in a diurnal pattern, with the highest value between 6 and 8 a.m., and the lowest normally around midnight. Cortisol also acts as an anti-inflammatory signal, meaning that it acts as an "off switch" for the immune system, helping to prevent the inflammatory response. An elevation in cortisol has been demonstrated to contribute to insulin resistance, central obesity, dyslipidaemia and hypertension, and consequently a direct correlation between elevated cortisol and weight gain has been established. Regarding obesity, in female subjects with abdominal obesity, void of depression, it has been demonstrated that an exaggerated ACTH and cortisol response exists.[7]

Dysregulation of the stress system or a maladaptive neuroendocrine response has the potential to result in disturbances in growth and development, and may ultimately result in other health consequences including psychiatric, endocrine/metabolic, and/or autoimmune imbalances, as well as vulnerability to diseases.[8] It has been documented that stress-induced hypercortisolism and visceral obesity and their cardiovascular and other sequelae increase the all-cause mortality risk of affected subjects by 2-3-fold, and curtail their life expectancy by several years.[3] If not controlled ACTH hypersecretion

(Continued on next page)

Could **Your Patient** be Suffering as a Result of a Hypersensitivity to METALS?

Hypersensitivity to metals in items such as implants, dental fillings, and the environment causes an ongoing immune response and chronic inflammation.[1]

Metal exposure in hypersensitive patients may be the root cause of symptoms such as:

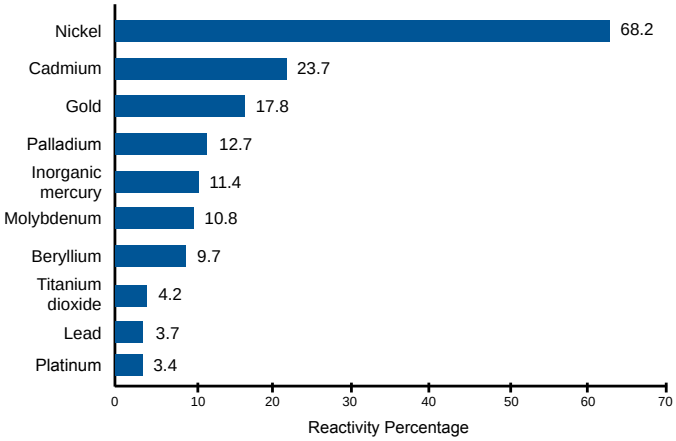
- Fatigue
- Insomnia
- Migraine
- Depression
- Pain
- Dermatitis
- Anxiety
- Arthralgia

MELISA® (MEmory Lymphocyte Immuno-Stimulation Assay)
THE WORLD'S LEADING TEST FOR IDENTIFYING METAL HYPERSENSITIVITY.

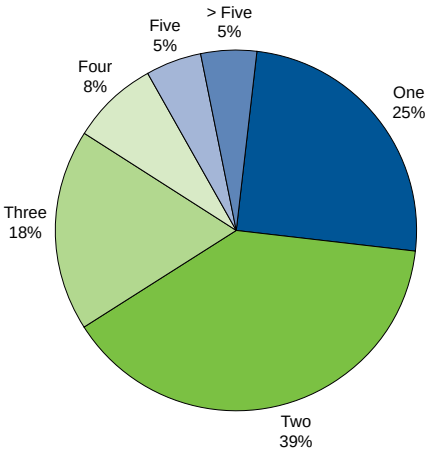
MELISA® measures Type-IV hypersensitivity to metals. Unlike hair, urine, and serum analysis that measure levels, MELISA® measures lymphocyte reactions to identify hypersensitivity. Even trace levels of metals can lead to inflammation in hypersensitive patients.

Symptomatic patients are commonly sensitive to more than one metal.[2]

Frequency of Metal Sensitivity in More Than 700 Symptomatic Patients[2]



Patients with Sensitivities to More Than One Metal[2]



70-80% of patients who tested positive to metals with MELISA® improved after removing the offending metal.[3]

NEUROSCIENCE
Improving Health Through The Nervous System

For more information visit www.neuroscienceinc.com/MELISA.

- ALUMINUM
- ARSENIC ACID
- BERYLLIUM
- CADMIUM
- CHROMIUM
- COBALT
- COPPER
- ETHYLMERCURY
- GOLD
- INORGANIC MERCURY
- LEAD
- MANGANESE
- METHYLMERCURY
- MOLYBDENUM
- NICKEL
- PALLADIUM
- PHENYLMERCURY
- PLATINUM
- SILVER
- THIMEROSAL
- TIN
- TITANIUM CALCIUM
- TITANIIM DIOXIDE
- VANADIUM

1. Martin, S.F. T Lymphocyte-Mediated Immune Responses to Chemical Haptens and Metal Ions: Implications for Allergic and Autoimmune Disease . *Int Arch Allergy Immunol* 2004;134:186-198.

2. Valentine-Thon, E., Muller, K. et all. LTT-MELISA is clinically relevant for detecting and monitoring metal sensitivity. (2006) *Neuro-Endocrinol. Lett.* 27 Suppl 117-24.

3. Stejskal VD, Danersund A, et all (1999). "Metal-specific lymphocytes: biomarkers of sensitivity in man". *Neuro-Endocrinol Lett.* 20 (5): 289-298.

frequently results in Cushing's disease.[9] Other diseases have been correlated to an excess production of adrenal androgen. For example, it has been estimated that in patients with polycystic ovarian syndrome, 20-30% produce an excess of adrenal androgen, resulting in elevated levels of dehydroepiandrosterone sulfate (DHEAS). Accordingly, in patients with PCOS, as a consequence of the response to ACTH stimulation a "generalized hypersecretion of adrenocortical products" has been observed.[10]

Nutritional Support for Healthy Adrenal Function

An extensive body of research provides important insights into nutritional support for optimal adrenal function. It is well accepted that stress increases the need for many nutrients, and a variety of factors affects the function of the adrenal glands. These may include dietary, environmental and/or innate mechanisms. Dietary factors are important contributors of adrenal stress. For example excess dietary carbohydrates or diets low in protein put additional stress on the adrenals. Inadequate or poor quality water also affects the adrenals due to inadequate oxygenation of the tissues. Prolonged or persistent hyperfunction may consequently result in unwanted health consequences, including Cushing syndrome, hyperaldosteronism, or adrenogenital syndromes.[11] A potential end result of adrenal hyperfunction is the excess production of one of the three corticosteroids; cortisol, aldosterone or adrenal androgens.

In children and adolescents adrenal hyperfunction may ultimately result in stunted growth and short stature in adults. Growth hormone has also been observed to be decreased in patients with adrenal hyperfunction.[12,13] Consequently, adrenal stress results in a greater need for many nutrients.

L-Tyrosine for Catecholamine Synthesis

Dietary L-Tyrosine is characteristically obtained via the metabolic conversion of phenylalanine. It functions as a key precursor in the synthesis of the catecholamines; epinephrine, norepinephrine and dopamine, and, coupled with iodine, functions as a key component in the production of thyroxine (T_4) and triiodothyronine (T_3). During stressful situations, catecholamine release is amplified, which over time may result in depleted levels. As a precursor of the catecholamies, alterations in L-tyrosine availability may impact the synthesis of dopamine and norepinephrine. L-Tyrosine has been noted to have a beneficial effect during increased neuronal firing rates, as in times of stress, and to prevent the decline in cognitive function associated with physical stress.[14] Thus, during times of stress, L-Tyrosine is considered a conditionally essential amino acid.

Vitamins associated with Adrenal Support

Vitamin C. The concentration of vitamin C in the adrenal glands is among the highest in the body, being roughly 100 times that of blood plasma levels.[15] As such they are extremely sensitive to inadequacies in vitamin C. In catecholamine synthesis, vitamin C is required as a co-factor in the conversion of dopamine to norepinephrine.[16] In humans vitamin C secretion occurs as part of the stress response via hormone regulation, specifically in response to stimulation via the hormone adrenocorticotrophic (ACTH). Following ACTH stimulation the mean adrenal vein vitamin C level increased approximately four fold, and then subsequently returned to near pre-stimulation levels approximately 15 minutes thereafter. Peak adrenal vitamin C and cortisol concentrations have been strongly correlated (r^2=0.35, P<0.001), suggesting a local action of vitamin C on the adrenal glands. Additionally, it has been noted that, although being of unknown function, the increase in vitamin C secretion suggests that "adrenal vitamin C secretion is an integral part of the stress response."[17] Stress, fever and viral infections, as well as habitual actions, such as smoking and alcohol use, cause a rapid decline in the blood level of vitamin C.[18]

Pantothenic Acid. Pantothenic acid is a cofactor in the synthesis of coenzyme A (CoA). CoA plays an important part in cellular respiration, as well as in the biosynthesis of many important compounds including fatty acids, cholesterol and acetylcholine.[19] Animal studies have documented morphological damages in the adrenal cortex with pantothenic acid deficiency.[20,21,22,23,24,25] Early experiments in animals also indicated that following prolonged pantothenic acid deficiency, extensive damage to the adrenals resulted, which was attributed to the adrenals inability to immediately utilize pantothenic acid. It was subsequently concluded that pantothenic acid deficiency results in an imposed stress upon the adrenal cortex, which in turn results in exhaustion, and consequently, adrenal hypofunction.[26] In spite of the fact that deficiencies are generally thought of as being rare, a deficiency in pantothenate results in fatigue and generalized malaise.[27]

Vitamin B_6. Vitamin B_6 serves as a coenzyme in well over 100 reactions, most of which are transaminase (aminotransferase) reactions. It plays an important role

(Continued on next page)

in the synthesis of the neurotransmitters γ-aminobutyric acid (GABA), serotonin, dopamine, norepinephrine and epinephrine.[28] As a physiological modulator of steroid hormone action, Vitamin B_6 has been associated with modulation of the expression of a diverse array of hormonally responsive genes.[29] For efficient function, both the nervous and immune systems require an adequate supply of vitamin B_6.[30, 31,32,33] Vitamin B_6 is also required for the conversion of tryptophan to niacin and serotonin,[34,35] as well as for the conversion of tyrosine to dopamine. In one study, a deficiency in vitamin B_6 was correlated to a slower extracellular dopamine release (43% longer with deficiency).[36] Dopamine is known to be an active participant in the secretory modulation of both aldosterone and catecholamine from the adrenal gland.[37] Dopamine depletion is correlated with physical and/or psychological stress.

Vitamin E. Vitamin E is found in all cells in the human body, and functions primarily as an antioxidant. The adrenal cells, along with the pituitary, platelet and testicular cells, contain the highest cellular concentration of vitamin E.[28] In animal studies vitamin E deficiency was demonstrated to predispose tissues to lipid peroxidation.[38] Conversely, vitamin E consumption affords protection against the effects of mineral toxicity, attributed to reversing the alterations in adrenocortical activities brought on by toxic mineral levels.[39] In another study, the use of alpha tocopherol during times of significant stress was demonstrated to decrease lipid peroxidation in both the liver and the brain, while simultaneously preventing depletion in glutathione levels, which are routinely depleted by stress. Adrenal sensitivity to ACTH is also increased with vitamin E use.[41]

Thiamin. Thiamin, a water-soluble B-complex vitamin, is involved in many bodily functions, including its requirement in the metabolism of carbohydrates, as part of the coenzyme thiamin pyrophosphate (TPP). In the absence of thiamin, a slowing or complete blocking of enzymatic activity occurs. As part of the citric acid cycle, essential for energy production, thiamin functions as a component in the decarboxylation of α-ketoglutaric acid to succinyl CoA.[28] In animal studies corticosterone levels have shown to be significantly increased with thiamin deficiency.[42,43]

Riboflavin. Like thiamin, riboflavin is also a water-soluble vitamin. It participates in normal cell function, growth and energy production. Riboflavin serves as a crucial component in converting food into energy via the manufacturing of flavin adenine dinucleotide (FAD). FAD is required for electron transport and ATP production in the Krebs cycle. Ariboflavinosis (riboflavin deficiency) is associated with weakness, cheilosis (fissures in the skin at the angles of the mouth), angular stomatitis (inflammation of the mucous lining of the mouth) and anemia. Individuals particularly susceptible to deficiency include the elderly, those with chronic illnesses or those with alcohol dependency.[44] Stress increases the need for riboflavin due to an increase in fatty acid oxidation. Riboflavin deficiency has been correlated to adrenal cortex dysfunction in animals.[45]

Niacin. Niacin's primary cellular function is as a coenzyme for NAD^+ and $NADP^+$, both of which function in the maintenance of cellular oxidation-reduction reactions. In addition to its varied cellular functions, NAD is used as a substrate for the production of poly-ADP-ribose (PARP). PARP is a nuclear enzyme activated by DNA strand breaks. It functions to synthesize polymers of ADP-ribose molecules, making it an important component in DNA repair.[46] Niacin intake has also been correlated with anxiety reduction.

Minerals associated with Adrenal Support

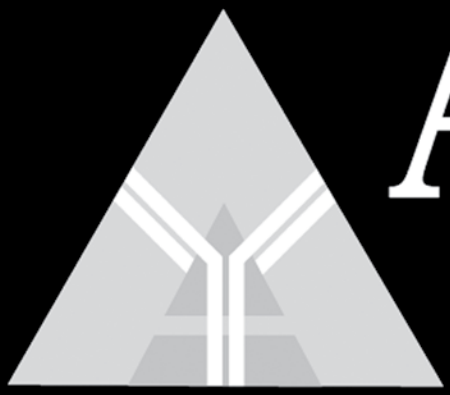
Minerals can also be beneficial components for adrenal support, functioning as aides in sustaining the adaptogenic response of the adrenals.

Zinc. Zinc participates as an active component in over 300 different enzymes, and plays a vital role in many biological processes. As a cofactor for the antioxidant enzyme superoxide dismutase (SOD) it is an important component in cellular protection. It also functions in enzymatic reactions in both carbohydrate and protein metabolism.[44] Zinc deficiency and adrenal stress have been associated. In one study a correlation between zinc deficiency and prostaglandin production was noted, demonstrating that with deficiency interference in the production and/or function of the prostaglandins ensued.[47]

Copper. Like zinc and iron, copper is also involved in gene regulation and expression, specifically for the metallothioneins, or metal-binding proteins. Studies have suggested that copper plays a role in mitochondrial gene expression, noting a decrease in oxidative phosphorylation with deficiency. A number of enzymes require copper as a cofactor, and copper is necessary to balance zinc.

Manganese. Manganese (Mn) is a required mineral for optimal adrenal glandular activity. It serves as a

(Continued on next page)



ALLETESS MEDICAL LABORATORIES

inhalant allergy

food sensitivity

candidiasis

customized wellness programs

Courier Service by
Federal Express at no charge

FOR MORE INFORMATION, PLEASE CALL
1.800.225.5404
OR LOG ON AT
WWW.FOODALLERGY.COM

component for energy metabolism, as a cofactor for enzymes of the citric acid cycle, and as a functional cofactor as part of the enzymatic structure of several additional enzymes. As an essential cofactor for Mn superoxide dismutase (MnSOD), it is an important participant in the cellular antioxidant defense mechanism.[48] It also functions as an important modulator in signal transduction pathways.[49] Recent evidence has denoted a correlation between Mn deficiency and the balance of endothelium-derived prostanoids, indicating the presence of oxidative stress in Mn deficiency, as a result of reduced activity MnSOD.[50]

Lithium and Rubidium. Lithium and rubidium, in trace amounts, function as relaxant minerals. Lithium has been shown to have general neuroprotective effects,[51] to offer protection against glutamate excitotoxicity, as well as to offer CNS neuroplasticity (changes in the brain organization as a result of experience).[52] The trace mineral rubidium (Rb) resembles potassium in terms of its method of absorption and excretion.

Acute stress impacts dopamine, increasing its release and metabolism.[53] Symptoms associated with neuropsychological issues have been coupled with disturbances in dopaminergic neurotransmission.[54] Dopamine, a known precursor to norepinephrine and epinephrine, also functions as a neurotransmitter.[55] Supplementation with lithium or rubidium was demonstrated to result in a decreased dopamine output.[56] Dopamine release in the brain has been shown to exert an important adaptagenic influence over specific behaviors, including emotion and cognition, as well as to affect mechanisms of reward and locomotional control.

Botanical Extracts for Adrenal Support

A number of botanicals have been identified as having adaptogenic properties with intake, along with a corresponding negligible disturbance in physiological function. In addition to established nutrients, several herbal extracts help support normal adrenal function. Many of these have their origins in Chinese or Ayurvedic traditions.

