Smokies Digest

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Cardiac Health

How to play the hand you're dealt...

Smokies Digest

CONTENTS

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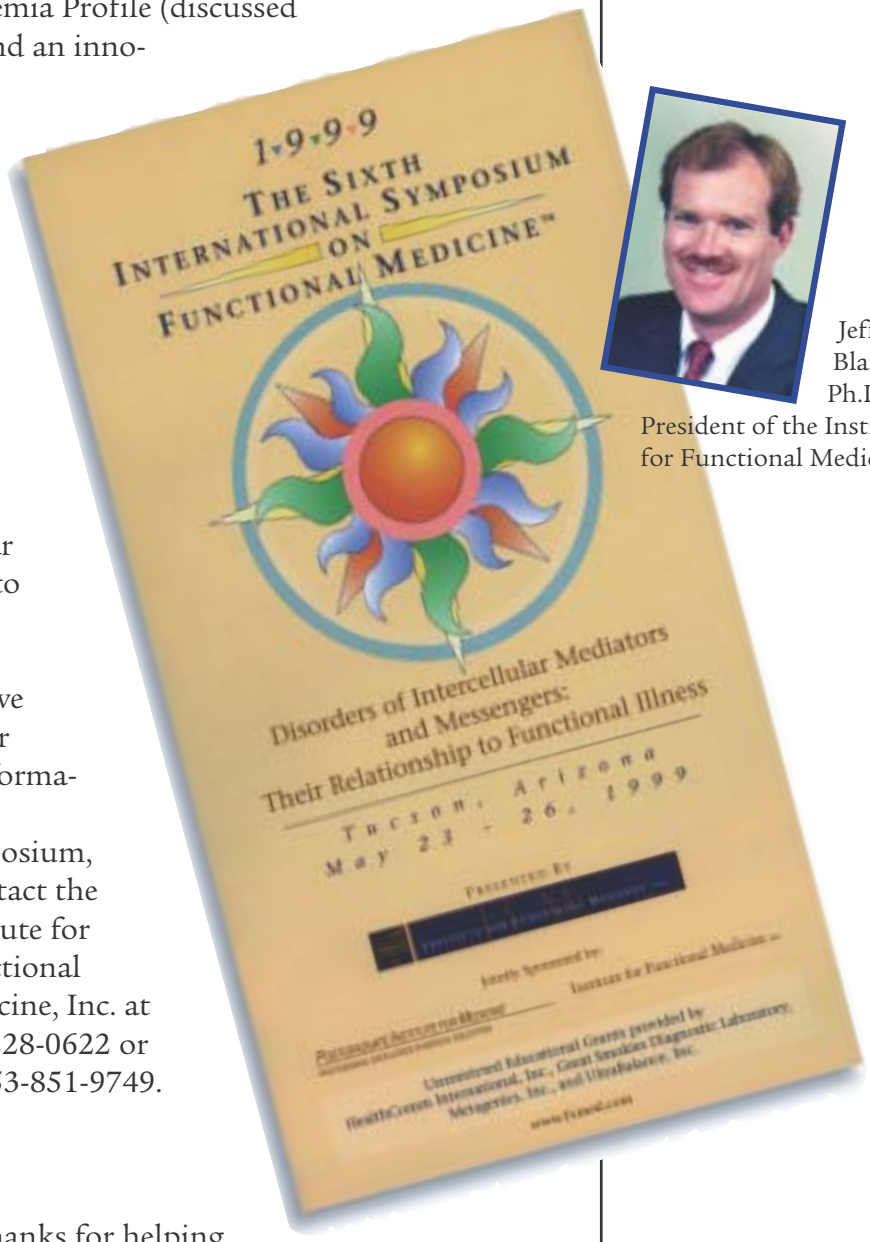
Stephen Barrie, N.D.
CEO

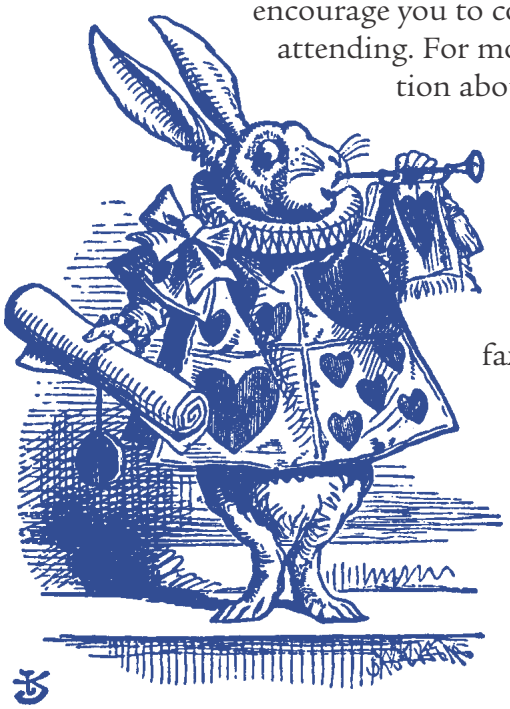
As we approach the new millennium, it is clearly an exciting time to be involved in healthcare.

Mainstream medicine is increasingly supporting the concepts behind our holistic approach to cardiac health, and innovators in the field of functional medicine continue to add to our understanding of the metabolic and molecular basis of health. At Great Smokies, we have already accomplished several goals in 1999 - the sensitivity enhancement of Inhalants Profile for allergies, the introduction of the Metabolic Dysglycemia Profile (discussed by John Furlong, N.D., in this issue), and an innovative Chronic Inflammation Profile currently under development. We look forward to introducing more cutting-edge assessments during the course of the year.



Jeffrey Bland, Ph.D.,
President of the Institute for Functional Medicine

Because we are always looking toward the future of medicine, we are also supporting once again the International Symposium on Functional Medicine with an unrestricted educational grant. This year's theme, "Disorders of Intercellular Mediators and Messengers," promises to stimulate a fruitful exchange of ideas among some of the most respected authorities in the field, and we encourage you to consider attending. For more information about the symposium, contact the Institute for Functional Medicine, Inc. at 800-228-0622 or fax to 253-851-9749.



Thanks for helping us continue to achieve our goals. We are indeed fortunate to have so many partners throughout the world.

INNOVATIVE PERSPECTIVES

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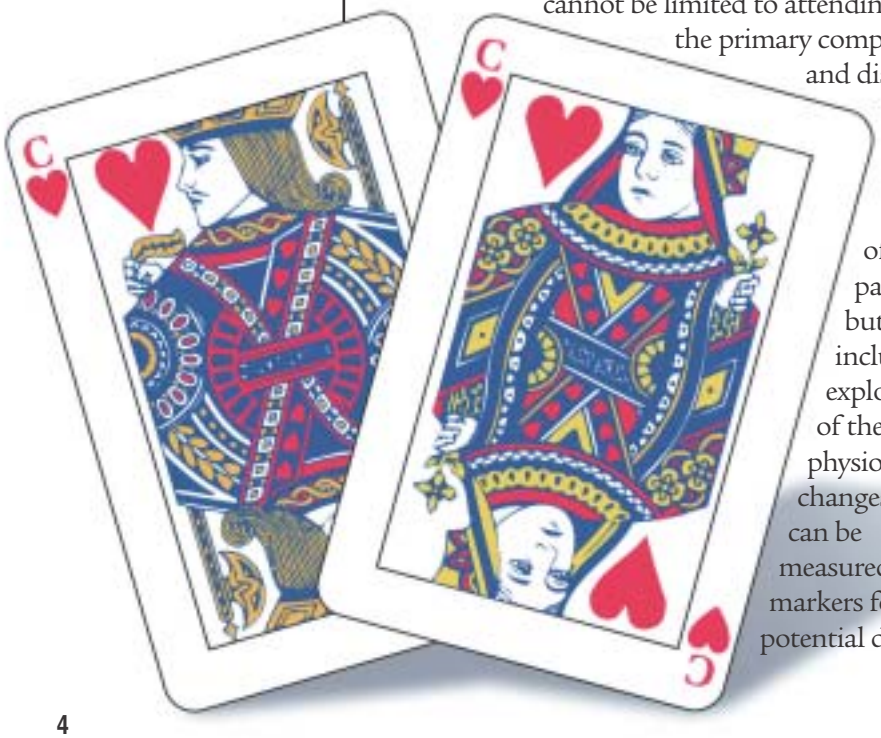
Functional Assessment for Cardiac Health:

Moving from the Parts to the Whole

by Alison Levitt, M.D.

As a Family Practice physician, I have always considered myself "holistic" and even "functional" in my approach to treating patients. I've tried to take into account important influences in a patient's life, such as social system, family history, diet, habits, ethics, and psychology. However, as I grow into my role as a functional assessment specialist for Great Smokies, learning more about functional assessment and medicine, I've come to realize just how much more is involved.