Achyranthes. In the Chinese pharmacology, the action of Achyranthes is said to invigorate the blood, and to expel blood stasis.[57] It is used in Yang tonic formulations. Its functionality is said to revolve around its ability to guide other herbs to the kidneys, genitals, and legs.[58]

Damiana (*Turnera diffusa*). Damiana is a small shrub with an aromatic leaf, found predominantly in Mexico, Southern and Central America. Like Achyranthes, Damiana is also designated as a yang tonic, and is suggested to aide with energy. It is considered a strengthener for the nervous system, and is viewed as a nervous restorative.[59,60] Its properties are indicated as stimulating to the nervous system and as a diuretic,[61] while its traditional use is as a general tonic for the nervous, endocrine, and reproductive systems.[44]

Gotu Kola (*Centella asiatica*). – In Ayurvedic medicine Gotu Kola is an herb viewed as an important component in rejuvenation, as well as one of the chief herbs for revitalizing the nerves and brain cells. The following properties have been attributed to its actions; mildly antibacterial, anti-viral, anti-inflammatory, anti-ulcerogenic, anxiolytic, a cerebral tonic, a circulatory stimulant, a diuretic, nervine and vulnerary.[62] Punturee, *et. al.,* demonstrated that *C. asiatica* has immunostimulating activity regarding both non-specific cellular immune responses and humoral immune responses. Additionally, they noted the inhibition of TNF-α with an ethanol extract of *C. asiatica*, implicating that it may be an important component in downregulating inflammation.[63]

Sichuan Teasel (*Dipsacus asperoides*). According to the Chinese tradition, *Dipsacus asperoides* (DA) is said to tonify the liver and kidneys, and to promote the movement of blood.[64] A crude polysaccharide fraction (DAP-1) from the root of DA has been shown to have a stimulating effect on the mitogenic activity of lymphocytes, as well as to suppress the phagocytic activity of macrophages.[65]

Asiatic Dogwood. (*Cornus officinalis)*. *Cornus officinalis* (CO) is popular in traditional medicine, and is known for its tonic, pain-relieving, and diuretic properties.[66] In addition to its use as a tonifier for liver and kidney deficiency, indicated by such symptoms as lightheadedness and dizziness, it is also said to tonify the essence and assist the yang.[64] The aglycons of anthocyanins have been shown to possess strong antioxidant activities.[67,68] Likewise, the anthocyanins of CO were confirmed to possess strong antioxidant activity.[69]

Basil (*Ocimum basilicum*). Basil is a popular culinary herb, as well as a medicinal herb in Thailand, India and Turkey.[70] It is said to affect the lungs and stomach meridians, and its actions are indicated as being stimulatory to the adrenal cortex.[71] The chief compounds isolated from basil include eugenol, citral and geraniol,[72] as well as rosmarinic acid, a natural phenolic compound shown to inhibit complement-dependent inflammatory processes.[73]

(Continued on next page)

Schisandra (*Schisandra chinensis*). *Schisandra chinensis* (SC) has been utilized in traditional Chinese medicine (TCM) for over 2000 years, as both a tonic and a calmative. As a tonic, one of its uses is to support mental function. It is considered an adaptogenic herb, which functions in the harmonization of the system. More recently, SC has been utilized to increase resistance to disease and stress, boost energy levels (void of caffeine associated jitteriness), increase both mental and physical endurance, to improve vision, and to support both the musculoskeletal and immune systems.[74] Modern Chinese research suggests that SC may have a protective effect on the liver, as well as possessing immune accentuating properties. Gomisin A, an isolated component from SC was demonstrated to have relaxant properties, demonstrating an "anti-stress" effect.

Tinospora cordifolia. The use of *Tinospora cordifolia* (TC) for debility and dyspepsia in Ayurvedia is common. The root of TC is documented as having anti-stress properties, as well as immune supporting properties.[77,78] In animal studies an aqueous extract of TC was demonstrated to have advantageous properties with adrenaline-induced hyperglycemia.[79,80,81]

Taken collectively, the components discussed above provide nutritional support for the adrenal glands, consisting of herbal adaptogens, and supportive vitamins and minerals. These components serve to aide in supporting bodily functions when the body is under stress, as well as in supporting normal cortisol values, which may be especially important in certain conditions, such as obesity, Syndrome X and hyperinsulinism. Stress, a poor diet and environmental toxins are known contributors of adrenal malfunction, factors which have been termed "diseases of civilization."[82]

Rachel Olivier, MS, ND, PhD serves as a Physician Advisor for Biotics Research Corporation.

1) Seyle H. A syndrome produced by diverse nocuous agents. *Nature* 1938;138:32.
2) Haussmann MF, Vleck CM, Farrar ES. A laboratory exercise to illustrate increased salivary cortisol in response to three stressful conditions using competitive ELISA. *Advan Physiol Educ*. 2007;31:110-115.
3) Chrousos GP. The role of stress and the hypothalamic-pituitary-adrenal axis in the pathogenesis of the metabolic syndrome: neuro-endocrine and target tissue-related causes. *Int J Obes Relat Metab Disrd.* 2000 Jun;24 Suppl 2:S50-5.
4) Jubiz W. **Endocrinology A Logical Approach for Clinicians**. 1979. McGraw-Hill Book Company.
5) Bjorntorp P. Body fat distribution, insulin resistance, and metabolic diseases. *Nutrition*. Sep 1997 13 (9):795-803.
6) Bjorntorp P, Holm G, Rosmond R. Hypothalamic arousal, insulin resistance and type 2 diabetes mellitus. *Diabet Med.* May 1999;16(5):373-383.
7) Vicennati V, Pasquali R. Abnormalities of the hypothalamic-pituitary-adrenal axis in nondepressed women with abdominal obesity and relations with insulin resistance: evidence for a central and a peripheral alteration. *J Clin Endocrinol Metab*. 2000 Nov;85(11):4093-8.
8) Straitakis CA and Chrousos GP. Neuro-endocrinology and pathophysiology of the stress system. *Ann N Y Acad Sci.* 1995 Dec 29;771:1-18.
9) www.vivo.colostate.edu/hbooks/pathphys/endocrine/hypopit/acth.html.
10) Yildiz BO, Azziz R. The adrenal and polycystic ovary syndrome. *Rev Endocr Metab Disord.* 2007 Oct 12; [Epub ahead of print]
11) http://www.physiol.ucl.ac.uk/endocrinology/year1_endocrine_CAL/ad/ad.htm
12) Savage MO, Scommegna S, Carroll, PV, Ho JTF, Monson JP, Besser GM, Grossman AB. Growth in Disorders of Adrenal Hyperfunction. *Hormone Research* 2002;58 (Suppl. 1):39-43.
13) Magiakou MA. Growth in disorders of adrenal hyperfunction. *Pediatr Endocrinol Rev*. 2004 Aug;1 Suppl 3:484-9. Review.
14) Young SN. L-tyrosine to alleviate the effects of stress? *J Psychiatry Neurosci* 2007;32:224.
15) http://en.wikipedia.org/wiki/Vitamin_C.
16) Levine M. New concepts in the biology and biochemistry of ascorbic acid. *N Engl J Med*. 1986 Apr 3;314(14):892-902.
17) Padayatty SJ, Doppman JL, Chang R, Wany Y, Gill J, Papanicolaou DA, Levine M. Human adrenal glands secrete vitamin C in response to adrenocorticotrophic hormone. *Am J Clin Nutr.* 2007 Jul;86(1):145-9.
18) Naidu KA. Vitamin C in human health and disease is still a mystery? An overview. *Nutrition Journal* 2003, 2**:**7.
19) http://en.wikipedia.org/wiki/Pantothenic_acid.
20) Morgan AF, Simms HD. *Science*. 1939;89:565.
21) Daft FS, Sebrell WH. *Pub Health Rep*., USPHS. 1939;54:2247.
22) Nelson AA. *Pub. Health Rep*., USPHS. 1939;54: 2250.
23) Daft FS, Sebrell WH. *Pub Health Rep*., USPHS. 1940;55:1333.
24) Ashburn LL. *Pub Health Rep*., USPHS. 1940;55: 1337.

(Continued on next page)

25) Deane HW, McKibbin JM. *Endocrinology*. 1946; 38:385.
26) Hurley LS, Morgan AF. Carbohydrate Metabolism and Adrenal Cortical Function in the Pantothenic Acid-Deficient Rat. *J Biol Chem*. 1952 Apr;195 (2):583-90.
27) Tahiliani AG, Beinlich CJ. Pantothenic acid in health and disease. *Vitam Horm*. 1991;46:165-228. Review.
28) Berdanier C. **Advanced Nutrition Micronutrients**. 1998. CRC Press.
29) Allgood VE, Cidlowski JA. Vitamin B6 modulates transcriptional activation by multiple members of the steroid hormone receptor superfamily. *J Biol Chem*. 1992 Feb 25;267(6):3819-24.
30) Gerster H. The importance of vitamin B6 for development of the infant. Human medical and animal experiment studies. *Z Ernahrungswiss* 1996; 35:309-17. [PubMed abstract]
31) Bender DA. Novel functions of vitamin B6. *Proc Nutr Soc* 1994;53:625-30. [PubMed Abstract].
32) Chandra R and Sudhakaran L. Regulation of immune responses by Vitamin B6. *NY Acad Sci* 1990; 585:404-423. [PubMed abstract]
33) Trakatellis A, Dimitriadou A, Trakatelli M. Pyridoxine deficiency: New approaches in immunosuppression and chemotherapy. *Postgrad Med J* 1997; 73:617-22. [PubMed abstract]
34) Leklem JE. Vitamin B6. In: Shils ME, Olson JA, Shike M, Ross AC, ed. **Modern Nutrition in Health and Disease**. 9th ed. Baltimore: Williams and Wilkins, 1999: 413-421.
35) Shibata K, Mushiage M, Kondo T, Hayakawa T, Tsuge H. Effects of vitamin B6 deficiency on the conversion ratio of tryptophan to niacin. *Biosci Biotechnol Biochem* 1995; 59:2060-3. [PubMed abstract]
36) Tang FI, Wei IL. Vitamin B-6 deficiency prolongs the time course of evoked dopamine release from rat striatum. *J Nutr*. 2004 Dec;134(12):3350-4.
37) Pivonello R, Ferone D, de Herder WW, de Krijger RR, Waaijers M, Mooij DM, van Koetsveld PM, Barreca A, De Caro ML, Lombardi G, Colao A, Lamberts SW, Hofland LJ. Dopamine receptor expression and function in human normal adrenal gland and adrenal tumors. *J Clin Endocrinol Metab*. 2004 Sep;89(9):4493-502.
38) Abidi P, Leers-Sucheta S, Azhar S. Suppression of steroidogenesis and activator protein-1 transcription factor activity in rat adrenals by vitamin E deficiency-induced chronic oxidative stress. *J Nutr Biochem*. 2004 Apr;15(4):210-9.
39) Chandra AK, Ghosh R, chatterjee A, Sarkar M. Amelioration of vanadium-induced testicular

(Continued on next page)

toxicity and adrenocortical hyperactivity by vitamin E acetate in rats. *Mol Cell Biochem*. 2007 Dec;306(1-2):189-200.
40) Tsiakitzis K, Kourounakis AP, Tani E, Rekka EA, Kourounakis PN. Stress and active oxygen species--effect of alpha-tocopherol on stress response. *Arch Pharm* (Weinheim). 2005 Jul;338(7):315-21.
41) Shorin IuP, Seliatitskaia VG, Kolosova NG, Kulikov VIu. Effect of alpha-tocopherol on the adrenal reaction to cold stress. *Biull Eksp Biol Med*. 1985 Jun;99(6):669-71. (Russian).
42) Hastings MM, Van JL. Sodium deprivation during thiamin deficiency in rats: hormonal, histological, and behavioral responses. *J Nutr*. 1981 Nov;111 (11):1955-63.
43) Gubler, CJ, Fujiwara, M, Dreyfus, PM. (1976) Biochemical changes in thiamine deficiencies. In: **Thiamine**. John Wiley and Sons, New York. 1976. pp. 121-142.
44) www.naturalstandard.com.
45) Riboflavin and adrenal cortex. *Nutr Rev* 1973 31:96-97.
46) Cervantes-Laurean D, McElvaney NG, Moss J. Niacin. In: Shils M, Olson JA, Shike M, Ross AC, eds. Modern Nutrition in Health and Disease. 9th ed. Baltimore: Williams & Wilkins; 1999:401-411.
47) O'Dell, BL, Reynolds G, Reeves PG. Analogous Effects of Zinc Deficiency and Aspirin Toxicity in the Pregnant Rat. J. Nutr. 1977 107: 1222-1228.
48) Malecki EA, Greger JL. Manganese Protects against Heart Mitochondrial Lipid Peroxidation in Rats Fed High Levels of Polyunsaturated Fatty Acids. J Nutr. 1996;126(1):27-33.
49) Welder FC. Biochemical and Nutritional Role of Manganese: an overview. In: Klimis-Tavantzis DJ, editor. Manganese in health and disease. 1st ed. Boca Raton, FL: CRC Press; 1994.p.2-37.
50) Kalea AZ, Schuschke DA, Harris PD, Klimis-Zacas DJ. Cyclo-Oxygenase Inhibition Restores the Attenuated Vasodilation in Manganese-Deficient Rat Aorta. J. Nutr. 2006 136:2302-2307.
51) Manji HK, Moore GJ, Chen G. Lithium up-regulates the cytoprotective protein Bcl-2 in the CNS in vivo: a role for neurotrophic and neuroprotective effects in manic depressive illness. J Clin Psychiatry. 2000;61 Suppl 9:82-96.
52) Hashimoto R, Fujimaki K, Jeong MR, Senatorov VV, Christ L, Leeds P, Chuang DM, Takeda M. [Neuroprotective actions of lithium] [Article in Japanese]. Seishin Shinkeigaku Zasshi. 2003;105 (1):81-6.
53) Crippen D. Agitation in the ICU: part one Anatomical and physiologic basis for the agitated state. Crit Care. 1999; 3(3): R35–R46.
54) Gainetdinov RR, Mohn AR, Bohn LM, Caron MG. Glutamatergic modulation of hyperactivity in mice lacking the dopamine transporter. *Proc Natl Acad Sci U S A*. 2001 Sep 25;98(20):11047-54.
55) http://en.wikipedia.org/wiki/Dopamine.
56) Gambarana C, Ghiglieri O, Masi F, Scheggi S, Tagliamonte A, De Montis MG. The effects of long-term administration of rubidium or lithium on reactivity to stress and on dopamine output in the nucleus accumbens in rats. *Brain Research* 1999;826(2):200-209.
57) Bensky D, Gamble Andrew (Compiler). **Chinese Herbal Medicine: Materia Medica.** Revised Edition. 1986. p. 284-85.
58) http://www.yahwehsaliveandwell.com/achyranthes.html.
59) Mills S. **The Complete Guide to Modern Herbalism**. 1994. Thorsons. Great Britain,.
60) Hoffman D. **The New Holistic Herbal**. 1990 Element, Dorset.
61) Ody P. **The Complete Medicinal Herbal**. 1993. Dorling Kindersley Limited, London.
62) http://en.wikipedia.org/wiki/Centella_asiatica.
63) Punturee1 K, Wild CP, Kasinrerk W, Vinitketkumnuen1 U. Immunomodulatory Activities of *Centella asiatica* and *Rhinacanthus nasutus* Extracts. *Asian Pacific J Cancer Prev.* 2005 6, 396-400.
64) Bensky D, Gamble A. **Chinese Herbal Medicine Materia Medica**. 1993. Eastland Press, Inc.
65) Zhang Y, Kiyohara H, Matsumoto T, Yamada H. Fractionation and chemical properties of immunomodulating polysaccharides from roots of Dipsacus asperoides. Planta Med. 1997 Oct;63 (5):393-9.
66) Kim, D.-K., Kwak, J. H. A Furan derivative from *Cornus officinalis*. *Arch. Pharmacal Res*. 1998, *21:* 787-789.
67) Wang, H, Nair, MG, Strasburg, G M, Chang, YC, Booren, AM, Gray, IJ, Dewitt, DL. Antioxidant and anti-inflammatory activities of anthocyanins and their aglycone, cyanidin, from tart cherries. *J. Nat. Prod.* 1999, *62*, 294-296.
68) Seeram, NP, Momin RA, Bourquin LD, Nair MG. Cyclooxygenase inhibitory and antioxidant cyanidin glycosides in cherries and berries. *Phytomedicine* 2001, *8*, 362-369.
69) NP Seeram NP, Schutzki R, Chandra A, Nair MG. Characterization**,** Quantification, and Bioactivities of Anthocyanins in *Cornus* Species. *J. Agric. Food Chem.* 2002 50:2519-2523.
70) http://www.natural standard.com/monographs/

(Continued on next page)

sweetbasil.
71) http://www.herbnet.com/BASIL2003.pdf
72) Lalko J, Api AM. Investigation of the dermal sensitization potential of various essential oils in the local lymph node assay. Food chem. Toxicol 2006;44(5):739-746.
73) Renzulli C, Galvano F, Pierdomenico L, Speroni E, Guerra MC. Effects of rosmarinic acid against aflatoxin B1 and ochratoxin-A-induced cell damage in a human hepatoma cell line (Hep G2). J Appl Toxicol. 2004 Jul-Aug;24(4):289-96.
74) http://www.naturalstandard.com/index-abstract.asp?create-abstract=/monographs/news/news200507010.asp.
75) http://en.wikipedia.org/wiki/Schisandra.
76) Park JY, Lee SJ, Yun MR, Seo KW, Bae SS, Park JW, Lee YJ, Shin WJ, Choi YW, Kim CD. Gomisin A from Schisandra chinensis Induces Endothelium-Dependent and Direct Relaxation in Rat Thoracic Aorta. Planta Med. 2007 Dec 7; [Epub ahead of print]
77) Zhao TF, Wang X, Rimando AM, Che C. Folkloric medicinal plants: *Tinospora sagittata var. cravaniana* and *Mahonia bealei*. *Planta Med* 1991;57:505.
78) Nayampalli S, Ainapure SS, Nadkarni PM. Study of antiallergic acid Bronchodilator effects of *Tinospora cordifolia*. *Indian J Pharm* 1982;14:64-6.
79) Mahajan VR, Jolly CI. A new hypoglyceamic agent from *Tinospora cordifolia* Miers. *Indian Drugs* 1985;**23**:119-20.
80) Grover JK, Vats V, Rathi SS. Anti-hyperglycemic effect of Eugenia jambolana and *Tinospora cordifolia* in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. *J Ethnopharmacol* 2000;73:461-70.
81) Stanely M, Prince P, Menon VP. Hypoglycaemic and other related actions of *Tinospora cordifolia* roots in alloxan-induced diabetic rats. *J Ethnopharmacol* 2000;70:9-15.
82) Selye H. Studies on adaptation. Endocrinology 1937 21:169. ◆

Gluten Sensitivity Packs™

Advanced Gluten Sensitivity & Immune Support Formula

Maintaining a healthy and balanced immune system is important for encouraging a healthy digestive system, healthy joints and skin, as well as nearly every other organ system in the body.

With today's challenging lifestyles, NuMedica's® Gluten Sensitivity Packs™ help support a balanced immune system and help maintain a higher level of health.

Each daily packet contains a powerful combination of 5 formulas:

- **1 Omega 600™ EPA/DHA**
- **2 Anti-Inflammex™**
- **1 D3 - 5000™**
- **1 L-Glutamine™ 500 mg**
- **1 BrocColinate™**

Comprehensive: Combines powerful intestinal support, anti-inflammatory and immune support with the amino acid L-Glutamine, omega 3 fatty acids and sulforaphane glucosinoate.

- **Just one packet daily for easy, single dosage**
- **Travels well in pocket, bag or purse**
- **Combined packaging for greater value**

Formulated to contain NO gluten or wheat.

Targeted Nutrition, Convenient Packets

Gluten Sensitivity Packs™ 30 Packets

gluten free

NuMedica®
Achieving Physiological Balance

9503 E. 55th Place | Tulsa, OK 74145 | (866) 787-5175 | www.numedica.com

The Evolution of Enzyme Treatment Adopted from the Trophoblast and the Origins of Cancer

by: Nicholas J. Gonzalez, M.D. and Linda L. Isaacs, M.D.

In our office, we offer an aggressive nutritional regimen for the treatment of cancer and other degenerative disease. Our therapy, in its most general sense, consists of three basic components; individualized diets, individualized supplement programs, and detoxification routines such as the coffee enemas. For cancer patients, we also specifically prescribe large doses of orally ingested pancreatic enzymes, taken around the clock, which we believe provide the main anti-cancer element in our therapy.

The use of pancreatic enzymes against cancer has a long history, going back to Dr. John Beard (1858-1924), the English zoologist and embryologist who spent most of his research career at the University of Edinburgh in Scotland. By Beard's day, the main categories of pancreatic enzymes had been identified, the proteases that reduce proteins into simple amino acids, the amylases that cleave complex carbohydrates into simpler sugars, and the lipases that break down triglycerides into fatty acids. Physiologists of the time knew that the pancreas secreted these various enzymes along with bicarbonate into the duodenum during meals for digestion. But Beard proposed as early as 1902 that trypsin, the main pancreatic proteolytic enzyme, in addition to its known digestive responsibilities, represented our body's main defense against cancer – and would serve as an ideal cancer treatment. Subsequently, Beard tested his enzyme hypothesis in both animal models and in human patients, with great success, as reported in the scientific literature of his day. Unfortunately, more due to medical politics than anything else, Beard's useful treatment never became accepted medical practice, and when he died in 1924, he died in obscurity, his enzyme approach relegated to no more than a footnote to medical history.

During his lifetime, Dr. Beard recommended only injectable preparations of pancreatic enzymes as a cancer treatment assuming that for his specific purposes, orally ingested preparations would be of little value. The active components such as trypsin are proteins, and like any other protein ingested by mouth would face a series of formidable barriers, beginning with the hydrochloric acid present in the stomach. Any active enzymes that might survive this initial assault would then be subjected to auto-digestion within the alkaline duodenum. Should any trypsin remain, it could do little systemically; scientists at the time already knew the protease to be a fairly large molecule that, they believed, could not possibly pass through the intestinal mucosa.

By 1900, a number of pharmaceutical firms in Europe and in the US manufactured powdered enzyme products, designed as a treatment for diphtheria, a world-wide scourge until the advent of vaccines for the disease. The diphtheria bacillus killed its host by elaborating a tough fibrous membrane in the throat that could, if unchecked, lead to suffocation. In an animal model of the disease, a preparation of trypsin locally applied in the larynx appeared to dissolve this deadly tissue and when tested in humans, the enzyme worked quite well. An early reference to the successful treatment in humans dates from the October 23, 1886 issue of the *Journal of the American Medical Association.*[1]

By 1900, two companies, Merck and the New York based Fairchild, affiliated with Burroughs Wellcome, marketed trypsin preparations derived from animal sources for treatment of the disease. An old catalogue of Fairchild we have uncovered from 1898 lists, as one of its products: "TRYPSIN. (FAIRCHILD.) ESPECIALLY PREPARED AS A SOLVENT FOR DIPHTHERITIC MEMBRANE."[2(p57)] It seems around that time, companies such as Fairchild began marketing injectable preparations in addition to those intended for direct application.

By 1907, the initial successes reported in the literature generated considerable interest in Beard's enzyme treatment of cancer. In response to this enthusiasm, a growing number of firms began selling their own "trypsin" specifically as a cancer treatment in addition to those available from Merck and Fairchild. With trypsin formulations widely available, physicians both in the US and in Europe began applying the therapy, usually without consulting Beard, and with variable results. As both positive and negative reports began to filter into the literature, Beard began to suspect that many of the available preparations had little potency and hence, little efficacy. He himself, after testing various products, recommended only

(Continued on next page)

the enzymes available from Fairchild, which he thought most effective clinically.[3]

Manufacturers of pancreatic enzymes in those days faced numerous difficulties bringing a potent formulation to market. Then, as now, all commercial enzymes were extracted from the glands of animals, such as cattle and pigs, slaughtered for their meat. In the animal pancreas, the acinar cells synthesize and store the proteolytic components as inactive precursors such as trypsinogen and chymotrypsinogen, to protect the gland itself. During meals, in response to both hormonal and neural stimulus, the exocrine cells release their supply of inactive proteases directly into the pancreatic ducts. The ductal cells themelves secrete a bicarbonate-rich fluid, which along with the enzymes ultimately empties into the duodenum. Since the proteolytic component works best in a slightly alkaline pH, the accompanying bicarbonate neutralizes any acid arriving from the stomach during digestion, and in so doing creates the ideal environment for the enzymes to begin their work.

In the duodenum the intestinal enzyme enterokinase secreted by the mucosal cells cleaves off a small six amino acid terminal from trypsinogen, converting the precursor into the active enzyme.[4(p227)] Trypsin can then rapidly begin activating other trypsinogen and chymotrypsinogen molecules in a cascade effect.

At room temperature in the presence of even small amounts of moisture, the precursors can begin spontaneously converting into active enzymes, even in the absence of enterokinase. After only a few trypsin molecules so transform, these can then rapidly set off the activation process. Consequently, in an animal pancreas sitting in a slaughterhouse waiting to be collected for drug company use, all the enzymes can convert into the active configuration unless cooled on ice and processed very quickly. Since trypsin and chymotrypsin are themselves proteins, the potent enzymes can begin attacking one another, rendering the mixture into a collection of inert peptide fragments and amino acids.

From our readings in the literature, it seems that in Beard's era, the manufacturers used a very simple process to extract the enzymes, first mincing the glands in cold water, pressing the mixture, then removing the active component with alcohol. The alcohol would then be allowed to evaporate off, leaving the desired enzyme fraction.[5]

We suspect the procedure was neither exacting nor refined, the final preparation most likely containing little in the way of potential enzyme activity. To make matters worse, those products intended for injectable use were provided in an aqueous solution in vial form, an ideal environment for the auto-digestion process to begin. Fairchild did market a dry powdered "trypsin" meant to be mixed with water immediately before injection, but even this proved so unstable that by 1907, as Beard reports, the company discontinued its sale.[6]

In the November 16, 1907 issue of *Lancet,* P. Tetens Hald, M.D., "Formerly Assistant in the Pharmacological Institute of the University of Copenhagen" and a Beard proponent, published the results of his evaluation of six popular enzyme products available at the time, including those marketed by Merck and Fairchild.[7] In his research, he employed the same method used today to assess proteolytic activity, the casein digestion test. This simple assay measures the amount of the milk protein casein curdled over time by a known quantity of pancreas product. Today, laboratories measure enzymatic potency much the same way, rating activity with a 1-10X USP system, in which each unit signifies the product has digested 25 times its weight of casein. So, a gram of a "1X" product can digest 25 grams of casein, a gram of a "4X" product, 100 grams, and so on.

Dr. Hald contacted the manufacturers of the various products he analyzed in his laboratory, none of whom provided him with any information about the stability of the formulations they sold commercially. To his surprise, his assays revealed the potencies varied enormously, up to a factor of 400, and that the activity levels rarely correlated with the company's claims, as stated on the bottle or in its literature.

Dr. Hald writes:

The results are interesting in several respects. First, they show that preparations obtained from different makers vary exceedingly in strength. Thus the strongest of the preparations examined was 400 times more active than the weakest one. The feeble action of the preparations obtained from Zanoni and from Freund and Redlich was very striking.

Secondly, Table III shows that even the preparations of the same class may present considerable differences in strength. In one brand one of the supplies was even between 30 and 40 times stronger than the other one.[7]

In his 1911 book *The Enzyme Treatment of Cancer*, Dr. Beard himself bemoaned the dearth of standardized and potent enzyme preparations, a situation that led to inevitable treatment failures when physicians utilized products of

(Continued on next page)

poor quality. He actually quotes a Merck publication from the time, in which the writer discusses the confusion in the field:

The actual position of affairs in the past few years can best be described by quoting the impartial opinion of a competent author. On p. 340 of *E. Merck's Annual Report of Recent Advances in Pharmaceutical Chemistry and Therapeutics* (Darmstadt, vol. xxii., August, 1909) one may read regarding trypsin: "The mode of action and the value of pancreas preparations in cancer has not yet received a wholly reliable explanation. Great difficulties are encountered because the preparations used by the various investigators differ greatly in respect to their chemical properties, their purity, and in the amount of active substances they contain, and often these factors are not fully known to the student of the literature, or to the physician who has used them and describes their action. Further difficulties arise when pancreatin [whole pancreas product] and trypsin are described as substances of equal value, and how shall we gauge the action of pancreatin and trypsin ampullae whose mode of preparation and whose composition is not mentioned in the original paper, neither is there any mention made of their sterility or the method by which they have been sterilized? …So long as the solutions of pancreatin and trypsin are treated as secret remedies no one will be able to form a clear picture of the value of trypsin treatment from the many publications which have appeared."[6(p198)]

In reference to the above, as an aside we find it interesting that by 1909 Beard's hypothesis had generated interest sufficient enough to warrant thoughtful discussion in the annual report of a major international pharmaceutical company. The above exposition also adds support to Beard's contention that the mixed results for enzyme treatment being reported in the literature most likely reflected no flaw in the theory, only variations in the quality of product.

A number of factors contributed to the decline of interest after 1911 in Dr. Beard's trophoblastic hypothesis and his enzyme approach to cancer. Certainly, the enthusiasm for the X-ray, discovered in 1895 by Röntgen, helped push Beard's treatment into the background.[8;9] After all, two-time Nobel Laureate Madame Curie, widely admired and respected at all levels of society, had vigorously championed the mysterious invisible rays as a non-toxic cure for all cancer, a breakthrough the press promoted with great enthusiasm. Beard had no such media savvy science star to praise his ideas about the use of enzymes against malignant disease. And it would not be until after Beard's death in 1924 that researchers began to appreciate the severe limitations of radiation treatment, which in reality worked well against only a few cancers. Even for those tumors that did respond initially, usually the disease recurred with a vengeance and the therapy once thought to be harmless actually could be quite toxic. An entire generation of radiation researchers died as a result of cavalier exposure to the rays, including Madame Curie herself who eventually succumbed to radiation-induced aplastic anemia.[10] By then, Beard was long forgotten.

Above and beyond the influence of personality, the vagaries of the media, and the realities of scientific politics, we suspect that poor quality enzyme products did much to undermine Beard's treatment. In a sense, Beard was a victim of his own fame. The initial successes reported in the literature prompted many doctors to begin using any number of enzyme formulations without first consulting Beard about dosing and quality, with inevitable poor or mixed results. The disappointments fueled the backlash in the journals, to the point that after 1911, few doctors of Beard's generation even considered the treatment for their patients.[11]

Subsequently, F.L. Morse, M.D. in St. Louis during the late 1920s and early 1930s,[12] and Frank Shively, M.D., a Dayton, Ohio surgeon active during the 1960s,[13] rediscovered Beard's earlier papers and used injectable formulations of the pancreatic enzymes in their treatment protocols with reported success. Then in the 1960s, William Kelley, D.D.S. first appeared on the scene, with his complex cancer treatment involving a whole foods diet, large amounts of various nutritional supplements, detoxification routines, and prodigious doses of pancreatic enzymes ingested orally – but never injected.

Kelley claimed he discovered the anti-cancer properties of oral pancreatic enzymes serendipitously, without any apparent previous knowledge of Dr. Beard. Kelley had been a successful orthodontist with a serious interest in nutrition, practicing in Grapevine, Texas, when in the early 1960s while he was only in his mid-30s, he became devastatingly ill. His doctors eventually diagnosed advanced pancreatic cancer, though he never underwent tissue sampling – not uncommon in the days before CT scans and needle biopsies. In desperation, with four children dependent on him, Kelley devised his own nutritional program to slow the disease, including a largely organic, vegetarian raw foods type diet, a variety of supplements, and detoxification routines such as coffee enemas. He also added high doses of oral pancreatic enzymes to his regimen, not because of any familiarity with Beard's hypothesis of which he was at the time ignorant, but to help relieve his severe digestive distress – as occurs commonly in patients with pancreatic malignancy.

(Continued on next page)

Kelley's digestion was so poor, he began ingesting huge amounts of pancreatin around the clock hoping to keep his worsening symptoms – including excruciating pain whenever he ate - at bay. He discovered that with large doses, his tolerance for food improved and – to his surprise – his large tumors, palpable through the abdominal wall, seemed to regress. Perplexed, and ever the serious student, he scoured the medical literature looking for evidence that someone else might have observed an anti-cancer effect for the pancreatic enzymes. His search eventually led him to Dr. Beard's book and papers from 50 years earlier, but by that point, Kelley claimed, he had already worked out the rudiments of his treatment.