In a functional approach to medicine, the absence of disease does not necessarily mean true health. The focus of assessment and treatment in functional medicine, then, cannot be limited to attending to the primary complaints and diseases of patients, but must include an exploration of the physiologic changes that can be measured as markers for potential disease, as well as for potential optimal health and wellness. So it's not surprising that a functional approach to cardiac health would also involve assessments of nutritional and metabolic factors that influence healthy cardiac function.



This comprehensive approach, this new paradigm for viewing health, presents challenges for me as a doctor trained in allopathic medicine. Instead of classifying disease and treating the symptoms, the focus shifts to seeking the mediators responsible for the symptoms–the functional triggers throughout the body that activate the mediators–and then altering the patient's environment to progress toward optimal health for that individual.

It's not that conventional medicine is oblivious to all this or that it totally disregards human individuality. Still, medical doctors are trained to see the individual patient primarily within the context of his or her disease, rather than to recognize the biochemical individuality of every person and the way this uniqueness can affect the manifestation of disease. Overcoming this myopia really does require a shift in paradigms from a cause-and-effect model of health to one that is more fluid. Considering the kind of rigid training many of us receive, this is not an easy task.

But that's just where the concept of "complementary" or "integrative" medicine plays an important part. And nowhere is the value of this kind of medicine better illustrated than in the exciting developments surrounding the issue of cardiovascular health, where the past eighteen months have seen an explosion

of mainstream research challenging the limits of the cholesterol model of cardiovascular disease (CVD).

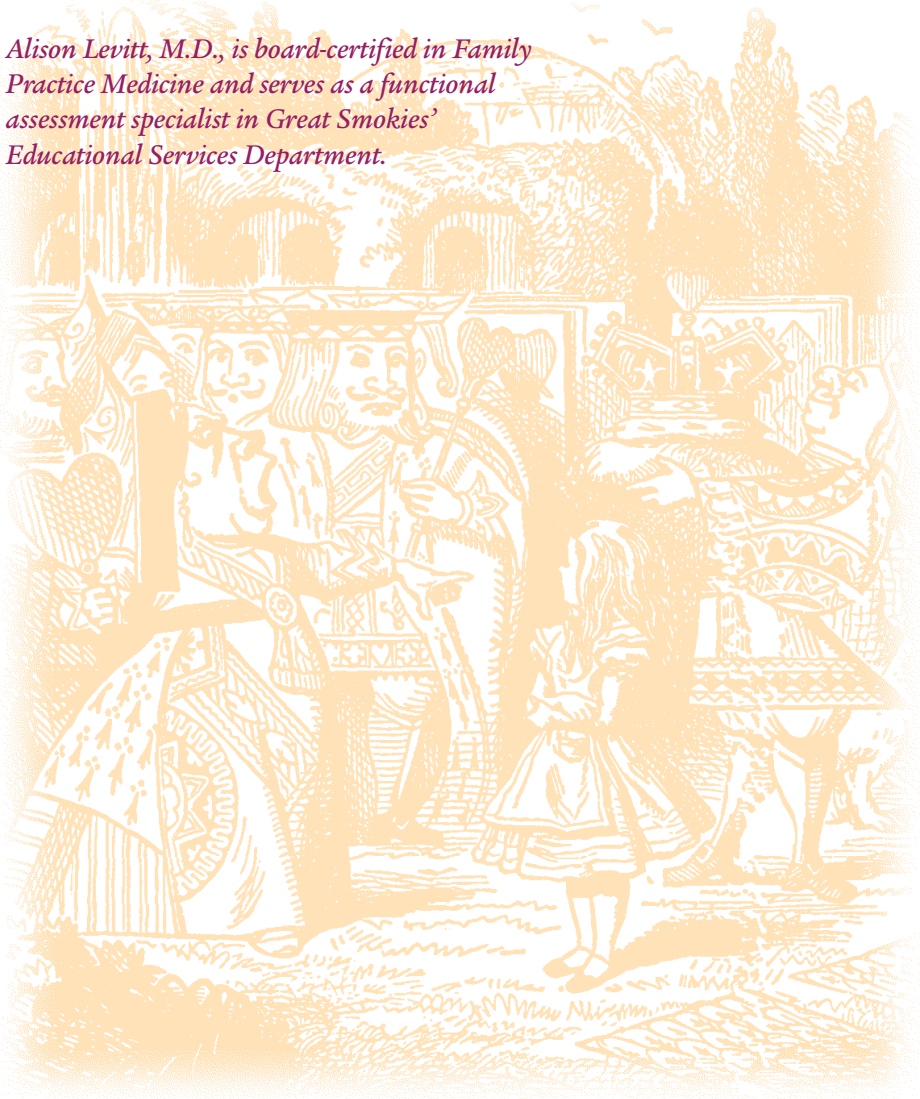
This issue of the Smokies Digest explores these new developments in cardiac assessment through the innovative functional medicine approach. This approach not only includes evaluating conventional measurable markers like total cholesterol, LDL, HDL, and triglycerides, but also examines other factors that may contribute to cardiovascular disease and health such as lipoprotein(a), homocysteine, C-reactive protein (CRP), and fibrinogen – all included on the Comprehensive Cardiovascular Assessment featured in this issue's case study. These independent markers can help identify CVD factors in individuals with very few or none of the conventional characteristics.

The markers on this innovative test are also put into perspective with an informative evaluation of their individual importance and synergistic effects. For example, Lp(a) is not only an independent factor for heart disease, it also acts in synergy with other factors. If it is found to be elevated in the face of a high LDL and total cholesterol, it adds to the deleterious effects. In addition, an elevated lipoprotein(a) has been shown to counteract the beneficial effects of an elevated HDL.

Several of the other markers have also gained considerable support from recent studies. Just this year, the American Heart Association issued a qualified endorsement of homocysteine screening. Several studies this year have also indicated that measuring baseline CRP can predict the likelihood of first heart attacks, especially in patients who were not seen as high risk. More importantly, testing for CRP in addition to total cholesterol proved to be a better predictor than testing for cholesterol alone.

The CRP marker brings me to my next point, which explains the beauty of a functional medicine model. Because CVD is always attended by inflammation and oxidative stress, the CRP marker for inflammation is especially important for assessing cardiovascular health. A large body of evidence has emerged to implicate free radicals, lipid peroxides, and oxidized LDL as inducers of atherosclerosis. Against continual oxidative stress, chronic inflammation is set into motion, which is what led researchers to look at CRP in the first place. My point is that metabolic activity throughout the body, including hyperinsulinemia, hormone imbalance, essential fatty acid metabolism, amino acid abnormalities, oxidative stress, toxic load, and detoxification impairment, all impact an individual's overall health and, more specifically, his or her cardiac health status.

Alison Levitt, M.D., is board-certified in Family Practice Medicine and serves as a functional assessment specialist in Great Smokies' Educational Services Department.



INNOVATIVE PERSPECTIVES

All of these evaluations are performed under rigorous quality control conditions that meet the requirements of our College of American Pathologists' certification.

For more information or to order the Comprehensive Cardiovascular Assessment or any other Great Smokies' test, call 800-522-4762.

CASE STUDY

Dysglycemia and Hyperhomocysteinemia: Cardiac Case Study

by Mark Hyman, M.D.

"After reviewing the core of his problem, insulin resistance, we discussed strategies for managing his case. I advised him to evaluate other, hidden indicators of cardiovascular disease with the Comprehensive Cardiovascular Assessment."
Mark Hyman, M.D.

Charles was fairly typical of patients I see, a hard-working 61-year-old executive, looking for an edge in preventing aging and degenerative diseases with lifestyle changes and natural therapies. He described himself as healthy, yet as I listened to his story of frequent travel, rich meals, and lack of exercise, coupled with his father's history of angina and his mother's Type 2 diabetes and stroke, I knew there was a bad mix of genetics and lifestyle. We searched together in our first visit for the usual risk factors for cardiovascular disease. He did have hyperlipidemia and was on Zocor™ 20mg. He has tried both Mevacor™ and Niacin™ in the past without success. He quit smoking 24 years ago. He denied having hypertension or diabetes, but had a high intake of sugar and truncal obesity.

He had been seen in another clinic and had a total cholesterol of 238, triglycerides of 158, HDL of 37, and LDL of 175. His ratio of cholesterol/HDL was 6.43 while on the Zocor™. In looking through his previous records, I discovered his glucose had crept up over the last few years from 109 to 120 to 132. His Alanine Transaminase (ALT) was also mildly elevated. He had been placed on many supplements, including a multi-vitamin, vitamin C, vitamin E, magnesium, DHEA, garlic, CoQ10, selenium, fish oil, and folic acid 800mcg.

After reviewing the core of his problem, insulin resistance, we discussed strategies for managing his case. I advised him to evaluate other, hidden indicators of cardiovascular disease with the Comprehensive Cardiovascular Assessment. Even though he was still taking Zocor™, his profile showed a total cholesterol of 272, an HDL of 42, an LDL of 230, triglycerides of 118. His cholesterol to HDL ratio was 6.4. His homocysteine was markedly elevated at 17. His RBC folic acid and B-12 levels were normal. All his other independent risk factors, including Lp(a), C-reactive protein, and fibrinogen, were normal.