From that very personal experience began Kelley's foray out of conventional orthodontics into the controversial world of nutritional cancer therapeutics. By the late 1960s, having long abandoned dentistry, he refocused his attention on treating, with his nutritional regimen, the very ill drawn from all over the country, most diagnosed with advanced malignancy. With the publication of his 1969 book *One Answer to Cancer*,[14] Kelley for better or worse secured his position as a preeminent alternative cancer therapist, and inevitably as a target for the mainstream medical world which then, as now, had little use for proposed nutritional approaches to the disease.

Kelley intently studied the writings of Beard, who strongly insisted the treatment needed to be applied via injection. Nonetheless, for the duration of his career, Kelley only recommended oral formulations. Injectable preparations were still available in the US until 1966, when the FDA in its wisdom enacted a regulation removing them from the marketplace, perhaps in response to Dr. Shively's practice. In any event, as a dentist, Kelley lacked the legal right to prescribe injectable enzymes, so the question was moot. Most importantly, even if such products remained available and even if he had the authority to use them, his own experience treating himself, and his subsequent experience with hundreds of patients taught him that oral preparations worked very well despite Beard's claims to the contrary.

From the early 1900s, oral formulations of pancreatic enzymes were available with and without prescription in the US and Europe for a variety of uses, including treatment for diphtheria as well as digestive problems. A Dr. C.C. Rice, who published the first report we have been able to identify of a patient successfully treated with enzymes, recommended the Fairchild injectable preparation along with an oral supplement known as "Holadin."[15] In the decades that followed, physicians prescribed these oral products for their patients diagnosed with pancreatic insufficiency such as occurs with pancreatitis or cystic fibrosis, though no one until Kelley used them as a primary cancer treatment.

By 1950, the commercial demand for pancreatic enzymes such as trypsin had expanded greatly beyond their limited pharmaceutical application. For example, leather tanners used proteolytic enzymes to speed up curing, and candy manufacturers learned that trypsin, when added during the processing of chocolate, helped create a smoother product.

But the commercial suppliers still relied on the old mincing and alcohol method of extracting proteolytic enzymes from the animal gland, a very inefficient technique that gave a 10-15% yield.[5] A potential bonanza awaited anyone who might develop a more efficient enzyme purification process.

The biochemist Ezra Levin of Champaign, Illinois, active during the 1940s and 1950s and at the time one of the leading experts in the manufacture of pancreatic enzymes, believed he had done just that. His lengthy 1950 US patent entitled *Production of Dried, Defatted Enzymatic Material* detailed his crowning achievement, an elaborate multi-step process for extracting active enzymes from the gland that he insisted was more efficient and more cost effective than the previous methodology.[5] Instead of removing a portion of the enzymes from the pancreas tissue, leaving most behind in the discarded residue, Levin's new method involved first extracting the fat with appropriate solvents. Then any remaining water would be evaporated off via vacuum distillation, leaving all the enzymes in the remaining powder that yielded, at least theoretically, a very potent product.[5] In a sense, Levin had reversed the traditional procedure in which the enzymes were extracted from the pancreatic tissue, with the water, fat, and most of the enzymes remaining behind as waste.

Levin saw as an added benefit that during the process, most if not all the precursors such as trypsinogen would also simultaneously activate, to yield a product of high potency with purported minimal processing losses; a product which Levin and his customers thought most ideal for pharmaceutical as well as industrial use.

Levin had made two assumptions, as he perfected his method. First, he believed that the fat in the gland – and the pancreas is a fatty gland – had no useful purpose beyond its role as a storage depot for excess calories, and needed to be removed. To him, fat seemed little more than inert filler. Second, he always assumed the more activated the product, the better.

On the first page of his patent, an introductory summary of his method reflects his two basic assumptions:

(Continued on next page)

"Our High Volume Equals Substantial Savings"

SAVE UP TO 80% ON LABORATORY TESTING

Doctor's Choice is a professional health care organization offering licensed health care professionals an easy and convenient way to get discounted laboratory tests. Whether you have a low-volume or a high-volume practice, we are certain that we can save you money.

ANA	$7.50	INSULIN	$8.50
CORTISOL	$9.50	PROGESTERONE	$12.00
CRP	$7.50	PSA	$9.00
DHEA	$21.00	T3, FREE	$9.00
ESTRADIOL	$18.00	TESTOSTERONE	$13.50
GLIADIN AB PNL	$25.50	TPO ANTIBODY	$10.50
HEMOGLOBIN A1C	$8.50	VAP	$42.00
HOMOCYSTEINE	$17.00	VITAMIN D, 25-OH	$28.00

BIOCHEMICAL LABORATORIES · Oncolab™ · Quest Diagnostics® · GENE SMART™ · ALLETESS MEDICAL LABORATORY · CHROMOSOMAL LABORATORIES, INC. · MEDTOX® · IBT Laboratories · Diagnos-Techs, Inc. Clinical and Research Laboratory

DOCTOR'S CHOICE™

Professional Laboratory & Diagnostic Services

P.O. Box 337, Washington Depot, CT 06794 • Telephone: 888-852-2723 • Facsimile: 888-952-2723

www.DoctorsChoice.net • Info@DoctorsChoice.net

By the present invention, trypsinogen is converted to trypsin and chymotrypsinogen to chymotrypsin by preactivation to a maximum and is then dried and defatted simultaneously as hereinafter described, while this high enzymatic activity is held substantially without change, to produce highly active raw powders equal in activity to the fresh gland.[5]

Levin actually created a company, Viobin, for years a subsidiary of A.H. Robbins, to manufacture and market his enzyme products. The Levin method proved so successful that by the 1960s, Viobin provided most of the enzymes used in the US, both for pharmaceutical and other industrial purposes. Even other manufacturers that ventured into the enzyme business themselves relied on variations of the Levin patent.

Throughout the 1970s, Kelley designed his own extensive line of supplements, produced by a number of different companies. At one point, he told me he had gone through 14 such firms in 20 years, changing when he felt quality control failed to meet his standards, which in the supplement industry in those days tended to be lax. However, whatever company name might appear on the label, Kelley insisted the pancreatic raw material be purchased from Viobin, which he always claimed to be the best available enzyme. The various distributors he used would purchase the pancreatin in bulk powdered form and encapsulate the material, with the final product bottled and distributed under Kelley's personal label. Even though other suppliers approached him, for all of Dr. Kelley's 20 years in practice as a nutritional therapist, he stuck by Viobin through the years of his great success and his growing reputation.

The Levin method could be adjusted, by shortening or lengthening the processing time, to provide pancreatin of various potencies as measured on the 1-10X scale, with 1X representing the least, and 10X, the maximum possible activity. During the 1970s, Viobin actually sold pancreatin of various activity levels, a number of which Kelley tried out over the years. Eventually, after vacillating back and forth from weaker to stronger then back to weaker formulations, he settled for a time on the 4X which provided more than half of the total potential enzyme content as inactive precursors.

By the time I (Dr. Gonzalez) met Kelley during the summer of 1981, he had become convinced that the more active the oral product, the better the effect against cancer. He wanted 8-10X, nothing less, for all his patients. He seemed at times almost fanatical about the issue of enzyme strength, insisting he wanted no precursors in his formulation. I even traveled with Kelley to Wisconsin to meet with the manufacturer he used at the time, to discuss with them his new plans for the strongest supplement possible, containing only 10X pancreatin. I also met several times with representatives of Viobin, to discuss their enzymes and the feasibility of providing large amounts of the 10X material.

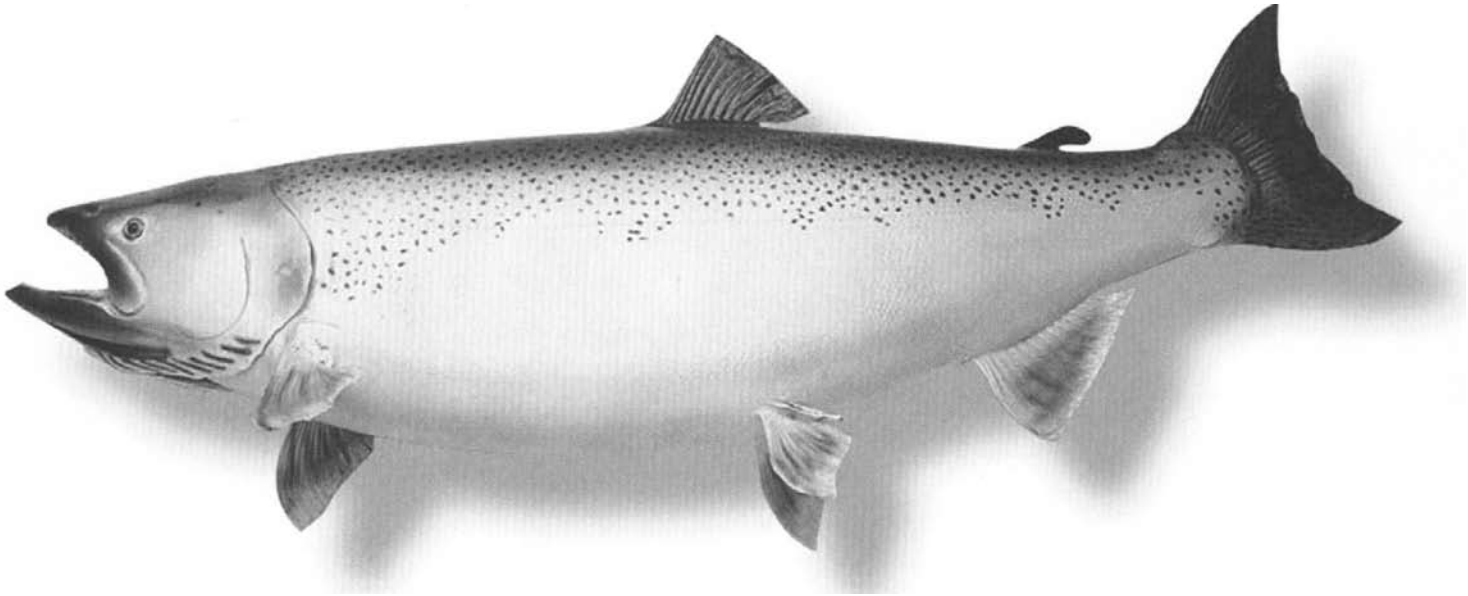
As I pursued my investigation of Dr. Kelley's therapy and practice over the next five years under my mentor, the late Robert A. Good, M.D., Ph.D., I concentrated my efforts primarily on Kelley's results with advanced cancer. As a side project, I also tried to evaluate the relative efficacy of the different pancreatic formulations he had recommended during his time in practice. From Kelley's records and our conversations about the issue, I had a fairly good idea of which strength of enzyme he used during which period.

From my review of Kelley's patient charts on a year by year basis, it seemed to me that his greatest success as a practitioner occurred during the decade 1970-1980, when he relied primarily on the 4X pancreatin, containing a high percentage of inactive precursors. After 1981, he opted for increasingly more activated product, eventually settling on the 10X potency. However, it appeared that his success declined markedly as he prescribed a "stronger" preparation. Admittedly, other factors might have come into play: beginning in 1981, Kelley himself withdrew from direct patient care, turning his therapy over to a constellation of "Kelley Counselors" whom he had trained via a series of weekend seminars. Though he had over the years certified over 1000 such practitioners, only several dozen were active at the time I met Kelley, and these consisted of a very mixed group of people, in both educational background and ability. Some were practicing physicians, dentists, and chiropractors, others had no professional education in health care whatsoever. While a number I found to be very competent and dedicated, including several who lacked formal medical training, many were far less so. It would be hard to sort out the influence of this dramatic shift in the administration of his program on its successful application.

Regardless of the cause, I could track a significant fall off in responders beginning about 1982 – in fact, during the years 1984-1985, as I actively brought my research to a close, I knew of only one impressive result, a patient with stage IV Hodgkin's disease whose cancer regressed completely on the enzyme therapy. This single success during that time represented a far different situation than Kelley's glory days of the 1970s when, by my investigation of his charts, many hundreds of patients with properly diagnosed cancer had done well. But this patient was to my knowledge the last great success, and by 1986, Kel-

(Continued on next page)

Save Your Heart With Me



Today, more than ever, people are becoming aware of the need to watch their diet and take the necessary supplements to promote good health for their heart.

SAMOLINIC from The Key Company, is an excellent source for the fatty acids that help you maintain a healthy heart.

SAMOLINIC contains 500 mg. of Norwegian Salmon Oil and 500 mg. of Black Currant Seed Oil in a softgel form.

Call or visit our website to order a supply of **SAMOLINIC** today.

The KEY COMPANY

Finest Health Products Since 1959

800.325.9592

thekeycompany.com

ley in great frustration had closed his organization, essentially cutting off his treatment after 20 years. He believed that "disloyal" counselors and greedy supplement manufacturers had effectively sabotaged his life's work.

I finished my project under Dr. Good in 1986, but sadly Kelley turned increasingly paranoid, at one point thinking I had been sent by the CIA to steal his therapy for the government. After 1987, I had no further direct contact with Kelley, who for a long time essentially disappeared from view.

When my colleague Dr. Linda Isaacs and I subsequently arrived in New York in the fall of 1987 determined to salvage Kelley's treatment, we knew if we were to succeed in practice, we needed a reliable source of enzymes. As I thought about the situation, I realized we must determine the optimal composition for the enzyme product in terms of relative fat and protein content, as well as the ideal level of proteolytic activity – and hopefully find a source that met our specifications.

I had already begun to move away from the Levin methodology as the best for manufacturing pancreatic enzymes. In terms of composition, I knew that he had designed his extraction method to remove as much fat as possible, which he perceived as useless filler. I thought in this regard Levin, as well as Kelley, who accepted without question Levin's dictates, had been wrong, that fat might allow for a more stable product and provide physiological benefit. By 1987, researchers had already begun to suspect that fat was not just a simple warehouse for storing excess energy, but a metabolically active tissue secreting a variety of enzymes and hormones that regulate the processing of sugars and fatty acids. Perhaps, I thought, the lipid component of the pancreas might itself provide some additional effect, a complement to the proteolytic activity. So as a first order of business, I decided to search for an enzyme preparation containing significant fat.

Ezra Levin also assumed that the more active the product the better, the mantra Kelley again professed to me with total conviction. But I knew from my exhaustive evaluation of Kelley's files that as he opted for a more potent enzyme formulation, his response rate fell significantly. In frustration, he assumed he only needed to prescribe an even stronger enzyme, or change encapsulators, etc., instead of retracing his steps and going backward to the less active 4X enzymes he had earlier used with great success.

I became convinced that as brilliant as Kelley had been in his prime, he had erred in his later years by assuming that "purer and stronger" is always unquestionably better. I suspected that the fat depleted, highly activated supplements may have been prone to deteriorate once encapsulated, susceptible to rapid auto-digestion on the shelf. That may have been part of Kelley's problem during the mid-1980s. I also became convinced that the fat in the gland might not only help stabilize the mix, but provide synergistic factors to assist the proteolytic enzymes in their fight against malignant cells. Finally, I came to believe that an enzyme with less activity, with more of the total potential as precursor, might not only be more stable in the bottle, but more effective against cancer.

As a first order of business, I obtained samples of pancreatin from a number of suppliers who manufactured their own products. I also visited several health food stores and nutritional pharmacies in Manhattan, such as Willner's, purchasing a variety of pancreatic enzyme supplements. In the kitchen of my mother's home in Queens where we were staying at the time, I set up my own enzyme assay, using Knox gelatin as my protein substrate instead of casein, and the Viobin preparation Viokase as my standard by which to measure the activity of other products. I dissolved each capsule or tablet in a slightly alkaline solution to help promote the enzymatic reactions, and then observed the amount of gelatin digested over time. The assay, which I repeated many times over a number of weeks, worked quite well. Unfortunately, nearly all of the enzymes I tested seemed highly activated and highly processed, with all the fat removed.

Finally, I learned of the pancreas enzyme product derived from New Zealand pigs available from Allergy Research Group, a nutritional supplement company of some renown based in Northern California. As a start, I was happy about the source, since I had learned that New Zealand had perhaps the cleanest environment of any country on earth, as well as the strictest laws for raising animals for commercial use. Diseases such as hoof and mouth disease and trichinosis, I was told, had never been reported there.

I also wanted enzymes derived from the pig pancreas, thought to be most similar to the human organ. For decades, before the advent of genetically engineered preparations, physicians treated their diabetic patients with pig insulin, which proved to be quite similar in terms of amino acid structure to the human variety. In a similar manner, pig enzymes, I had learned from my conversations with Viobin scientists, most closely resembled ours, of all commercially available sources.