His therapeutic program included education about the links among insulin resistance, sugar intake, his weight, and his dyslipidemia. Understanding and managing his insulin resistance gave him a framework for making the necessary changes in lifestyle and diet.

After a cardiac stress test, he committed to regular aerobic exercise. I encouraged him to perform resistance training to increase his lean:fat ratio. He made dietary changes including reducing refined carbohydrates, increasing B-vitamin-containing foods, omega-3 fatty acids, and eating more regular meals with a balance of quality protein, fat, and carbohydrate. He also eliminated hydrogenated fats and red meat. I switched his medication from Zocor™ to Lipitor™. Despite supplements of multi-vitamin and

CASE STUDY

800 mcg of folic acid, his homocysteine remained quite elevated. I modified his supplements to include a high potency multi-vitamin, with extra vitamin E, vitamin C, taurine, n-acetyl-cysteine for improvement of liver function and antioxidant reserve, and CoQ10. I prescribed a B-complex that not only included B-6, B-12, and folic acid, but also betaine, which facilitates one of the four nutrient-dependent enzymatic reactions involved in homocysteine metabolism. In addition, for further reductions in cholesterol, I added guggulipid and garlic. To aid in improving liver function, often at the core of dyslipidemia and insulin resistance, I added milk thistle. To help control his glucose, he was placed on gymnema. EPA/DHA was continued to help facilitate insulin action and reduce triglycerides and lower blood pressure.

When he returned four months later for review, he had lost 15 pounds, was exercising regularly, and had dramatically improved his lipids and homocysteine. His follow-up profile revealed a total cholesterol of 192, an LDL of 144, and triglycerides of 99. His homocysteine had dropped from 17 to 9. His fasting glucose also improved from 132 to 111. After two more months his total cholesterol was down to 156, triglycerides to 74, and his LDL had dropped from an initial 230 to 106. We discussed the possibility of stopping his Lipitor™ if he continues his lifestyle and nutrient modifications.

Commentary

The importance of a multi-factorial approach to cardiovascular disease prevention is critical. Teasing out the complex factors of lipid status, insulin resistance, homocysteine metabolism, other factors, and genetics interacting with lifestyle is essential to helping each individual.

Heart disease is not one disease. It is a label we ascribe to the final product of multiple metabolic and genetic variations that give rise to atherosclerosis. The complexity and individual uniqueness of this process is underscored by the case discussion. One patient may have normal lipids, but a high homocysteine, as in the 50- year-old Irish professor I recently treated who had six older brothers with heart disease—three dead and three with Coronary Artery Bypass Grafts.

Elevations of homocysteine in other patients may require a wide range of nutrient doses to correct, because of genetic variations in nutrient-dependent enzymes. In yet another patient, the core dysfunction may be insulin resistance, a largely unrecognized modern epidemic: there are over twelve million Americans with diabetes, and half of them are completely unaware of their added risk to develop CVD. Periodontal disease or an occult Chlamydia infection may initiate a chronic inflammatory process, setting the stage for atherosclerosis. Some patients have a genetic predisposition to lipid abnormalities such as those with familial dyslipidemia or apo-E4 double allele, some of which are responsive to diet, and others requiring medication. Identifying biochemical and genetic variations and their mismatch with lifestyle can aid us in more refined and aggressive disease prevention and life enhancement.

Mark A. Hyman, M.D., currently serves as a Medical Director at Canyon Ranch in the Berkshires, an internationally acclaimed health resort. He received his B.A. in Asian Studies and graduated Magna Cum Laude with a Medical Doctor degree from the University of Ottawa. His varied experiences include postgraduate training in Family Medicine (and board certification), practice in Beijing and Hong Kong, emergency medicine in inner city Springfield, MA, and rural family practice and backcountry medical rescue. Along with his interest in Eastern medicine, Buddhism, and Yoga, Dr. Hyman has studied preventive and integrative medicine, as well as clinical mind/body medicine with Herbert Benson at Harvard.

"It is now clear that abnormalities of molecular processes may be the basis of many cardiovascular diseases...."

Eugene Braunwald, M.D., Heart Disease: A Textbook of Cardiovascular Medicine (1997)

TEST SUPPORT

Getting information and ordering tests is easier than ever—

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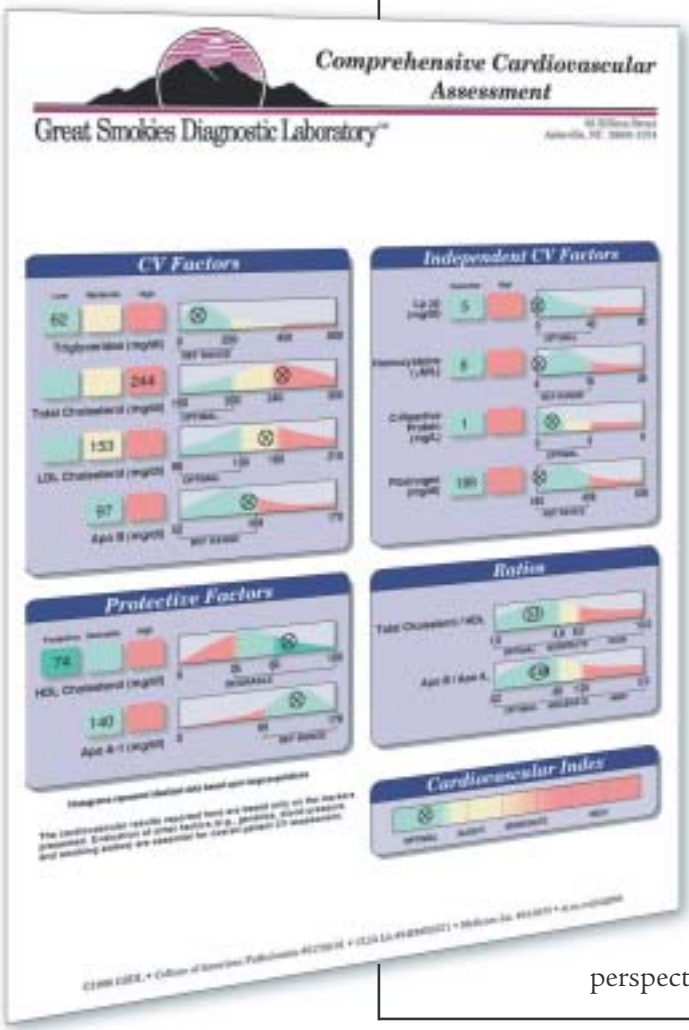
The Cardio Report:

A Precision Tool for the Physician

by Alison Levitt, M.D.

Preventive cardiology is the most effective way of reducing the morbidity and mortality associated with cardiovascular disease (CVD), the number one cause of death in America today. However, what constitutes "preventive cardiology" is rapidly expanding beyond running routine laboratory tests such as a lipid profile and counseling patients on appropriate diet, smoking cessation, diabetic control, and ways to lower their blood pressure. Increasingly, as in Dr. Mark Hyman's case study, cardiovascular disease is being seen as the product of multiple metabolic, genetic, and environmental influences.



Great Smokies' Comprehensive Cardiovascular Assessment offers the practitioner a broader individual laboratory assessment of cardiac health, taking into account several unique and modifiable markers such as Lp(a), homocysteine, C-reactive protein (CRP), fibrinogen, Apo B, and Apo A-1, in addition to conventional lipid markers. Placed into the proper perspective – as they are in the report and commentary for this test - they can help define overall CVD status and help guide the physician toward a unique and specific treatment plan for each patient. Using information from the mosaic of independent markers and ratios on the Comprehensive Cardiovascular Assessment, physicians can better treat the many patients who do not have conventional risk factors when they experience their first myocardial infarction (MI), estimated to be as many as 50% of CVD patients.

In Dr. Hyman's case study, homocysteine is elevated. This amino acid has received much attention as a key independent factor for heart disease that is modifiable with nutritional intervention. In recognition of the importance of methionine metabolism, the American Heart Association earlier this year issued an advisory urging homocysteine testing for at-risk patients and a diet with sufficient levels of folic acid, vitamin B-6, and B-12.

Another of the markers on the GSDL cardio profile, Lp(a), is considered the most atherogenic of all lipoproteins. The Apo A-1 component of Lp(a) is thought to act like an adhesive, drawing LDL and other atherosclerotic deposits. Elevated levels of Lp(a) translate into a higher possibility for premature cardiovascular disease.

C-reactive protein, an acute-phase marker of inflammation, infection, and trauma, serves as an independent factor for MI and stroke. This relationship has led to important research into a possible infectious etiology to heart disease involving *C. pneumoniae* and *H. pylori*.

The likelihood of stroke and MI are compounded with an elevated fibrinogen. Fibrinogen is also an acute-phase reactant that participates in the clotting process by promoting plaques, thrombus, and endothelial damage. When both fibrinogen and LDL are elevated, there can be up to an eight-fold increase in likelihood for MI. Increasingly, it is becoming clear that cardiovascular disease is not simply a result of hyperlipidemia and hypertension. The cardiovascular profile at GSDL offers the clinician a unique perspective on this complex syndrome by providing accurate test results and interpretation so that, as a clinician, you can make informative, precise recommendations for your patients. The cardiovascular profile test report is easy to interpret for you and your patient, while providing valuable innovative information that could make the difference between life and death.

TEST SUPPORT

Cardio QA and Lab Developments

by Uta Levinson, M.S.

Great Smokies' Comprehensive Cardiovascular Assessment boasts an enviable record of performance on in-house and external competency testing for all of its markers. Whenever possible, we participate in periodic surveys submitted by the College of American Pathologists (CAP) and New York State (NY). For markers with no external competency, Great Smokies has developed its own comparisons with results from other labs and in-house, split sample measures to evaluate reproducibility and accuracy. Every marker is surveyed three to eight times a year, depending on availability.

The results are impressive, to say the least...

- For the conventional lipid markers – triglycerides, HDL, LDL, and total cholesterol – we've passed CAP and NY competency surveys with perfect scores ever since we introduced the Comprehensive Cardiovascular Assessment.
- We've achieved perfect scores from CAP on the Apo A-1 and Apo B markers.
- We received a high rating on NY's first homocysteine survey – which was conducted as a trial with a limited number of participating labs – and our performance in comparison to other labs has been very good.
- NY has just introduced a survey for fibrinogen.
- We're relying on internal controls for Lp(a), which is still an experimental marker.
- We have performed very well on in-house C-reactive protein surveys, although this is an area where we are not entirely satisfied with available technology, and we run samples with elevated results twice to insure sensitivity.

Our current research and development efforts are focused on achieving greater sensitivity for the C-reactive protein marker to better suit our lower reference range cut-off and to improve service. We have also recently switched from chromatography to immunoassay technology to achieve a more rapid evaluation of plasma homocysteine, which improves turnaround time for clients and provides us a wider window of opportunity for verifying high results or suspicious peaks.

Uta Levinson, M.S., is the supervisor of Great Smokies' Chemistry Lab. Prior to assuming that position in 1997, Ms. Levinson worked for three and one-half years as an associate in the Research Department.

"Whenever possible, we participate in periodic surveys submitted by the College of American Pathologists (CAP) and New York State (NY). For markers with no external competency, Great Smokies has developed its own comparisons with results from other labs and in-house, split sample measures to evaluate reproducibility and accuracy."

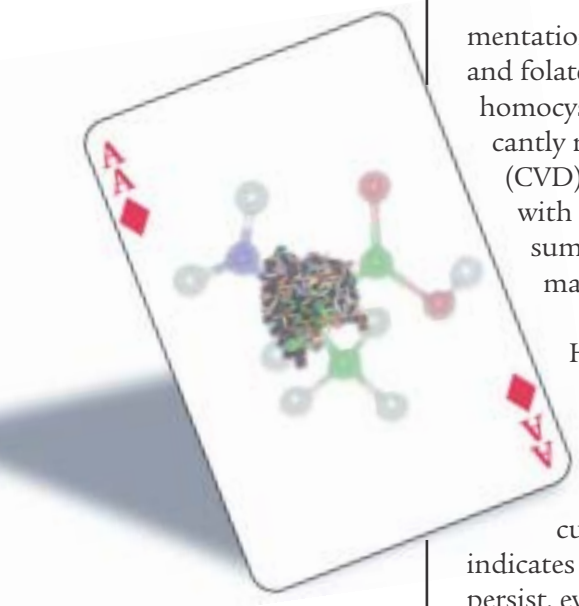
Uta Levinson, M.S.

Biochemical Dimensions

Solving the Mystery of B Vitamin Supplementation with Amino Acids Analysis

By Jon Pangborn, Ph.D.

"With the remarkable variation among patients in terms of their nutritional requirements, determining the proper dosage to bring down homocysteine levels can be accomplished quickly and effectively with Amino Acids Analysis."
Jon Pangborn, Ph.D.



The plasma homocysteine assay offered as part of the Comprehensive Cardiovascular Assessment can alert physicians to excess levels of this amino acid. In most cases, supplementation of vitamin B-6, vitamin B-12, and folate is sufficient to reduce homocysteine to normal levels and significantly reduce cardiovascular disease (CVD) risk, especially when combined with dietary changes to reduce consumption of fats and junk food that may be deficient in magnesium.

However, factors besides homocysteine can predispose to CVD, such as taurine insufficiency. Also, monitoring therapy with the Comprehensive Cardiovascular Assessment sometimes indicates that high levels of homocysteine persist, even despite what is usually an adequate supplement regimen. In cases of homocysteinemia and homocysteinuria, dietary, toxic, or other factors can limit bioavailability of these important nutrients. Genetic factors may cause an unusually increased need for B-6, B-12, and/or folate. If this is not compensated for, an overproduction of homocysteine thiolactone from methionine results, due to decreased remethylation or transsulfuration of homocysteine. Excess homocysteine thiolactone consequently stimulates several detrimental changes in the body, ultimately stimulating molecular abrasion on the endothelial cell, causing smooth muscle cell hyperplasia and fibrosis.

In such cases, the question facing healthcare providers is an important one: just how much supplementation is necessary for these kinds of patients? With the remarkable variation among patients in terms of their nutritional requirements, determining the proper dosage to bring down homocysteine levels can be accomplished quickly and effectively with Amino Acids Analysis. Because of marked biochemical individuality, what is sufficient for one patient may be entirely inadequate for another—even one whose age, weight, and general health are almost identical. Proper assessment can answer the question of dosage without the risks and delays of trial-and-error dosing.

The urine and plasma Amino Acids Analyses offered by Great Smokies Diagnostic Laboratory are practical laboratory tests to determine phenotypical and functional variation in human ability to properly metabolize methionine and homocysteine, as well as to produce adequate taurine. An intermediate in the metabolism of methionine, homocysteine, when elevated, has been correlated repeatedly with increased susceptibility to cardiovascular disease, including myocardial infarcts and occlusive arterial conditions. Amino Acids Analysis (plasma and urine) assesses homocysteine metabolism and levels of 40+ other amino

acids, including taurine, as well as the metabolic cycles that affect them, and evaluates the functional availability of vitamin B-12, B-6, and folate.

For patients with disturbed methylation/transsulfation pathways (a condition occurring in approximately one in 75 otherwise healthy individuals), a 24-hour urine Amino Acids Analysis with oral methionine challenge is often needed to identify and stimulate specific pathways. This test can identify patients whose elevated homocysteine (and altered folate cycle) are not apparent through standard serum vitamin B-12 analysis. Methionine challenge assessment can pinpoint at which of many metabolic junctures vitamin B-6, folate, and vitamin B-12 availability is impaired. The Amino Acids Analysis can also determine serine deficiency, an unusual cause of homocysteine elevation.

An oral loading of L-methionine at 25mg/kg body weight, given in divided doses during the day of the urine collection, provides a challenge by which the test highlights weaknesses in methionine metabolism. The methionine loading can also be done during the day prior to a morning blood draw for an overnight-fasting plasma Amino Acids Analysis to check for homocystinemia. This highly specialized assessment is the gold standard of metabolic analysis of homocysteine and is indicated when other, less specialized tests can not pinpoint why high levels persist despite therapy.

A new addition to our reports on Amino Acids Analysis provides additional information for physicians concerned with cardiac health interventions. In addition to the detailed commentary provided with our standard amino acid report, Interpretation at a Glance focuses on the complex interactions of amino acid metabolism. The report's colorful bar chart specifies presumptive needs for:

--Three specific vitamins...B-6, B-12, and folate
--Two critical vitamin groups...B-1, B-2, B-3, and lipoic acid
--The lipid soluble vitamins... A, D, E, and beta-carotene
--Five minerals which serve as major enzyme activators...magnesium, manganese, molybdenum, zinc, and iron
--Alpha-ketoglutarate, the major amino group receptor in metabolism

Because other factors influence overall health and cardiac function, physicians will find additional information on the Interpretation at a Glance report also helpful. Information about presumptive needs is then related to conditions implied by abnormalities, including:

--Nitrogen insufficiency or excess
--Impaired xenobiotic detoxication
--Susceptibility to occlusive arterial disease
--Collagen or skeletal disorders
--Susceptibility to neurological disorders
--Gastrointestinal dysfunction
--Endocrine dysfunctions or hormonal imbalances
--Infection or gut dysbiosis
--Disordered renal transport (with urine analysis)

As this list suggests, Great Smokies Amino Acids Analysis can help solve some of the mysteries of supplementation. If interventions don't seem to be working as the patient is monitored by re-testing, it is often useful to examine metabolic precursor pathways. Amino Acids Analysis answers the most important question in supplementation--the level of bioavailable nutrients. Because of an individual's unique metabolic patterns, the level of supplementation that is required by the body and that is bioavailable may be much different than the level of dosing would suggest.