Most importantly, the Allergy Research Group (ARG) specifications described their pancreas supplement as a

(Continued on next page)

freeze dried product, minimally processed, *with the fat intact*, yet it still tested active at moderate levels by my own assay - exactly what we wanted. Though the material had not been intentionally activated as per Levin, I suspected during the handling of the glands, some of the precursors spontaneously converted, fortuitously to the precise level we thought ideal. Then, with freeze drying complete, all activation would come to a halt, leaving a stable product with most of the proteolytic enzymes in the precursor form.

I contacted the founder of ARG, Dr. Stephen Levine, and introduced myself, explaining my plan to open up a practice and my need for good quality enzymes. Though I was virtually unknown at the time, he agreed to provide me with as much of the product as we required. With a supply of enzymes guaranteed, in late 1987 we opened our practice with great optimism in an office in Manhattan. To our relief, this enzyme worked quite well, confirming my belief that a minimally processed lightly activated preparation, with the fat intact, was ideal for our purposes. One of my first successes dated from December 1987, a woman diagnosed with inflammatory breast cancer who had developed metastases into the bone while receiving chemotherapy. Told she had terminal disease, she somehow learned about us and began our program. She is alive today, over 21 years later, in excellent health with all scans long ago showing complete regression of her disease.

We treated all our early successes, right up until 1995, with pancreatic enzymes available from ARG. Between 1995 and 1998, we entered into a research and development arrangement with Procter & Gamble, who generously provided extensive financial support as well as a team of scientists to help us determine definitively the best enzyme formulation for our purposes. The company spent considerable time, effort, and money evaluating our enzymes, even sending researchers to New Zealand to observe first hand the entire processing of the pancreas glands from slaughterhouse to finished material. With such assistance, we eventually refined the methodology still further, to help guarantee consistent manufacture of a stable, modestly active, minimally processed product with most of the enzymes – but not all - in the precursor form, and with a certain percentage of fat remaining. Working with our New Zealand supplier, we developed a method to help assure the desired potency with each batch, without the need for Levin's complicated system of fat extraction and vacuum distillation. Today, we still rely on that same enzyme preparation, which we find works even more effectively than our earlier supplement.

About the Authors:

Dr. Nicholas Gonzalez: Dr. Gonzalez graduated from Brown University, Phi Beta Kappa, magna cum laude. He worked as a journalist, first at Time Inc., before pursuing premedical studies at Columbia University and receiving his medical degree from Cornell University Medical College in 1983. During a postgraduate immunology fellowship under Dr. Robert A. Good, considered the father of modern immunology, Dr. Gonzalez's investigated the nutritional regimen developed by the dentist Dr. William Kelley and used in the treatment of advanced cancer. Dr. Gonzalez's research has been funded by The Procter & Gamble Company, Nestle, and the National Cancer Institute/National Institutes of Health. For more information, see his website at www.dr-gonzalez.com.

Dr. Linda Isaacs: Dr. Isaacs has been working with Dr. Gonzalez in his private practice and research efforts since 1985. She graduated from the University of Kentucky, Phi Beta Kappa with High Distinction, and subsequently received her medical degree from Vanderbilt University School of Medicine. She completed a residency in Internal Medicine at the Department of Veteran's Affairs Medical Center at New York University Medical School and is Board Certified in Internal Medicine.

Excerpted from: *The Trophoblast and the Origins of Cancer: One solution to the medical enigma of our time* by Nicholas J. Gonzalez, M.D. and Linda L. Isaacs, M.D.

ISBN 978-0-9821965-0-2. $49.95. 220 pages including references, full color illustrations and index.

New Spring Press
PO Box 200
New York, NY 10156
www.newspringpress.com

References:

1) Porter W. Some practical suggestions on the treatment of diphtheria. *J Am Med Assoc.* 1886;7:454-455.
2) *Fairchild's Hand-Book of the Digestive Ferments*. New York, NY: Fairchild Bros. & Foster; 1898.
3) Beard J. Trypsin and amylopsin in cancer. *Med Rec.* 1906;69:1020.
4) Bhagavan NV. *Medical Biochemistry*. Boston, MA: Jones and Bartlett Publishers International; 1992.
5) Levin E. Production of dried, defatted enzymatic material. *U S Patent Office.* 1950;1-7.

(Continued on page 41)

CERTIFY YOUR STAFF

DRUG TESTING
DOT PHYSICALS

Each Training Kit Includes:

- DVD showing a live Drug Screen
- Sample Forms
- Step by Step Instructions
- Marketing Ideas and Suggestions
- Recommended Pricing
- Sample Contracts & Invoices
- Drug Screen Labs and Contact Information

$100

Plus shipping

DVD included of an actual DOT Physical performed by a Physician and Staff ……***includes forms and procedures***

For further information (or purchasing) the DOT/Drug Kit please contact Amanda Saunders, Laboratory Administrator for Kessinger Diagnostic Centre at 573-341-8292

NEW

HCG

Human Chorionic Gonadotropin

Now Available From
Professional Health Products®

®

Homeopathic HCG eliminates the need for daily injections and is a more cost effective form for patients.

Phone: (800) 955-1769 ***Fax: (817) 467-7567***

Hair Mineral Analysis to Define Past or Low Level Chronic Exposures

by: E. Blaurock-Busch, PhD

Hair mineral analysis (HMA) reflects how efficiently the root was nourished (or intoxicated) via the blood stream. As long as metals circulate, hair tissue will be supplied.

- This feeding and storing mechanism continues over time. Therefore, hair mineral levels reflect how well or poorly the hair tissue was supplied over time. While blood and urine testing reflects the present metal status only, HMA values indicate what happened over time.
- As long as toxins circulate in the blood stream, hair will be supplied. A 'normal' mercury or lead range in hair does not necessarily exclude a metal burden. If a metal such as Hg has fully crossed the blood brain barrier and no additional exposure exits, Hg will no longer be detected in the circulating blood stream. Or, if metals are tightly bound in tissue (such as fat tissue), little may find its way into blood or urine.
- Since mercury is no longer circulating and thus not supplying the hair root, it will not be detectable in hair either.
- This principle largely applies to metals capable of crossing the blood brain barrier.
- Some chelating agents such as DMSA (Dimercapto Succinic Acid) cross the blood brain barrier, binding metals, rerouting them back into the bloodstream where these metals *temporarily* circulate until excreted.
- This temporary circulation is often misinterpreted. Some chelation therapists believe that the redistribution of brain metals into the blood stream causes these circulating toxins to be transported to organ cells where they are stored, causing intoxication of other organ systems. This is a theoretical, but unlikely probability. If this possibility would exist, all chelation would lead to redistribution of chelator-bound metals into other organ cells. This is an unlikely scenario. When a metal is tightly bound to a chelating agent it will not be easily 'dropped'. If that were the case, chelation therapy would be endangering patients rather than detoxifying them; *it would not cause detoxification but metal redistribution and the end effect would not be an improvement in metal-related health problems as we generally see, but a change in metal-related health symptoms.*
- Hair tissue storage depends on the body's protein-metal binding ability, which decreases with age. This actually means that in older, grey-haired persons the bodily system is less likely to supply hair tissue with nutrients and toxins. In fact, hair mineral analysis of grey haired persons generally shows low-borderline metal concentrations. If elevated levels of any toxins are seen, we need to be concerned. The same is true for children. Light-haired children have a lower protein-metal-binding capacity, and again, elevated levels of any toxin are a sign of overexposure, and the exposure may have happened in utero. We often see high mercury hair levels in young children who have not been exposed during their lifetime. Investigation into the mother's history often indicates amalgam treatment during pregnancy, repeated immunization with thiomersal-containing vaccines, or high fish consumption as seen in Asian countries.

Improvement in method development and increased instrument sensitivity have improved the spectroanalysis of all specimen, including hair. Unfortunately, misinterpretation of hair mineral analysis results abound. By now, it is a well-established fact that sodium and potassium levels in hair do not represent a patient's nutritional status, but are generally an indication of an inadequate sample preparation process.

In spite of all the negative information, hair is a useful diagnostic tool for the evaluation of long term metal exposure and there is an accumulation of evidence that hair mineral analysis provides important information about chronic under-nutrition. While sample collection is rather simple, and no time constraint applies to the storage of hair, critical minds have lost interest due to negative publicity. This is unfortunate, because no other test allows us to view long term metal exposure with such ease.

With the hope to improve understanding, I let the following research summaries speak for this test. The essential statements of these excerpts have been trimmed without changing content or meaning. High-

(Continued on next page)

lighted parts are commented by the author, reflecting her opinion.

1. Arsenic and other elements in hair, nails, and skin-scales of arsenic victims in West Bengal, India. Samanta G., Sharma R., Roychowdhury T., Chakraborti D. Department of Civil and Environmental Engineering, University of Houston, N 107 Engineering Bldg 1, Houston, TX 77204-4003, USA. gsamanta@mail.uh.edu. Sci Total Environ. 2004 Jun 29;326(1-3):33-47.

For the first time, biological tissues (hair, nails, and skin-scales) of arsenic victims from an arsenic affected area of West Bengal (WB), India were analyzed for trace elements. Analysis was carried out by inductively coupled plasma-mass spectrometry (ICP-MS) for 10 elements (As, Se, Hg, Zn, Pb, Ni, Cd, Mn, Cu, and Fe). A **microwave digester** was used for digestion of the tissue samples. To validate the method, certified reference materials--human hair (GBW 07601) and bovine muscle (CRM 8414)--were analyzed for all elements. The W test was used to study the normal/log normal distribution for each element in the tissue samples. For hair (n=44) and nails (n=33), all elements show log-normal distribution. For skin-scale samples (n=11), data are not sufficient to provide the information about the trend. Geometric mean, standard error, and range for each element were presented and compared with literature values for other populations. This study reveals the higher levels of toxic elements As, Mn, Pb, and Ni in the tissue samples compared with available values in the literature. **The elevated levels of these toxic metals in the tissues may be due to exposure of these elements through drinking water and food.** This study reveals that in the arsenic-affected areas of WB, the concentrations of other toxic elements in drinking water and foodstuff should be monitored to evaluate the arsenic poisoning.

Comment: for about 10years now, closed vessel microwave digestion (see picture from our laboratory) is used to prepare hair samples for analysis. As a result, the accuracy of the analysis of elements such as arsenic, mercury, and selenium improved dramatically. Before microwave digestion, hair was acid digested in open vessels under heat. This caused the more volatile metals to escape, resulting in false low values of metals such as arsenic, mercury and selenium.

In addition, the old spectroanalysis via MS-ICP was not ideal for testing these halogenic metals. The newest MS-ICP are utilizing cell technique which provides a high analytical accuracy, even for the most difficult elements. In our recent governmental round-robin, we achieved a near 100% accuracy, something that was impossible with previous instruments.

Mechanism of modern MS-ICP

(Continued on next page)

Because good health is VITAL

Keep blood sugar on the level.

Proper blood sugar levels are important for living a healthy, active lifestyle. Vital Nutrients offers a family of supplements designed to help liver function and energy levels, while also maintaining healthy blood sugar levels. At Vital Nutrients, nothing is more important than the quality of our supplements. Using U.S. laboratories, we test every finished product and conduct comprehensive testing on all raw materials before we bring them together. When it comes to offering superior quality and clinically effective supplements, nobody beats Vital Nutrients.* Call (888) 328-9992. See monographs under research at www.vitalnutrients.net.

VITAL NUTRIENTS

THE LEADER IN QUALITY ASSURANCE

Vital Nutrients products are independently tested in the U.S. for authenticity, potency, heavy metals, solvent residue, herbicide and pesticide residue, aflatoxins, stability and bacteria, yeast, and mold counts.

Compliant with FDA GMPs

Natural Products ASSOCIATION™ GMP certified

*This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Modern technique improved metal testing for all human and animal specimen, including hair samples. Hair analysis will not eliminate the need for blood or urine testing, but provides valuable information for the diagnosis of long term exposure.

2. Maternal Fish Consumption, Hair Mercury, and Infant Cognition in a U.S. Cohort

Emily Oken,[1] Robert O. Wright,[2,3] Ken P. Kleinman,[1] David Bellinger,[4,5] Chitra J. Amarasiriwardena,[3] Howard Hu,[3,5] Janet W. Rich-Edwards,[1,6] and Matthew W. Gillman[1,7]

[1]Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, Massachusetts, USA; [2]Department of Pediatrics, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, USA; [3]Channing Laboratory, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA; [4]Department of Neurology, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, USA; [5]Department of Environmental Health, [6]Department of Epidemiology, and [7]Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA

Address correspondence to E. Oken, Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim, 133 Brookline Ave., Boston, MA 02215 USA. Telephone: (617) 509-9835. Fax: (617) 859-8112. E-mail: emily_oken@harvardpilgrim.org

Fish and other seafood may contain organic mercury but also beneficial nutrients such as n-3 polyunsaturated fatty acids. We studied whether maternal fish consumption during pregnancy harms or benefits fetal brain development. We examined associations of maternal fish intake during pregnancy and maternal hair mercury at delivery with infant cognition among 135 mother-infant pairs in Project Viva, a prospective U.S. pregnancy and child cohort study. We assessed infant cognition by the percent novelty preference on visual recognition memory (VRM) testing at 6 months of age. Mothers consumed an average of 1.2 fish servings per week during the second trimester. Mean maternal hair mercury was 0.55 ppm, with 10% of samples > 1.2 ppm. Mean VRM score was 59.8 (range, 10.9-92.5). After adjusting for participant characteristics using linear regression, higher fish intake was associated with higher infant cognition. This association strengthened after adjustment for hair mercury level: For each additional weekly fish serving, offspring VRM score was 4.0 points higher [95% confidence interval (CI) , 1.3 to 6.7]. However, an increase of 1 ppm in mercury was associated with a decrement in VRM score of 7.5 (95% CI, -13.7 to -1.2) points. VRM scores were highest among infants of women who consumed > 2 weekly fish servings but had mercury levels ≤ 1.2 ppm. **Higher fish consumption in pregnancy was associated with better infant cognition, but higher mercury levels were associated with lower cognition. Women should continue to eat fish during pregnancy but choose varieties with lower mercury contamination.**

Comment: Hair mineral analysis reflects long term exposure. It can be used to evaluate the mercury status in women before pregnancy occurs, allowing for nutritional corrections and adequate detoxification measures.

3.Mercury and Selenium Concentrations in Maternal and Neonatal Scalp Hair: Relationship to Amalgam-Based Dental Treatment Received During Pregnancy

Razagui I.B-A.; Haswell S.J. Biological Trace Element Research, Volume 81, Number 1, July 2001 , pp. 1-19 (19)

(Continued on next page)

Mercury and selenium concentrations were determined in scalp hair samples collected postpartum from 82 term pregnancy mothers and their neonates. Maternal mercury and selenium had median concentrations of 0.39$^{\mu}$g/g (range 0.1-2.13$^{\mu}$g/g) and 0.75$^{\mu}$g/g (range 0.1-3.95$^{\mu}$g/g), respectively, and corresponding median neonatal values were 0.24$^{\mu}$g/g (range 0.1-1.93 $^{\mu}$g) and 0.52 g/g (range (0.1-3.0$^{\mu}$g/g). **Amalgam-based restorative dental treatment received during pregnancy by 27 mothers (Group I) was associated with significantly higher mercury concentrations in their neonates ($p < 0.0001$) compared to those born to 55 mothers (Group II) whose most recent history of such dental treatment was dated to periods ranging between 1 and 12 yr prior to pregnancy.** In the Group I mother/neonate pairs, amalgam removal and replacement in 10 cases was associated with significantly higher mercury concentrations compared to 17 cases of new amalgam emplacement. Selenium concentrations showed no significant intergroup differences. The data from this preliminary study suggest that amalgam-based dental treatment during pregnancy is associated with higher prenatal exposure to mercury, particularly in cases of amalgam removal and replacement. **The ability of a peripheral biological tissue, such as hair, to elicit such marked differences in neonatal mercury concentrations provides supporting evidence of high fetal susceptibility to this form of mercury exposure.**

Comment: Transplacental movement of mercury has been documented. This is another study speaking against dental treatment with, or removal of, amalgam during pregnancy. It also supports infant hair testing.

4. Hair Element Concentrations in Females in One Acid and One Alkaline Area in Southern Sweden
Ingegerd Rosborg, Bengt Nihlgård, and Lars Gerhardsson . AMBIO: A Journal of the Human Environment. Vol 32, Issue No7, Nov. 2003 pp. 440–446

Concentrations of 34 trace elements in hair have been determined in 47 females from an acid region in southern Sweden, who were compared with 43 females from an alkaline area. The concentrations of these elements in hair and drinking water were determined by inductively coupled plasma optical emission spectroscopy and inductively coupled plasma mass spectrometry. **The hair concentrations of boron and barium were significantly higher ($p < 0.001$) in hair samples from the acid region, the hair levels of calcium, strontium, molybdenum, iron, and selenium were significantly higher ($p < 0.001$) in the alkaline region.** For some metals, e.g. calcium, lead, molybdenum, and strontium, there were positive correlations between the concentrations in hair and water ($r_s = 0.34–0.57; p \leq 0.001$), indicating the importance of intake from minerals in water. The increased ratio of selenium/mercury concentrations in hair samples obtained in the alkaline district ($p < 0.001$) indicates that these subjects may have better protection against the toxic effects of mercury.

Comment: Metal uptake is influenced by pH, a fact we recognize and pay attention to during chelation treatment.

5. Hair iron content: possible marker to complement monitoring therapy of iron deficiency in patients with chronic inflammatory bowel diseases?

E Bisse, F Renner, S Sussmann, J Scholmerich and H Wieland . Department of Clinical Chemistry, University Hospital, Freiburg im Breisgau, Germany. Clinical Chemistry, Vol 42, 1270-1274, Copyright © 1996 by American Association for Clinical Chemistry
Measurements of the concentration of iron in hair from 10 patients with chronic inflammatory bowel diseases and from 10 healthy controls showed that the iron concentrations were significantly ($P < 0.05$) lower in patients before iron intake than in controls. Three weeks after beginning iron treatment, the hair iron concentrations were found to be significantly correlated ($r = 0.68$; $P < 0.05$) to reticulocyte counts. **Changes in the hair iron concentrations were accompanied by similar changes in the concentrations of the markers most commonly used to diagnose and monitor iron deficiency. The results suggest that quantification of** hair **iron may be useful to complement evaluations of the body iron status.**

Comment: None needed.

6. Serum and hair trace element levels in patients with epilepsy and healthy subjects: does the antiepileptic therapy affect the element concentrations of hair?

A. İlhan[a] , Efkan Uz[b,] Sinem Kali[a,] Ahmet Var[c,] and Omer Akyol[b a] Department of Neurology, İnönü University, Turgut Özal Medical Center, 44069, Malatya, Turkey[b]Department of Biochemistry, İnönü University, Turgut Özal Medical Center, 44069, Malatya, Turkey-[c]Department of Biochemistry, Firat University, Faculty of Medicine, Elazig, Turkey
Eur J Neurol 6:705–709 © 1999 Lippincott Williams & Wilkins

(Continued on next page)

Abstract:

In this study, hair magnesium (Mg), zinc (Zn), copper (Cu), and manganese (Mn) levels, and serum Zn and Mg levels were measured by atomic absorption spectrophotometer in patients with epilepsy (n = 33) and healthy subjects (n = 21), and results obtained were statistically compared. The mean hair Cu, Mg, and Zn levels of epileptic patients were significantly lower than the levels of control subjects. There was no significant difference between epileptic patients and control subjects in respect to the mean Mn levels. Mean serum Mg levels in epileptic patients showed significant difference, but serum Zn levels were similar among both groups. When the effects of anticonvulsant therapy on Cu, Zn, Mn, and Mg in the hair, and Mg and Zn in the serum were analyzed in epileptics, there was no significant difference between the patients with or without therapy. Likewise, the mean trace element levels in epileptics showed no significant difference according to the type of antielpileptic drug and seizure, and gender. **We suggest that the changed element status (Zn, Mg, and Cu) in hair play an indicator role in the diagnosis of epileptic patients.**

Comment: Hair mineral evaluation of epileptic patients should be part of the patient evaluation process.

This article is an edited excerpt of the upcoming book, ***Antidota, Handbook of Chelation Therapy*** *(also called Clinical Metal Toxicology) by E.Blaurock-Busch, available through Micro Trace Minerals, Boulder, Colorado and Hersbruck, Germany.*

For information, contact service@microtrace.de or info@microtraceminerals.com or contact the author at ebb@microtrace.de ◆

Evolution: Continued from page 33

6) Beard J. *The Enzyme Treatment of Cancer*. London: Chatto and Windus; 1911.
7) Hald PT. Comparative researches on the tryptic strength of different trypsin preparations and on their action on the human body. *Lancet.* 1907;170:1371-1375.
8) Wilhelm Conrad Röntgen - biography. http://nobelprize.org/nobel_prizes/physics/laureates/1901/rontgen-bio.html. Accessed June 26, 2008.
9) Wilhelm Conrad Röntgen. http://en.wikipedia.org/wiki/Wilhelm_Rontgen. Accessed June 26, 2008.
10) Marie Curie. http://en.wikipedia.org/wiki/Marie_Curie. Accessed June 26, 2008.
11) Weinstein JW. Dr. Beard's theory in the crucible of test. An experimental study of the trypsin treatment in cancer. *N Y State J Med.* 1908;9:400-402.
12) Morse FL. Treatment of cancer with pancreatic extract. *Wkly Bull St Louis Med Soc.* 1934;28:599-603.
13) Shively FL. *Multiple Proteolytic Enzyme Therapy of Cancer*. Dayton, OH: John-Watson Printing and Bookbinding Co.; 1969.
14) Kelley WD. *One Answer to Cancer*. Los Angeles, CA: Cancer Book House; 1969.
15) Rice CC. Treatment of cancer of the larynx by subcutaneous injection of pancreatic extract (trypsin). *Med Rec.* 1906;70:812-816. ◆

The Integrative Practitioner's Solution for Optimal Patient Health

Nutritional Supplements, Acupuncture and Oriental Medicine, Skin and Personal Care, Vitamins and Minerals, Herbs, Veterinary Products, Medical Supplies, and Homeopathic Remedies

At Emerson Ecologics, we want practitioners like you to concentrate on improving the lives of your patients. It's what you do best. And because your patients look to you for the right healthcare balance, you need a reliable partner to help deliver the right healthcare solution.

For thirty years, Emerson Ecologics has provided confidence and peace of mind to you and your patients. Today, we are proud to be the professional's preferred, one-stop source for the highest quality nutritional products, customer service, and care solutions.

- Over 20,000 products from 250 of the world's top manufacturers
- Nationwide delivery guaranteed to arrive at your door within two business days
- Staff of healthcare practitioners available for peer-to-peer counseling
- Committed to increasing awareness of quality manufacturing practices through the Emerson Quality Program℠ (EQP)

EMERSON ECOLOGICS®

Solutions for Optimal Patient Health

Order online at www.emersonecologics.com or by calling us direct at 800.654.4432. Key Code: EEOI10

Abstracts of Interest

Submitted by: Emerson Ecologics

Niacin Beats Zetia as an Addition to Statin Therapy in a Randomized Trial

by: Steve Austin, N.D.

Reference: Taylor AJ, Villines TC, Stanek EJ, et al. Extended-release niacin or ezetimibe and carotid intima-media thickness. *N Engl J Med* 2009; Nov 15 E-publication ahead of print.

Design: Randomized unblinded intervention trial

Participants: 317 patients with a history of coronary artery disease (CAD) or at high risk for CAD who had been taking a statin drug (for 6±5 years) that had resulted in low-density lipoprotein cholesterol (LDL) levels <100 mg/dL and who had high-density lipoprotein cholesterol (HDL) levels <50 mg/dL for men or <55 mg/dL for women entered the trial, of whom 208 completed the trial.

Study Medication and Dosage: All patients continued to take statin drugs. Patients were randomized to add either 10 gm/day Zetia (ezetimibe), a drug known to further lower LDL levels, or time-release niacin (TRN) with a target dose of 2,000 mg/day. Of those assigned to TRN, 75% achieved the 2,000 mg/day dosage with the rest taking doses ranging from 500 mg/day to 1,500 mg/day. (While not specifically stated, it is likely that those taking lower doses did so as the result of intolerance to TRN at the full target dose.) The intervention lasted 14 months.

Primary Outcome Measures: Change in carotid intima-media thickness after 14 months, changes in lipid levels, and major cardiovascular events (e.g., myocardial infarction, revascularization, and death from CAD)

Key Findings: Mean HDL levels rose 7.5 mg/dL in the TRN group (P=0.001), while falling 2.8 mg/dL in the ezetimibe group. Mean LDL levels in the ezetimibe group declined by 17.6 mg/dL (P=0.001), compared with a 10.0 mg/dL decline in the TRN group (P=0.001). Significant reductions in triglyceride levels were also reported in both groups. Carotid intima-media thickness declined significantly in the TRN group (P=0.003) but not in the ezetimibe group.

The incidence of major cardiovascular events was 1% in the TRN group (2/160) versus 5% in the ezetimibe group (9/165) (P=0.04 for the difference). Of those events, 7 patients given ezetimibe died during the course of the trial compared with only one death in the TRN group. Three patients withdrew from the ezetimibe group due to drug side effects compared with 17 patients receiving TRN (NS).

Practice Implications: This is the first clinical trial to compare the effects of statins plus niacin (as TRN) with the effects of statins plus ezetimibe. The outcome was strikingly clear, with TRN coming out the winner.

Both arms of the trial continued to take statin drugs as they had been doing before the trial's onset. Statin therapy alone has been shown to lower LDL and decrease the risk of coronary events. Historically, LDL levels are viewed as integral to the disease process and not simply as markers. Thus, most researchers and practitioners have believed that virtually anything that lowers LDL will lower the risk of CAD. Indeed the vast majority of agents or lifestyle changes that have been studied fit this pattern. These new findings therefore contradict our previously-held beliefs; the researchers conclude, " . . . our findings challenge the usefulness of LDL cholesterol reduction as a guaranteed surrogate of clinical efficacy . . . "

The conventional drug studied, ezetimibe, had previously been proven to add to the LDL-lowering effects of statins, but had not been proven to achieve primary or secondary prevention of cardiovascular disease in the process. The new findings appear to suggest that ezetimibe-induced reductions in LDL buy no clinical benefit and may actually increase atherosclerosis (as indicated by the increase in carotid intima-media thickness) while quintupling the risk of cardiovascular events, at least when compared with the findings in the TRN group).

The link between the extent of LDL-lowering and worse clinical outcomes in the ezetimibe group was uncovered in *post hoc* analysis. As a result, we should view the ezetimibe data with caution. *Post hoc* analyses often provide misinformation. If one hunts long enough, eventually by chance, statistical significance will attach to something. By chance alone, one observation in 20 should achieve statistical significance. Thus, the LDL-lowering effect of ezetimibe may not have been responsible for the apparent disease progression reported by these researchers in subjects for whom the decrease in LDL was most profound. Nonetheless, these data provide no reason to consider ezetimibe a therapeutic addition to treatment with statin drugs.

(Continued on next page)

Unlike ezetimibe, niacin (either in crystalline or time-release forms) is known to raise HDL levels while also reducing or stabilizing atherosclerosis and decreasing the risk of coronary events.

The amide form of vitamin B3 (niacinamide) is not used to treat patients with CAD because despite its excellent safety profile, it does not lower lipid levels. Crystalline niacin, which does lower LDL while raising HDL levels, is often avoided by cardiologists because of the high incidence of side effects both acute (e.g., gastrointestinal distress, headaches, and flushing) and chronic (e.g., elevations in serum uric acid, glucose, and liver enzymes). TRN avoids most (though not all) of the acute problems associated with standard (crystalline) niacin, but has been linked with a higher incidence of hepatotoxicity.

While the difference in side effects between ezetimibe and TRN did not achieve statistical significance, it probably was the result of real problems caused by niacin and perhaps specifically by the time-release form of it. Patients assigned to large (500–2,000 mg/d) doses of TRN require monitoring for ALT and AST levels as well as fasting glucose and uric acid levels.

These findings suggest that when possible (dependent upon the patient's tolerance to TRN) TRN should now be added to statin therapy.

Two Randomized Folic Acid/Cancer Trial Reports: More Data but Confusion Still Reigns

by: Steve Austin, N.D.

References:

A) Wu K, Platz EA, Willett WC, et al. A randomized trial on folic acid supplementation and risk of recurrent colorectal adenoma. *Am J Clin Nutr* 2009; E-published ahead of print October 28th.
B) Ebbing M, Bonna KH, Nygard O, et al. Cancer incidence and mortality after treatment with folic acid and vitamin B_{12}. *JAMA* 2009;302;2119–26.

Designs:

A) Data taken from two randomized double blind intervention trials
B) Data taken from two randomized double blind intervention trials

Participants:

A) 672 adults from the Nurses' Health Study and the Health Professionals Follow-up Study with a history of adenomatous polyp formation
B) 6,837 adults from the Norwegian Vitamin Trial and the Western Norway B Vitamin Intervention Trial with a history of ischemic heart disease

Study Medication and Dosage:

A) 1 mg/day folic acid (FA) or placebo for 3–6.5 years
B) 800 mcg/day FA and 400 mcg/day vitamin B_{12} with or without vitamin B_6 or placebo for a median of 39 months, with an additional 38 months of post-treatment follow-up

Primary Outcome Measures:

A) Recurrences of adenomatous polyps
B) CA diagnosis, CA mortality, and all-cause mortality

Key Findings:

A) The overall risk of adenoma recurrence was nonsignificantly lower in the group receiving FA supplementation (relative risk: 0.82; P=0.22). When subjects were divided by baseline plasma folate levels, those who were relatively folate-deficient (defined as a plasma folate ≤7.5 ng/mL) experienced a statistically significant 39% decrease in the risk of suffering an adenoma recurrence (P=0.01). In contrast, those with better folate status experienced a 28% increased risk of adenoma recurrence, though that trend did not achieve statistical significance (P=0.27).
B) As expected, supplementation with vitamin B_6 had no effect on the primary endpoints. Although FA and B_{12} were administered together, the researchers have no reason to think the B_{12} component would affect CA risks one way or the other. As a result, the potential effect of vitamin B_{12} was mostly ignored by the authors and by most of those who have subsequently commented on these new findings.

   Those assigned to groups receiving FA supplementation experienced a 21% increased risk of being diagnosed with CA (P=0.02), a 38% increased risk of dying from CA (P=0.01) and an 18% increased risk of dying from any cause (P=0.01). Each of these risks increased slightly when the analysis was limited to those who took FA for more than six months. Although most of the higher risk was due to an increase in lung CA (most of it in smokers past and present), the actual difference between the number of lung CA diagnoses and lung CA deaths in the FA/B_{12} groups versus the placebo group did not achieve statistical significance. When the cases of lung CA were removed from the data, the overall increased risk for a CA diagnosis fell to 16%, which was no longer statistically significant.

Practice Implications: The *JAMA* trial combines data from two Norwegian trials, each of which had previously discovered nonsignificant increases in CA risk with FA supplementation. The pooling of data from these two trials in an attempt to achieve the power to uncover a significant relationship is related to the format of meta-analyses. There's nothing inherently wrong with this approach. Indeed, the pooling of data in the other new report, also from two different trials (Health Profes-

(Continued on next page)

Affordable Lab Testing

Professional Co-op Gets You the Results You Need - With Integrity!

Here's What Professional Co-op Will Do For You

- **Convenient ordering of tests**
- **Timely results with e-mail reports**
- **Patient access to draw locations in your area**
- **Lower lab test pricing then you'll get on your own**
- **A deeper knowledge of your patients that allows you to provide more comprehensive treatment**

Then You Can Build Relationships with Chemistry

PCS

PROFESSIONAL CO-OP™

P: 866-999-4041

F: 866-999-9175

www.ProfessionalCo-op.com

AMERICA'S LAB GROUP™

Testing Done Through LabCorp®

Service With Integrity Since 2001

sionals Follow-up and Nurses' Health Study [HPF/NHS]) presents a somewhat-related attempt to gain sufficient power to uncover whether FA supplementation is having a true effect (positive or negative) on the risk of precancerous polyps. However, the *JAMA* researchers had already noticed nonsignificant increases in CA risk in both previous Norwegian trials before they put the data together—increased risks that had not initially been primary endpoints in either trial. One could argue that this creates a set up to find the outcomes reported before the investigation even began. Nonetheless, we need to ask, why did both Norwegian trials find significant increases in CA risk as a function of FA supplementation? While this question remains unsettling, we must keep in mind that previous FA intervention trials, also in which CA diagnoses and deaths were not primary endpoints but *were* being followed, have not reported increased CA incidence or CA mortality (*N Engl J Med* 2006; 354:1567–77; *JAMA* 2008;300:2012–21).