Jon Pangborn, Ph.D., serves as elemental and amino acid analysis clinical specialist and consultant for Great Smokies. Since 1981, he and his wife Chris have also operated Bionostics, Inc., a technical consulting firm. In addition, Dr. Pangborn is Adjunct Professor of Nutritional Biochemistry, Union Institute (Cincinnati, OH).

Amino Acids Analysis support materials now available -
· Application Guide
· Mini-Guide to Interpretation at a Glance Report
· Audiotape

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Introductions

The New Metabolic Dysglycemia Profile and Early Identification

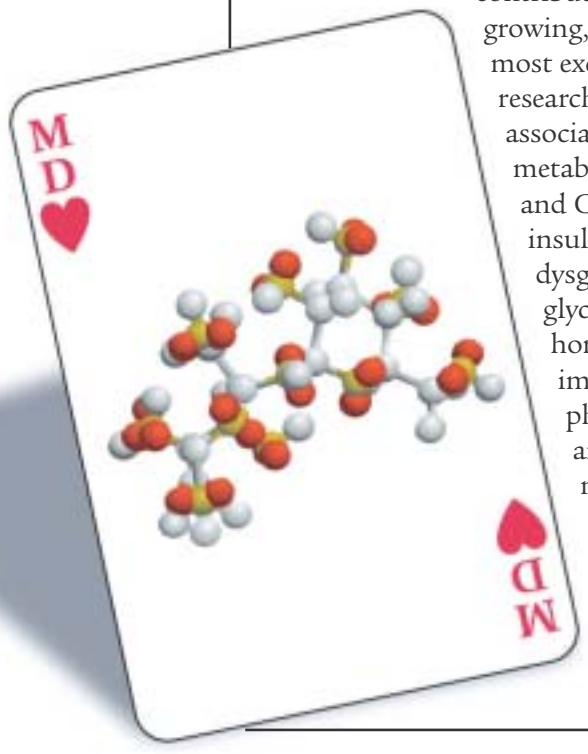
by John Furlong, N.D.

"The importance of metabolic dysglycemia has yet to receive the wide-spread attention it apparently deserves if one looks at sheer numbers of cases. One recent article in the Lancet showed the rising incidence of Type II diabetes in graphic terms, with an estimate that, globally, the incidence of diabetes will double within the next five years."

John Furlong, N.D.

Working with patients with various types of heart disease used to be a straightforward matter - look at family history, cholesterol levels, and perhaps glance quickly at stressors, and voilá! you've got a treatment plan. Statistics indicate that this type of approach, along with the public awareness of being "heart-smart," has indeed resulted in improvements of morbidity and mortality statistics for cardiovascular disease (CVD). Still, CVD continues to remain the leading cause of death in the US, and it's become clear that more than the conventional risk factors are responsible.

Fortunately, awareness of other causes and contributing factors is growing, and some of the most exciting recent research involves the association between metabolic dysglycemia and CVD, including insulin resistance, dysglycemia, protein glycation, and hormonal imbalance. To help physicians identify and treat metabolic dysglycemia, Great Smokies has modified its Glucose and Insulin Tolerance Test, added two markers of protein glycation (Hemoglobin A1c and Fructosamine), and included measurement of DHEA-S, cortisol, and IGF-1 for a new comprehensive assessment, the Metabolic Dysglycemia Profile. As an option, physicians can also order a lipid profile that includes trigycerides, total cholesterol, HDL, LDL, and uric acid.



The importance of metabolic dysglycemia has yet to receive the wide-spread attention it apparently deserves if one looks at sheer numbers of cases. One recent article in the *Lancet* showed the rising incidence of Type II diabetes in graphic terms, with an estimate that, globally, the incidence of diabetes will double within the next five years. This trend is a reflection of western culture's more sedentary lifestyle, intakes of carbohydrate-rich diets and, to some degree, genetic predisposition among populations experiencing rapid growth.

There are reasonably accurate and simple measures, such as the waist-hip ratio, that can help categorize patients who require further testing with the Metabolic Dysglycemia Profile. The new American Diabetes Association (ADA) screening criteria state that ALL middle-aged patients should be assessed for potential for diabetes, and other sources, including the Centers for Disease Control's Cost-effectiveness Work Group, argue that significantly EARLIER evaluation is certainly cost-effective and worthwhile among certain populations of people at high risk. Fortunately, we have many preventive tools with which to modify the gradual develop-

ment of insulin resistance, impaired glucose tolerance, and eventual diabetes - nutritional approaches, phytomedicines, and pharmacologic agents all show effectiveness in their particular arenas. With the Metabolic Dysglycemia Profile 2-hour glucose-load component, people at risk can be identified as much as ten to fifteen years before symptoms develop.

Insulin resistance and hyperglycemia are critical factors in overall health as they both have multi-system influences. For example, high insulin levels make for lower DHEA levels and lower IGF-1 levels in adults. Deficiencies of these two hormones have been linked with some of the more common trends in the aging process: decreased muscle mass, fatigue, and bone loss, as well as sub-optimal immune function and impaired overall emotional well-being. By seeing insulin as an instigating factor and by correcting inordinately elevated levels, many additional problems may be avoided.

A key consideration in this tendency toward excessive carbohydrate diets, with elevations in mean glucose levels and insulin over a lifetime, is the concept of protein glycosylation. With high glucose levels over time, a non-enzymatic process occurs that causes irreversible changes in many types of tissue proteins. The most familiar gauge of these changes is the hemoglobin A1c test used to evaluate response to treatment for (or diagnosis of) dysglycemia and diabetes. The modified proteins produced by the glycosylation process have been linked to the development of microvascular problems, autoimmune conditions, and the modified collagenous structures, all of which contribute to morbidity in the diabetic/dysglycemic population. Moreover, when the potential for glycosylation exists, increased oxidative stress will tend to make the situation worse, further limiting the mobility which is so important for maintaining positive health habits.

Clearly, the search for fitness has seen better days. More and more Americans are obese and the metabolic ramifications of this are beginning to be understood in the context of insulin and glycosylation rather than in the context of weight loss and "ideal weight." The metabolic realities that render people very literally unable to lose weight even with significant caloric restriction are based upon the changes wrought by insulin and glucose combined with predisposition and the interplay of other hormones and stress. Assessment with the Metabolic Dysglycemic Profile will reveal the interplay of these physiological processes, and the test can be used to monitor a variety of therapeutic interventions (diet, exercise, supplements) that may be employed to achieve optimal metabolism.

The recognition of cardiovascular disease as a major scourge in our "advanced" culture and chosen lifestyles shows how we must look across disciplines and specialties towards a more holistic view of health, healing, and medical practice. By considering the ramifications of an accentuated insulin cascade over years and decades, we are able to identify increased CVD risk and do something to prevent disease. Metabolic dysglycemia not only contributes to the leading cause of mortality, but it also impacts various and sundry other serious conditions including renal failure, autoimmune disease, cancer, Alzheimer's disease, arthritis, as well as the blindness and amputation resulting from diabetes.

John Furlong, N.D., spent ten years in private practice and has taught anatomy and physiology. Dr. Furlong joined the educational staff of Great Smokies in 1996.

Components of Great Smokies' innovative Metabolic Dysglycemia Profile include:

- *Glucose and Insulin Tolerance to identify metabolic patterns leading to diabetes and dysglycemia at fasting and two hours later with glucose challenge*
- *Glycated Hemoglobin A1c to measure blood sugar levels over a six to eight week period of therapy – early warning of risk for advanced protein glycation*
- *Fructosamine to evaluate short-term (two to three week) blood sugar levels in response to recent interventions*
- *DHEA-S, cortisol, and IGF-1 at fasting to pinpoint the metabolic shifts which affect glycemic control, cardiac health, and lean muscle*
- *(Optional) Lipid profile to assess total cholesterol, triglycerides, HDL, LDL, and uric acid as indications of specific dietary needs for the individual*

Call 800-522-4762 to order a companion packet and test kits.

TEST APPLICATIONS

Element Influences on Cardiac Health

by Bob Smith
Vice-President of Elemental Analysis

"Depletion of such key elements as cobalt (essential for cobalamin metabolism), copper, selenium, chromium, magnesium, calcium, and, most recently, potassium has been linked to cardiovascular disease, as have disturbances in the zinc/copper and calcium/magnesium ratios."
Bob Smith

Elemental Analysis of hair, blood, or urine samples can yield important information concerning cardiac health. Levels of both toxic and nutritional elements—as well as certain critical ratios–impact the function of heart and arteries. Considered as a part of global assessment of cardiac function, the results of Elemental Analysis pinpoint the elusive causation of chronic conditions and disease states.

CHOOSING THE BEST SAMPLE TO TEST

Great Smokies currently offers three types of tests for Elemental Analysis with an additional two (white blood cells for chromium and fasting blood plasma) under development—

- Packed blood cells (erythrocytes)
- Urine, random-time and 24-hour specimens
- Head hair from the nape of the neck

Hair element testing is best viewed as a means to monitor element imbalances and environmental toxicity with follow-up blood testing or provocative urine testing useful for confirming hair toxic element findings (Amino Acids Analysis is useful for confirmation of many nutrient elements). Urine is an appropriate sample to assess the excretion of potentially toxic elements, providing a window into levels retained in the body. Urine is also the sample of choice for monitoring detoxification therapies. Using blood plasma or erythrocyte as the sample for testing, on the other hand, is always indicated in cases of recent exposure. Some samples yield more information about specific elements than others, and environmental considerations may affect the healthcare provider's selection.

TOXIC ELEMENTS

Acute excesses of several toxic elements can also affect cardiac health, among them thallium, which can cause serious cardiovascular problems including myocardial necrosis. However, there is intriguing research indicating that chronic low-level mercury, lead, and nickel ingestion may also be related to cardiovascular disease (CVD).

Recent data suggest that intake of mercury from non-fatty freshwater fish and the consequent accumulation of mercury in the body are associated with an increased incidence of acute myocardial infarction, as well as death from cardiovascular disease in general, possibly due to the promotion of lipid peroxidation by mercury. Interest has also grown in the possible ill effects of mercury liberated from dental amalgam fillings.

With long term exposure, lead accumulates in bone, where it may be stored for years before mobilization because of bone mineral turnover. This latent lead toxicity can then disturb regulation of fibrinolytic protein release from subendothelial cells through intercellular calcium-independent pathways. The resulting effects on platelet aggregation can increase CVD risk considerably.

Nickel, a less publicized toxic element, exerts its damaging effects through immune dysregulation, with elevated IgG, IgA, IgM, and decreased levels of IgE being observed in patients with high hair levels of nickel. Most exposure leading to elevated hair levels is via dust from nearby industries including electrometallurgical emissions. Nickel is also found in many processed foods, and there is evidence that some individuals may absorb it through the skin. Nickel accumulates with age and smoking, perhaps explaining why tissue levels are highest in patients who died of cardiovascular disease. Nickel's negative effect on immunoglobulin levels may explain its possible cumulative impact on cardiac function.

NUTRITIONAL ELEMENTS

Depletion of such key elements as cobalt (essential for cobalamin metabolism), copper, selenium, chromium, magnesium, calcium, and, most recently, potassium has been linked to cardiovascular disease, as have disturbances in the zinc/copper and calcium/magnesium ratios. The elements silicon and cadmium have also been found to influence heart and vascular function. Studies have established direct and, for some elements, inverse ratios used in interpretation of test results.

Along with its effects on glucose and insulin metabolism, chromium's role in the regulation of carbohydrate and lipid metabolism may account for its beneficial influence on cardiac health. Chromium supplementation increases insulin sensitivity and reduces circulating insulin—a key to proper function of the heart and circulatory system.

In retrospective studies, high calcium in the hair was related to low aortic calcium, and a low hair calcium was an early and sensitive indicator of arteriosclerosis and other pathology of the cardiovascular system – including the enhanced dietary uptake of toxics such as lead resulting from calcium deficiency. It has been demonstrated that antioxidant supplementation along with vitamin D can increase hair calcium levels. In terms of interpretation of test results, these studies suggest that an inverse relationship exists between hair calcium and cardiovascular disease.

In one study of elderly patients, a higher hair magnesium level was associated with higher rates of regional cerebral blood flow. Low magnesium has been linked with complications of diabetes and the impact of dysinsulinemia on heart function, and a recent study presents evidence that hypomagnesium may contribute to coronary heart disease. Clinical observations regarding calcium and magnesium appear to support the importance of a proper ratio between these elements for reduction of cardiovascular disease.

CONCLUSION

The vast majority of chemical reactions that govern cellular processes are in turn regulated by enzymatic reactions. Enzyme catalysts most often require mineral cofactors to operate and can be damaged by toxic load. For these reasons, Elemental Analysis of hair, blood, and urine can yield important information for the formulation of a comprehensive prevention and treatment protocol to ensure maximum protection of cardiac health.

Bob L. Smith, Vice-President-Elemental Analysis, has developed understanding of element levels and health conditions using specimens. He is recognized as an authority on the effects of nutrition and toxic element exposure on human health and behavior, and he lectures worldwide on the topic.

TEST APPLICATIONS

Great Smokies performs its Elemental Analysis-Hair in one of the only "clean rooms" in the industry. After washing samples with Triton and 18-megamo DI (de-ionized) water, digested samples are examined using Inductively Coupled Plasma Mass Spectrometer instruments.

Call 800-522-4762 to order test kits and support materials.

Cellular Chemistry

Oxidative Stress: Gradual Damage that Leads to Pathology

by Mary James, N.D.

"Without question, free radical damage is a major player in cardiovascular disease. Minimizing excess production of reactive oxygen species (including exposure to toxic metals) is of paramount importance, as is ensuring adequate intake of dietary antioxidants and the nutrient cofactors needed for endogenous antioxidants."

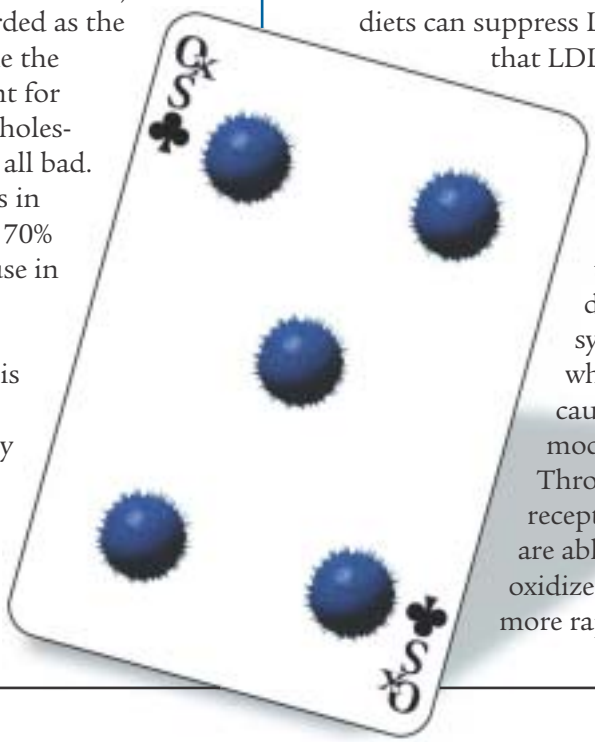
Mary James, N.D.

The importance of such significant risk factors as obesity, smoking, hypertension, diabetes, and serum lipid in the development of cardiovascular disease is well agreed upon. Perhaps less frequently acknowledged is the major contributing role played by oxidative stress, or free radical damage, in the body. This destructive process can be easily and accurately evaluated by Great Smokies' Oxidative Stress Analysis, which can pinpoint the metabolic deficiencies that accelerate the aging process and lead to degenerative cardiovascular disease.

Among lipid abnormalities, elevated LDL cholesterol (the "bad" cholesterol) has generally been regarded as the most problematic. While the term "bad" is convenient for simplicity's sake, LDL cholesterol is, of course, NOT all bad. Every day LDL receptors in our vessel walls take up 70% of circulating LDL for use in membrane and steroid hormone synthesis. Trouble begins when this LDL cholesterol is modified, particularly by oxidation. Oxidized cholesterol, in fact, appears to be a major instigator of the atherosclerotic process.

Like other tissues in the body, LDL becomes oxidized when antioxidants (endogenous or dietary) are inadequate for the amount of reactive oxygen species (ROS) being produced. An excess of ROS, resulting from conditions such as up-regulated metabolism or detoxification (cytochrome P450 enzyme activity), hypoxia, inflammatory processes, or cigarette smoking, can place a burden on our antioxidant systems, rapidly draining reserves. Plasma lipid peroxide levels in atherosclerotic patients have been found to be significantly higher than those of normal subjects, and increasing evidence supports the hypothesis that an increased intake of antioxidants leads to a lower risk of cardiovascular disease.

Various factors such as high saturated fat diets can suppress LDL receptors so that LDL is less efficiently taken up from the bloodstream. The excess LDL is then cleared by the reticuloendothelial (RES) system, a process which in itself causes oxidative modification of LDL. Through a special receptor, macrophages are able to absorb oxidized LDL at a much more rapid rate than non-



oxidized LDL, perhaps because it is the macrophage's job to scavenge damaged material in the body. In contrast to the LDL receptor, the expression of this scavenger receptor on the macrophage is not down-regulated by high intracellular LDL content. As a result, macrophages become engorged with LDL cholesterol, eventually forming the "foam cells" which compose the characteristic "fatty streaks" in atherosclerotic plaque. Aggravating the problem is the ability of oxidized LDL to prevent macrophages' return to the circulation, in essence trapping them in the intima of the artery wall. This, in turn, propagates the oxidation process further.