At first glance, it appears the findings of these two reports are in near-direct conflict. The *JAMA* research tells us that FA supplementation increases the risk of CA, while the HPF/NHS data suggest that FA supplementation does not increase the risk of precancerous changes and may actually reduce them in deficient populations.

I suspect editors at *JAMA* might defend the findings of the trial they published in part by turning to the ten-fold greater size of the *JAMA* trial sampling. While this factor should not be ignored, we need to keep in mind that the smaller the trial, the more difficult it is to obtain statistical significance. Both trials produced statistically significant findings. Besides, no matter how large the trial sampling might have been, while *JAMA* has published previous reports from the PHF/NHS authors, I believe it's unlikely they would have published this particular report, if only because natural medicine came out the winner. Medical politics aside, for the most part the outcomes of these trials do not directly conflict.

We might guess that a significant increase in CA incidence (let alone CA deaths) could hardly be due to *anything*—even cigarettes—in just the 6 ½ years of follow-up in the Norwegian trials. CA generally takes decades before it becomes clinically apparent. However, if latent undiagnosed CA had already existed in the FA-supplemented subjects who later were diagnosed with CA in bigger numbers than those in the placebo group, it is plausible that FA promoted those CA cells, revealing the disease prematurely. This would fit with current concerns about supplementing FA to middle-aged and older adults, many of whom have or will have undiagnosed CA.

The emerging view in the research community is that when CA is not present, the effect of supplemental folates or even synthetic FA may primarily be to help cells replicate normally, thus potentially *protecting* against CA. This view has some scientific support, but it remains a theory skating on ice yet too thin to depend upon. By studying only middle-aged and older adults (groups more likely to contain subjects with undiagnosed CA), neither of the new reports speaks to this issue (i.e., of potential CA prevention in children and young adults supplemented with FA).

The *JAMA* trial found an increased risk of lung CA (mostly in smokers), but the HPF/NHS report does not address that question. Even here, the *JAMA* researchers would have to admit that their concern should be considered tentative. It has not been reported elsewhere, nor did the increased risk of lung CA attain statistical significance in the new report. Thus, the appearance of that increased risk might simply have been due to chance.

And what of the concerns regarding adenoma recurrences and colorectal CA? Adenomas are *pre*cancerous changes. Thus, they lie in a gray area between the normal cells that might possibly be protected by FA supplementation on one hand, and CA cells that might be promoted by FA supplementation on the other. The findings of the HPF/NHS report suggest that those effects may be complex: protection in the folate deficient, countered by a nonsignificant trend toward an *increased* risk in those that were folate *suf*ficient. While the *JAMA* report does not deal with adenoma risk, the fine print shows that those given FA supplementation had precisely the same risk of colorectal CA as those given placebo (relative risk=1.00). The *JAMA* report did look at outcomes in subjects with particularly low folate status (those with plasma levels <3.9 ng/mL versus all others). But unlike the HPF/NHS report, that (higher versus lower plasma folate) analysis produced the same outcomes (data not supplied, P value "≥0.06"). In this respect alone, the findings of the two new reports are at odds, albeit with very different cut off points for folate-sufficiency versus deficiency.

A prospective analysis from the same HPF/NHS trials previously found that colorectal CA mortality was significantly *lower* in those with the highest plasma folate levels at baseline (*J Clin Oncol* 2008;26:3222–8). Two small trials have also shown a reduction in adenoma formation with FA supplementation. In one case, the reduced risk was statistically significant (*World J Gastroenterol* 2008;14:4492–8). In the other case, despite a greater than 50% reduction in risk, the effect was not statistically significant (*Dis Colon Rectum* 1994; 37:1340–1). In yet another attempted adenoma prevention trial, FA supplementation led to statistically significant increased risks of having an advanced lesion, multiple lesions, or diagnosis of non-colorectal cancers

(Continued on next page)

(*JAMA* 2007;297:2351–9). Thus, no clear picture has yet to emerge, with some data suggesting prevention, others showing no effect, and still other data suggesting an increase in risk.

How might clinicians best deal with the complex and unresolved relationship between CA and FA? I believe the broad picture remains much as it was before publication of these new reports. There is still hope but inadequate proof that supplementation of folates or even synthetic FA might reduce the risks of certain cancers if given to those with a very low chance of currently having undiagnosed CA—mainly the young. As for older adults, they are now less folate deficient than in the past as a result of the 1998 FDA-mandated fortification program. So far, however, Americans appear to remain deficient enough for further supplementation to buy some protection, at least according to the PHF/NHS data dealing with precancerous changes in the colon and rectum. In regard to other cancers, in middle-aged and older adults (particularly in those who are not folate deficient), there remains reason to fear that supplementation with synthetic FA (if not necessarily supplementation with natural folates, about which we know far less), may increase CA risks. It may be important to point out that we know little of the effects of unmetabolized FA--an issue that occurs as a result of supplementation with synthetic FA and not with intake of natural folates from food or from supplements. In any case, the potential for an increased risk of FA-induced CA is what the *JAMA* report appears to have uncovered. That conclusion is not directly contradicted by the findings of the HPF/NHS report.

The bottom line remains the same: until we know more, we need to avoid gratuitous use of synthetic FA. Keeping in mind that food fortification is probably less than sufficient for optimal neural tube defect prevention, FA supplementation in young women who could become pregnant should not be viewed as gratuitous.

I thank Dr. Richard Passwater for being the first to alert me to these reports even before they appeared, and sending me responses to the *JAMA* report by the Natural Products Association and the Council for Responsible Nutrition. I thank Dr. Alan Gaby for obtaining the text of the AJCN report. Thank you also goes out to Dr. Gaby and to Douglas Millar of Solgar Vitamins who shared with me the *JAMA* report with accompanying editorial immediately upon publication.

L-Tryptophan is Back
by: Alan R. Gaby, M.D.

United States regulatory agencies have recently reversed a 20-year ban on the over-the-counter sale of the essential amino acid L-tryptophan, and will once again allow it to be sold as a dietary supplement. The United States joins other countries such as the United Kingdom, Japan, and the Netherlands in letting the public have access to this valuable nutrient, which is often an effective treatment for depression, insomnia, and premenstrual dysphoric disorder.

In the 1980s, L-tryptophan was a very popular dietary supplement. However, over-the-counter sale of this amino acid was banned in 1989, after a manufacturing error by one of the world's five L-tryptophan producers introduced a contaminant into the product that resulted in more than 1,500 of cases of eosinophilia-myalgia syndrome, including 27 deaths. The manufacturing error was identified and corrected relatively quickly, and there have been no reports of eosinophilia-myalgia syndrome resulting from the use of uncontaminated L-tryptophan.

Now that L-tryptophan is back, it is important to be aware of ways to maximize its safety and efficacy. First, be aware of drug interactions. Because L-tryptophan increases serotonin levels, co-administration of L-tryptophan and antidepressants that increase serotonergic activity (such as selective serotonin-reuptake inhibitors [SSRIs], amitriptyline, or monoamine oxidase inhibitors) may increase both the efficacy and the toxicity of the drugs. If a patient is taking one of these medications, L-tryptophan should either be avoided completely or used with caution and in low doses (perhaps 500-1,000 mg/day), while monitoring for signs of serotonin excess (serotonin syndrome). There is one exception to this caveat: when initiating SSRI treatment, administration of up to 2 g per day of L-tryptophan for up to four weeks may accelerate the onset of the drug's antidepressant effect and protect against the development of insomnia, a frequent side effect of SSRIs in the early stages of treatment. However, patients should be monitored closely during this time, because serotonin excess can be life-threatening. Co-administration of L-tryptophan and a triptan (e.g., sumatriptan, zolmitriptan, eletriptan) may also lead to serotonin excess, and should be avoided. In addition, L-tryptophan and 5-hydroxytryptophan (5-HTP) each increase serotonin levels, and should not be taken together.

Second, the timing of L-tryptophan administration in relation to meals may influence its effectiveness. L-Tryptophan competes with other amino acids for intestinal absorption and for uptake into the brain. Taking L-tryptophan with a high-protein meal decreases its effectiveness, whereas taking it on an empty stomach increases its efficacy. L-tryptophan is most effective when taken on an empty stomach along with some carbohydrate (such as a small glass of orange juice or a

(Continued on next page)

piece of fruit). Eating carbohydrates causes the body to release insulin, which promotes the uptake of L-tryptophan into the brain.

The dosage of L-tryptophan used in clinical trials has usually ranged from 1 g per day to 6 g per day. In the treatment of depression, there may be a "therapeutic window," in that L-tryptophan may lose its efficacy if the dosage exceeds 6 g per day. In treating depression, L-tryptophan should be given in at least two divided doses per day, in order to minimize fluctuations in plasma tryptophan concentrations. For the treatment of insomnia, many people take 500 to 2,000 mg 30 minutes before bedtime. L-tryptophan appears to be most useful for people with mild insomnia, for healthy individuals who have longer-than-average sleep onset latency (the amount of time required to fall asleep), and for people who have clear awakenings three to six times during the night. For the treatment of premenstrual dysphoric disorder, a double-blind trial found that a dosage of 2 g three times per day during the second half of the menstrual cycle was beneficial. In my experience, as little as 500 to 1,000 mg taken at night during the last half of the menstrual cycle is sufficient to relieve dysphoric symptoms in some cases.

While 5-HTP appears to be an effective treatment for depression and insomnia, it may preferable to use L-tryptophan. Unlike 5-HTP, L-tryptophan is a building block for protein synthesis and is also metabolized to important compounds such as niacin and picolinic acid. Consequently, if a person is deficient in tryptophan, then supplementing with L-tryptophan would provide a broader spectrum of benefits than would treatment with 5-HTP.

References:

1) Levitan RD, Shen JH, Jindal R, Driver HS, Kennedy SH, Shapiro CM. Preliminary randomized double-blind placebo-controlled trial of tryptophan combined with fluoxetine to treat major depressive disorder: antidepressant and hypnotic effects. *J Psychiatry Neurosci* 2000;25:337-346.
2) Chouinard G, Young SN, Annable L, Sourkes TL. Tryptophan-nicotinamide combination in depression. *Lancet* 1977;1:249.
3) Chouinard G, Young SN, Annable L, Sourkes TL. Tryptophan-nicotinamide, imipramine and their combination in depression. *Acta Psychiat Scand* 1979;59:395-414.
4) Lindsley JG, Hartmann EL, Mitchell W. Selectivity in response to L-tryptophan among insomniac subjects: a preliminary report. *Sleep* 1983;6:247-256.
5) Steinberg S, Annable L, Young SN, Liyanage N. A placebo-controlled clinical trial of L-tryptophan in premenstrual dysphoria. *Biol Psychiatry* 1999;45:313-320.

Breast Cancer and Beauty Products: the Paraben Concern

by: Marianne Marchese, ND

Breast cancer is considered to be a multi-factorial process. Genetic, lifestyle, immune and environmental factors play a role. Part of the process leading to cancer is acquiring damage to genes that regulate normal cell growth. This damage or mutation can be caused in part by exposure to chemicals in the environment and in part by other factors. There are known risk factors for breast cancer that are generally agreed upon throughout the medical and scientific community. They include early menarche, late menopause, having a first child later in life or not having children at all, a history of a first degree relative with breast cancer, a carrier of the breast cancer gene, past exposure to ionizing radiation, obesity, excess alcohol and use of a combination of estrogen and progestin for four years or more in postmenopausal women.[1] But these factors only account for 10%-40% of breast cancers.

What accounts for the rest?

We may never know the full range of factors that lead to breast cancer but environmental factors must be considered. Chemicals in the environment can act like estrogen in the body. Breast tissue is extremely sensitive to estrogen stimulation which causes breast cell division.[2] Hormones such as estrogen, progesterone, prolactin and growth hormone affect growth and functioning of breast cells.[2] More than half of breast tumors depend on estrogen.[2] Environmental chemicals can act like hormones and other growth factors.[2] Environmental chemicals can affect the balance that controls breast cell division and growth.[3] One such chemical is parabens.

Parabens are a group of synthetic chemicals that we are exposed to everyday. They are in many cosmetics, shampoos, lotions, soaps and many other grooming products. They are what keep bacteria from growing in the product. Common parabens used in cosmetic and grooming products are methylparaben, ethylparaben, butylparaben, and propylparaben. Typically more than one paraben is used in a product and they are often used in combination with other chemical preservatives. Parabens were first approved for use in cosmetic products in 1984 when the Cosmetic Ingredient Review (CIR) determined they were safe. The CIR again looked at the safety of parbens in cosmetics in 2003 and 2005 and again determined that parabens are safe as used in cosmetics.

So what's all the fuss about parabens?

A 2004 study looked at 20 women with breast cancer and measured the tumor tissue for 6 different parabens.

(Continued on next page)

RETAIN YOUR PRIMARY CARE STATUS

- Prove Effectiveness of Natural Health Care Through Diagnosis
- Understand Blood Chemistries for Prevention & Wellness
- Learn How & When to Use Nutritional Supplementation

BECOME A

DIPLOMATE INTERNIST

PROGRAMS IN PROGRESS IN

LOS ANGELES, CA, DALLAS, TX & PORTLAND, OR

(SEE PAGE 2 FOR DATES)

Co-Sponsored with NUHS & ACA Council on Diagnosis & Internal Disorders

New Programs in Kansas City, MO & Hartford, CT

Register online at www.drkessinger.com/prohealth_seminars.html

FOR MORE INFORMATION CONTACT
VIRGINIA 573-341-8448
virginia@drkessinger.com
Fax: 573-341-8494

300 Hour
Chiropractic Family Practice *Diplomate Program*

☐ Dallas, TX ☐ Kansas City, KS ☐ Hartford, CT ☐ Los Angeles, CA ☐ Portland, OR

Name: _____

Address: _____ **City:** _____

State: _____ **Zip:** _____ **Phone:** _____

E-Mail: _____ **License #** _____ **State** _____

$300 per session — 10 days prior to seminar
$325 — less than 10 days.. or at the door

Chiropractic Students — $150 per session
SACA members — $125 per session

Credit Card # _____

Expiration _____ Type of Card _____

Checks payable to: ProHealth Seminars
720 Oak Knoll Rolla, Mo 65401

www.drkessinger.com

Phone 573-341-8448 Fax 573-341-8494

100% of samples had at least one paraben with methylparaben being the highest.[4] The study discussed the information in the context of the weak estrogen-like properties of parabens and the influence of estrogen on breast cancer. The study clearly had some flaws. First, it was a small sample of women all of which had breast cancer, and it did not compare this group to women without breast cancer. Also, it is important to note that the study did not show that parbens caused breast cancer but merely showed a correlation.

The question of parabens' estrogenicity has also been raised. One study in 2002 showed that parabens can act like estrogen in the body at the strength to cause breast cancer cells to grow and proliferate.[5] While a 1998 study found that the most potent paraben, butylparaben, had an estrogenic activity 10,000 to 100,000 fold less activity than endogenous estradiol.[7] Typically parabens used in cosmetics are at levels ranging from 0.01% to 0.03%. A 2005 review of the estrogenic activity of parabens found, based on maximum daily exposure estimates on the levels in cosmetics that parabens could not increase the risk associated with exposure to estrogenic chemicals.[7]

The Darbre study did bring up an interesting point of concern. The study showed that 5 of the 6 parabens widely used in cosmetics can be detected intact in human tissue. Often studies look at urine or blood levels of chemicals which show changed or metabolized effects of the chemical. This study showed unchanged, intact parabens stored in human tissue. A report published in the Journal of the American College of Toxicology in 1984 estimated that parabens are used in more than 13,000 consumer products.[8] Parabens are easily absorbed through the skin where most cosmetics are applied.[9] We know from body burden studies that the average American has at least one form of parabens stored in their body. In 2008, Dateline NBC ran a story about the body burden of chemicals. They measured 76 chemicals in 2 families. Each family consisted of a mother, father and two kids. All members of both families had low to moderate levels of parabens. This covers men, women, adults and children.[10] This finding is not surprising considering parabens are in 13,000 grooming and hygiene products.[11]

What should women do?

Is there a concern for women applying a weak estrogen to the skin every day through cosmetics, lotions, shampoos, sunscreens lotions, and soaps? Caution may be warranted based on the studies showing the weak estrogenic activity of parabens and their ability to penetrate the skin and be found intact in human breast cancer tissue. However, further research needs to be done comparing a large group of women with breast cancer to a large group of healthy women without breast cancer as well as more estrogenicity studies in the lab. In the meantime, look for products that are using phenoxyethanol, capryly glycol, potassium sorbate, ascorbic acid and grapefruit seed extract as alternative preservatives. However, each of these too come with controversy in regards to issues including whether or not they have sufficient antimicrobial effects, labeling as natural, and the nature of the chemical make-up.