Oxidized LDL is highly toxic to the vessel wall. In the presence of oxidized LDL, platelets are known to aggregate and adhere to sites of endothelial injury (a prerequisite to thrombotic MI and stroke). Platelet aggregation is prevented by prostacyclin; however, the biosynthesis of prostacyclin is inhibited by lipid peroxides. Oxidized LDL also appears to interfere with coronary artery flow by inhibiting the smooth muscle cell relaxation response to endothelial-derived relaxing factor (EDRF). Treatment with antioxidants has been demonstrated to reverse this process, improving coronary artery flow.

Finally, cell-mediated LDL oxidation *in vitro* typically requires the presence of transition metals such as iron or copper which facilitate synthesis of the potentially destructive hydroxyl radical. Removal of these metals by chelators serves to inhibit LDL oxidation. *In vivo*, the release of iron is known to occur when inflammation or injury lowers tissue pH. Interestingly, inflammation, as reflected by elevated levels of C-reactive protein, is increasingly recognized for its contribution to cardiovascular risk.

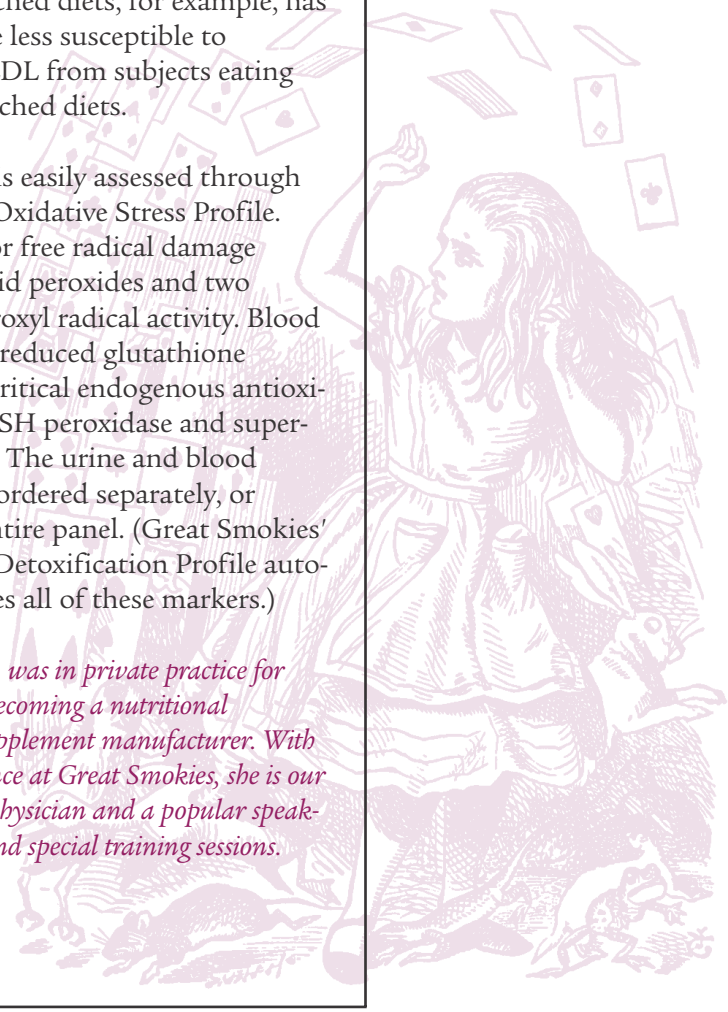
Adding to the load of free radicals in the body is mercury, a potent inducer of lipid peroxidation. A study in Finland demonstrated that men with the highest hair mercury content had a greater risk of both acute MI and CV death in general than those with a lower hair mercury content. Both the hair and urinary mercury associated significantly with titers of immune complexes containing oxidized LDL.

Without question, free radical damage is a major player in cardiovascular disease. Minimizing excess production of ROS (including exposure to toxic metals) is of paramount importance, as is ensuring adequate intake of dietary antioxidants and the nutrient cofactors needed for endogenous antioxidants. Since melatonin is a potent scavenger of both the hydroxyl and peroxyl radical, assessing melatonin levels is recommended. Balancing intake of easily-oxidized PUFAs with antioxidants, as well as with less-oxidized fatty acids, will also help control oxidation. LDL from subjects fed olive oil-enriched diets, for example, has been found to be less susceptible to oxidation than LDL from subjects eating linoleic acid-enriched diets.

Oxidative stress is easily assessed through Great Smokies' Oxidative Stress Profile. Urine markers for free radical damage include urine lipid peroxides and two markers for hydroxyl radical activity. Blood markers include reduced glutathione (GSH) and two critical endogenous antioxidant enzymes, GSH peroxidase and superoxide dismutase. The urine and blood markers may be ordered separately, or together as an entire panel. (Great Smokies' Comprehensive Detoxification Profile automatically includes all of these markers.)

Mary James, N.D., was in private practice for four years before becoming a nutritional consultant for a supplement manufacturer. With four years experience at Great Smokies, she is our senior laboratory physician and a popular speaker at conferences and special training sessions.

For more information or to order any of our functional assessments, call 800-522-4762



ENDOCRINE APPLICATIONS

Hormone Balance - Yet Another Factor in CV Protection

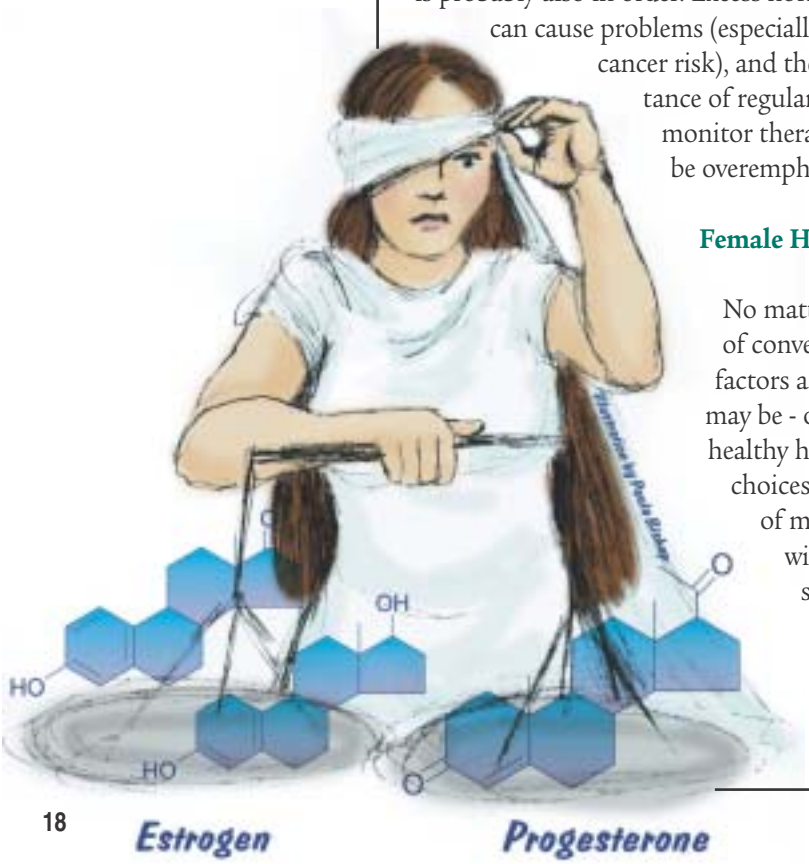
by Joseph Collins, N.D.

"An effective comprehensive strategy for combating CVD needs to include accurate assessment of hormone levels and regular monitoring to avoid the negative effects of hormone excess. Great Smokies offers salivary assessments of hormones beneficial to cardiac health (there is also a serum assessment for DHEA-S). To take full advantage of our resources in this area, call 800-522-4762."

Joseph Collins, N.D.

When it comes to helping the heart protect itself against cardiovascular disease (CVD), hormone balance is not usually the first thing that comes to a doctor's mind. However, assessment for hormone balance can often be the key to preventive intervention. Hormones, especially testosterone, estradiol, IGF-1, and DHEA, influence muscle tone, insulin sensitivity, and lipid metabolism. And it's hardly coincidental that just at the time in a person's life that hormone balance begins to swing toward the lower end of reference ranges, cardiovascular dysfunction also increases.

Before choosing to supplement hormone levels, however, accurate assessment is important. The operative term in hormone replacement therapy (HRT) is "balance," and the qualifier "delicate" is probably also in order. Excess hormone levels can cause problems (especially with cancer risk), and the importance of regular testing to monitor therapy cannot be overemphasized.



Female Hormones

No matter how free of conventional risk factors a woman may be - or how healthy her lifestyle choices - the onset of menopause, with the consequent drop in estrogen levels, places her at much higher risk for development of CVD. A preponderance of studies on women undergoing hormone replacement therapy (HRT) have pointed to the protective value of maintaining hormone balance in the post-menopausal years. There are factors that influence how great the protection is - such factors as whether a woman has had a first heart attack already, how her genetic disposition affects lipid metabolism, and how estrogen and progesterone are balanced in HRT. Still, for the woman without history of a previous cardiac event, HRT can be of significant benefit, probably because of estrogen's powerful antioxidant qualities.