Happi and *GCI* trade publications publish annual preservative issues that serve as a resource to manufacturers. Whole Foods Market has developed their "Premium Body Care" list of products that meet the standards they have set based on the most current safety and efficacy data, research and resources available. Premium Body Care booklets are available in Whole Foods stores.

References:

1) *State of the Evidence 2008: The Connection Between Breast Cancer and the Environment*, edited by Janet Gray, Ph.D., and published by the Breast Cancer Fund. www.breastcancerfund.org
2) DeBruin LS, Josephy PD. Perspectives on the chemical etiology of Breast Cancer. *Environ Health Perspect*. 2002;110:119-128.
3) Aschengrau et al, Occupational exposure to estrogenic chemicals and the occurrence of breast cancer: an exploratory analysis *AM J Ind Med.* 1998 ;34(1) :6-14
4) Darbre PD, et al. Concentrations of parabens in human breast tumors. *J Appl Toxicol*. 2004;24(1):5-13.
5) Byford JR, et al. Oestrogenic activity of parabens in MCF7 human breast cancer cells. *J Steroid Biochem*. 2002;80:49-60.
6) Routledge EJ, et al, Some alkyl hydroxy .benzoate preservatives (parabens) are estrogenic. *Toxicol Appl Pharmacol* 1998 Nov;153(1):12-9.
7) Golden R, Gandy J, Vollmer G. A review of the endocrine activity of parabens and implications for potential risks to human health. Crit Rev Toxicol. 2005;35(5):435-58.
8) Elder RRL Final report on the safety assessment of methylparaben, ethylparaben, propylparaben and butylparaben. *Journal of the American College of Toxicology* 1984;3:147-209.
9) Pedersen S, et al. In vitro skin permeation and retention of parabens from cosmetic formulations. *Int J Cosmet Sci.* 2007;29(5):361-367.
10) http://www.msnbc.msn.com/id/24230246/?pg=1#dtl_toxic
11) Elder RRL.Final report on the safety assessment of methylparaben, ethylparaben, propylparaben, and butylparaben. *Journal of the American College of Toxicology*. 1984;3:147-209.

Dr. Marchese, naturopathic physician, received her Doctorate of Naturopathic Medicine from the National College of Naturopathic Medicine in 2002. She currently is adjunct faculty at the Southwest College of Naturopathic Medicine and maintains a private practice in Phoenix AZ. Dr. Marchese is Vice President of the Arizona Naturopathic Medical Association and on the board of directors of the Council of Naturopathic Medical Education. She writes a bi-monthly column on environmental medicine in *The Townsend Letter* and lectures nationally on women's health and environmental medicine. www.drmarchese.com.◆

DABCIs and Where They Are

ALABAMA
Dr. Reginald Hug*
Birmingham, AL

ALASKA
Dr. David Mulholland
Anchorage, AK

Dr. Stan Throckmorton
Anchorage, AK

ARIZONA
Dr. R. Michael Cessna*
Tucson, AZ

Dr. Laura Frey
Tucson, AZ

Dr. Timothy Gerhart
Glendale, AZ

Dr. Kellie Gray
Glendale, AZ

Dr. Michael Stone
Tucson, AZ

ARKANSAS
Dr. Lance Clouse
Van Buren, AR

Dr. Douglas Smiley*
Siloam Springs, AR

CALIFORNIA
Dr. Jan Dooley
Arcata, CA

Dr. Jeffrey Greene
Los Angeles, CA

Dr. Jill Jordan
Carlsbad, CA

Dr. Andrew Lucas
Riverside, CA

Dr. Kathleen Power
Pasadena, CA

Dr. Rowen Richardson
Glendora, CA

Dr. Scott Soluk
Los Angeles, CA

Dr. Sylvie Wellhausen
Loma Linda, CA

Dr. Kelly Worth
Orange, CA

COLORADO
Dr. John Baer
Englewood, CO

Dr. Debra Carpenter
Pueblo West, CO

Dr. Terry Collinson
Colorado Springs, CO

Dr. Rita Cummings
Denver, CO

Dr. Paula Dechert
Denver, CO

Dr. Lewis Holm
Littleton, CO

Dr. William Kleber
Berthoud, CO

Dr. Reiner Kremer
Franktown, CO

Dr. Steven Lokken
Colorado Springs, CO

Dr. Duane Lowe
Colorado Springs, CO

Dr. David Paradiso
Colorado Springs, CO

Dr. Philip Pollock
Sterling, CO

Dr. Deborah Riekman
Colorado Springs, CO

Dr. Thomas Turner
Boulder, CO

Dr. Michael Vanaria
Boulder, CO

Dr. Brian Wilson
Englewood, CO

CONNECTICUT
Dr. Paul DiDomizio
Wolcott, CT

FLORIDA
Dr. John Findlay
W. Palm Beach, FL

Dr. David Frerking
Tavares, FL

Dr. Marguerite Gerger
Clearwater, FL

Dr. Janice Piro
Palm Harbor, FL

Dr. Susan Player
Clearwater, FL

Dr. John Podlaski
Ocala, FL

GEORGIA
Dr. Larry Haberski
Stone Mountain, GA

IDAHO
Dr. Uma Mulnick
McCall, ID

ILLINOIS
Dr. Delilah Anderson
Sandwich, IL

Dr. Jeffrey Bergin
Lindenhurst, IL

Dr. Stephen Boudro
Elmhurst, IL

Dr. Sharon DeFrain
Peotone, IL

Dr. Mete Durum
Arlington Heights, IL

Dr. Raymond Ferre
Decatur, IL

Dr. Mark Fredrick
Gurnee, IL

Dr. David Hepler
Lincoln, IL

Dr. William Hogan
Lombard, IL

Dr. Lester Holze, Jr.
Elgin, IL

Dr. Cindy Howard
Orland Park, IL

Dr. Frederick Hult
McHenry, IL

Dr. Grant Iannelli
Lombard, IL

Dr. Harry Jensen
Sterling, IL

Dr. Thomas Jensen
Sterling, IL

Dr. Theodore Johnson
Chicago, IL

Dr. James McGinn, Jr.
Crystal Lake, IL

Dr. Anthony Pantanella
Hoffman Estates, IL

Dr. Michael Poierier
Lombard, IL

Dr. Robert Pyne, Jr.
Palos Hills, IL

Dr. William Shelton
Lombard, IL

Dr. Douglas Stam
Bourbonnais, IL

Dr. Frank Strehl
Wheaton, IL

Dr. Melanie Tiahrt*
Alton, IL

Dr. Steven Zaeske
Orland Park, IL

Dr. Alex Zevan,III
Bloomingdale, IL

INDIANA
Dr. John Bernzott
Connersville, IN

Dr. Thomas Jansen
Kendalville, IN

Dr. William Lyden
Mishawaka, IN

Dr. Brian McGuckin
Valparaiso, IN

Dr. Robert Prather
Indianapolis, IN

IOWA
Dr. Gary Bowden
McGregor, IA

Dr. Darlene Ehlers
Tipton, IA

Dr. Robert Friedrichs
Mason City, IA

Dr. Tracy A. Stomgren
Glenwood, IA

Dr. Lynn Theesfield
Ames, IA

Dr. Zach Watkins
Johnston, IA

Dr. Anita Wubenna
Parkview, IA

KANSAS
Dr. Mark Albers
Wichita, KS

Dr. Lynn Betz
Auburn, KS

Dr. Ben Bowers
Wichita, KS

Dr. Richard Brown
Olathe, KS

Dr. Susan Buchanan-Cheney
Phillipsburg, KS

Dr. Ralph Cardin
Overland Park, KS

Dr. H.M. Chalker
Meade, KS

Dr. Dustin Cheney
Phillipsburg, KS

Dr. Rod Clements
Eldorado, KS

Dr. Paul Hughes
Edgerton, KS

Dr. Tobi Jeurink
Gardner, KS

Dr. Christena Nicholson
Overland Park, KS

Dr. Janie Pirner
Wichita, KS

Dr. Ron Young
Salina, KS

LOUISIANA
Dr. Robert W. Smith
Baton Rouge, LA

Dr. Stephanie Clay
Baton Rouge, LA

MARYLAND
Dr. Wayne Sodano
Bel Air, MD

MICHIGAN
Dr. Daniel M. McGregor
Prudenville, MI

MINNESOTA
Dr. Jeffrey Anderson
Edina, MN

Dr. Robert Bergan
Minneapolis, MN

Dr. Timothy Bertsch
Champlin, MN

Dr. Linda Bowers
Bloomington, MN

Dr. Russell DesMarais
St. Paul, MN

Dr. Joel Eichers
Chanhassen, MN

Dr. John Gerber
Blaine, MN

Dr. Timothy Gerhart
Red Wing, MN

Dr. Jedidiah Krauss
St. Louis Park, MN

Dr. Mac Beth Lindstrom
Slayton, MN

Dr. Todd McGillick
Gaylord, MN

(Continued on next page)

* Retired DABCI Practitioner

DABCIs and Where They Are

Dr. Thomas Miller
Coon Rapids, MN

Dr. Joseph Muldoon
Slayton, MN

Dr. Brenwyn Peddycoat
White Bear Lake, MN

Dr. Gregory Peterson
Winona, MN

Dr. Dane Roubos
Bloomington, MN

Dr. Sandra Spore
Stillwater, MN

Dr. Leslie Stewart
St. Paul, MN

Dr. Charles Strauman
St. Louis Park, MN

Dr. Terese Tomanek
Duluth, MN

Dr. Timothy Whelan
New Hope, MN

Dr. Jon Williams
Bloomington, MN

MISSOURI
Dr. David Clark
Oak Grove, MO

Dr. Charles Eckert
Raymore, MO

Dr. Jack Kessinger
Rolla, MO

Dr. Jay Kessinger
Rolla, MO

Dr. Kelley Kirchner
Kahoka, MO

Dr. Mable Leckrone
Liberty, MO

Dr. Duane Lowe
Maplewood, MO

Dr. Terry Nelson
Independence, MO

Dr. R Vincent Satterwhite
Kansas City, MO

Dr. Jeremy Thornton
Stockton, MO

Dr. Jeffrey S. Ware
Lake St. Louis, MO

Dr. Robert Wiehe
West Plains, MO

NEVADA
Dr. Howard Balduc
Las Vegas, NV

Dr. Craig Roles
Henderson, NV

NEW JERSEY
Dr. Jon Mastrobattista
Bernardville, NJ

Dr. Perry Ricci
Egg Harbor City, NJ

NEW MEXICO
Dr. John Dalton
Roswell, NM

Dr. John H. Gelhot
Albuquerque, NM

Dr. Shereen Jegtvig
Albuquerque, NM

NEW YORK
Dr. Ronald Safko
New York City, NY

Dr. John Zilliox
Amherst, NY

NORTH CAROLINA
Dr. William R. Armstrong
Laurenburg, NC

Dr. Phillip Arnone
Matthews, NC

Dr. Stephen Button
Mount Airy, NC

Dr. Karen Carrick
Raleigh, NC

Dr. Rick Davis
Conover, NC

Dr. Nikolas R. Hedberg
Asheville, NC

Dr. Dean Kenny
High Point, NC

Dr. Sandrine Martin
Cornelius, NC

Dr. Barbara Saunders
Garner, NC

Dr. Todd Smith
Winston-Salem, NC

Dr. Mark Yeager
Charlotte, NC

OHIO
Dr. Robert Gilbert
Mansfield, OH

Dr. Mark McAdoo
Athens, OH

Dr. Van Merkle
Dayton, OH

OKLAHOMA
Dr. Gerry Langston
Tulsa, OK

Dr. Mark Mercer
Mannford, OK

Dr. Richard Santelli
Bethany, OK

Dr. Michael Taylor
Tulsa, OK

OREGON
Dr. Daniel Beeson
Portland, OR

Dr. David Braman
Tuelatin, OR

Dr. Kathleen M. Galligan
Oregon City, OR

Dr. Edward M. Geller
Medford, OR

Dr. Usha Honeyman
Corvallis, OR

Dr. Steven Lumsden
Gresham, OR

Dr. Scott Northrup
Brookings, OR

Dr. Kristopher Peterson
Hermiston, OR

Dr. Thomas Richards
Beaverton, OR

Dr. James Siegel
Canyonville, OR

Dr. Mark Thomas
Cottage Grove, OR

Dr. David Wickes
Portland, OR

PENNSYLVANIA
Dr. Bruce Fink
Coudersport, PA

Dr. Mark Homison
Cranberry Township, PA

Dr. John LaHoda
Richboro, PA

Dr. Fredrick Osterberg
Red Lion, PA

SOUTH CAROLINA
Dr. Jon Bergrin
Florence, SC

Dr. Bruce Gwinnup
Charleston, SC

Dr. Peter Kfoury
Charleston, SC

Dr. Morgan Kutzner
Greenville, SC

Dr. Jacqueline McKool
Charleston, SC

Dr. Robert Pascal
Charleston, SC

Dr. Virginia Samuel
Columbia, SC

SOUTH DAKOTA
Dr. Roger Bommersbach
Brookings, SD

Dr. Roger Prill
Mitchell, SD

Dr. David Schwierert
Rapid City, SD

TENNESSEE
Dr. William Strauss
Lebanon, TN

TEXAS
Dr. Edward Brown
Dallas, TX

Dr. Ralph Burton
Kennedale, TX

Dr. Lance Carlton-Durrett
The Woodlands, TX

Dr. Janie Duke
Plano, TX

Dr. Steve Grimm
San Antonio, TX

Dr. Doreen Lewis-Overstrom
San Antonio, TX

Dr. Joe Lindley
Houston, TX

Dr. Tim McCullough
Houston, TX

Dr. Zachery McVey
League City, TX

Dr. Gregory Mrozinski
Houston, TX

Dr. Mike Prioux
Friendswood, TX

Dr. V.M. Thompsom
Arlington, TX

UTAH
Dr. Don Vradenburg
St. George, UT

VIRGINIA
Dr. Robert Duca
Dunn Loring, VA

Dr. Guntrang Khalsa
Herndon, VA

WASHINGTON
Dr. H. Earl Moore
Spokane, WA

WISCONSIN
Dr. Leslie Best
Madison, WI

Dr. Barbara Bradley
Wausau, WI

Dr. Kevin Branham
Eagle River, WI

Dr. Bernie Finch
Pepin, WI

Dr. Gwendolyn Gauerke
Iola, WI

Dr. Craig Gilbaugh
Ashland, WI

Dr. Kathleen Maedke
Milwaukee, WI

Dr. Cheryl Metzler
Green Bay, WI

Dr. Gina R. Schultz
Blanchardville, WI

Dr. David A. Sommerfield
Rice Lake, WI

Dr. Dean Willhite
Manitowoc, WI



TRUE STRENGTH

TRUST. IN NUTRITIONAL HEALTH.

Trust Douglas Laboratories, the choice of thousands of physicians for over 50 years.
Trust Douglas Laboratories for best-in-class, science-based natural supplements manufactured exclusively for health professionals. We are proud to offer you the largest and most innovative selection of premium-quality products and formulations to help promote the wellness of your patients. Together with health professionals like you, we have helped millions of patients improve their health and look forward to helping millions more because…

You trust Douglas Laboratories. Your patients trust you.

Trust Douglas Laboratories® for Complete Health.
Trust Douglas Laboratories® for the nutrients adults need with our world-class Ultra Preventive® X, a carefully balanced multivitamin formula that contains more than 50 nutritional ingredients. Douglas Laboratories® is proud to introduce our revised Ultra Preventive® X multivitamin with the following enhancements:

- **Now contains Folate from Metafolin®**
- **Now contains Organic Fruit and Vegetable Blend**
- **Now contains 1000 IU of vitamin D3 per serving**
- **Continues to carry the 5-Star Standard Gold rating from the Comparative Guide to Nutritional Supplements**

douglaslabs.com
1-888-DOUGLAB

DOUGLAS LABORATORIES®

CLINT PUBLICATIONS
720 OAK KNOLL
ROLLA, MO 65401

STAY INFORMED

ON THE LATEST IN

NATURAL HEALTH CARE

Subscribe to *The Original Internist* for only $50 annually

Name _____

Address _____

City _____ State _____ Zip _____

Phone _____ Fax _____ E-mail _____

☐ Check enclosed ☐ Bill my Visa/Master Card ☐ Bill my American Express

Credit Card Number _____ Expiration Date _____

Please return to Clint Publications, 720 Oak Knoll, Rolla, MO 65401 or call (573) 341-8448