In addition there are several specifically cardioprotective effects of estrogen such as:

- Lowering LDL (the "bad" cholesterol)
- Increasing HDL (the "good" cholesterol)
- Decreasing levels of lipoprotein (a), an independent factor for development of CVD that also compounds the effect of LDL
- Attenuating endothelin-1-mediated vasodilation, resulting in decreased blood pressure (BP) and increased coronary blood flow
- Decreasing homocysteine levels and enhancing the effects of supplementation of B-6, B-12, and folic acid
- Decreasing risk of hyperinsulinemia
- Possibly lowering levels of fibrinogen and decreasing platelet aggregation (currently under investigation)

Choosing the right balance of estrogen and progesterone is critical to effective HRT. Progesterone, whether natural or synthetic, blunts the

oncogenic effects of unopposed estrogen, restoring natural balance and exercising a beneficial effect on hypertension.

Androgens and Precursors

Although work is underway to isolate metabolites of estrogen that will not cause such side effects as gynecomastia in men, the primary hormones for cardiac protection in males are testosterone, IGF-1, and DHEA. As with female hormones, androgen replacement should be monitored carefully, because androgen excess may promote colorectal cancer.

Testosterone seems to affect cardiac health primarily through its ability to vasodilate coronary arteries. A host of studies have demonstrated the effect of adequate levels of this hormone on general well being, lean muscle mass, and healthy metabolism, including cardiac function and detoxification. Along with its other benefits in aging men, testosterone plays a role in establishing a foundation for cardiac health.

IGF-1, both on its own and as a monitoring analyte for growth hormone therapy, has long been employed in therapies to improve cardiac function. Among the beneficial effects associated with growth hormone therapy is a positive impact on lipid metabolism. This year, Swiss researchers provided even more evidence of the power of IGF-1 itself as a cardiac therapy. When researchers administered the hormone to a group of heart disease patients, the elevation of IGF-1 was followed by a decrease in insulin levels, an increase in heart stroke blood volume, a reduction in vascular resistance, and a lowering of left and right heart filling pressures. Along with previous studies, this one adds to the evidence that IGF-1 can stimulate heart muscle growth, increase insulin sensitivity, and lower lipid CVD risk markers.

Despite the controversy surrounding DHEA, researchers continue to discover links between this hormone and heart protection. A study presented at this year's American Heart Association Scientific Sessions concluded that DHEA acts very much as 17-ß-estradiol does in the attenuation of endothelin-1-induced vasoconstriction in coronary conductance vessels. If further research reproduces these findings, the protective value of DHEA in combating the microcirculatory dysfunction in CVD may soon be established.

Assessing and Monitoring HRT

An effective comprehensive strategy for combating CVD needs to include accurate assessment of hormone levels and regular monitoring to avoid the negative effects of hormone excess. Great Smokies offers salivary assessments of hormones beneficial to cardiac health (there is also a serum assessment for DHEA-S). To take full advantage of our resources in this area, call 800-522-4762. When test results arrive in your office, remember that you can schedule a consultation (at no additional charge) with me or one of my colleagues in Educational Services for advice on using test results and deciding about therapeutic approaches, including herbal, pharmaceutical, and lifestyle interventions.

Joseph Collins, N.D., has worked in both private and integrative group practices before joining the educational staff in 1996. Dr. Collins provides practical and technical support for practitioners. His special interest is assessment and management of endocrine function. Dr. Collins' book on the subject is scheduled for release this summer.

Visit the News section at our web site, www.greatsmokies-lab.com, for updates from the medical literature about the potential of hormone therapies, or e-mail cs@gsdl.com to receive the Connection newsletter at your home or office.

NUTRITIONAL COMPONENTS

Fatty Acids

Getting the Right Balance for a Healthy Heart

by T. Michael Culp, N.D.

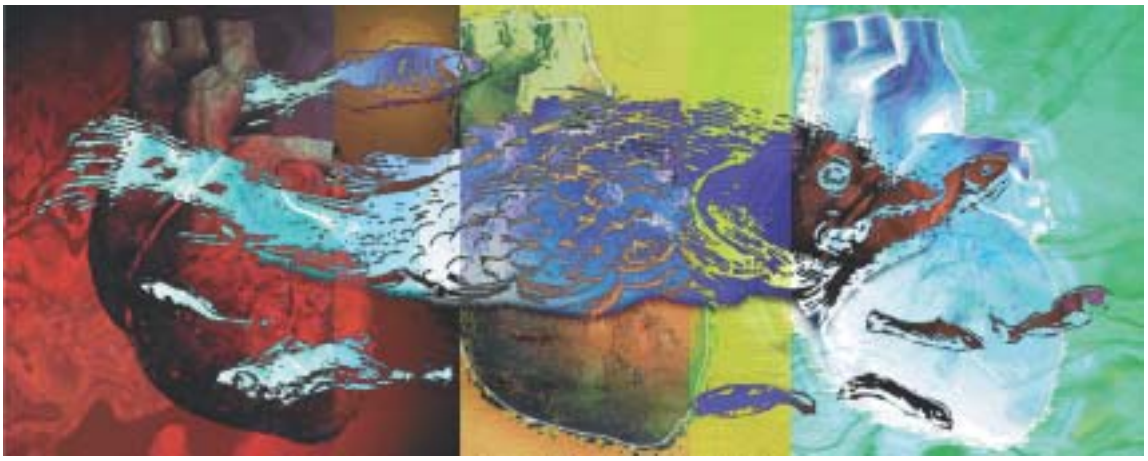
"How much fish oil or evening primrose is enough? How much is too much? Remember each patient is biochemically individual and will have different physiological needs."
T. Michael Culp, N.D.

Suggesting that the right balance of fats can lower cardiovascular disease (CVD) risk may sound a bit peculiar, but more than a decade ago, scientists started noticing a trend: people who ate more fish had much lower risk of developing heart disease. Men who ate fish only once a week reduced their risk of having a first heart attack by 70%. Men who eat fish regularly are also 42% less likely to die of a heart attack than men who do not eat fish. And men who have already had one myocardial infarction (MI) can reduce their risk of dying from a second MI merely by eating moderate amounts of fish.

Fish oils, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are believed to be largely responsible for these cardiovascular health benefits. Fish oils have been shown to lower triglycerides, to increase HDL cholesterol, to reduce the amount of circulating fibrinogen, and to lower blood pressure in hypertensives. EPA also directly reduces endothelial inflammation by inhibiting monocyte adhesion. Fish oil supplementation lowers homocysteine, CRP, and fibrinogen levels as well and decreases the tendency of platelets to aggregate, reducing the overall tendency toward inflammation in the cardiovascular system.

EPA, DHA, and alpha-linolenic acid (LNA) have all been shown to reduce blood pressure in hypertensives. Several mechanisms may be at work here. These omega-3 fats act to reduce the production of pro-inflammatory thromboxanes (made from omega-6 fats) and increase the production of anti-inflammatory thromboxanes (omega-3 derived), both leading to a reduction in blood pressure. The amount of available dihomogamma-linolenic acid (DGLA) in membranes is proportional to the series 1 prostaglandins produced, which are known to induce smooth muscle relaxation. And men given fish oil supplements had a 43% increase in nitric oxide production, allowing blood vessels to relax, further reducing blood pressure.

Certainly linked to cardiovascular disease risk is the emerging notion of Syndrome X, a term coined by researcher Gerald Reaven at Stanford University. Reaven, in studying adult-onset diabetes, recognized a common pattern of abnormalities accompanying the onset of diabetes. These include developing insulin resistance, central obesity, high blood pressure, increased serum triglygerides and decreased levels of HDL cholesterol. Reaven and others speculate that the increased



insulin resistance may be the underlying stimulus for all these problems. Insulin is critical for the proper transformation of essential fatty acids into prostaglandin precursors. Too much as well as too little can have disastrous consequences for the body's eicosanoid regulation. Specifically, too much insulin may increase the cell membrane stores of arachidonic acid and reduce the amount of DGLA, which will have the net effect of increasing the inflammatory readiness of the body. With insulin resistance, glucose cannot flow freely into cells and, in response to this functional hypoglycemia, the body secretes cortisol and glucagon to make more glucose available (raising blood sugar levels further, but having little effect at the cellular level). Unfortunately, the increased cortisol also causes triglyceride release from adipose tissues, affecting serum cholesterol and triglyceride levels, and contributes to heart disease as well as to abdominal obesity.

Great, but why not just give fish oils? Why do I need to measure essential fatty acid levels with Great Smokies testing? From the perspective of better diet habits, it is true that the vast majority of people would be better off just eating more oily fish. However, there are three major problem areas of EFA metabolism that can be identified using the EMFA test.

1) Genetic delta-6 desaturase enzyme dysfunction. Estimates run as high as 20% of the population having some degree of dysfunction. This can lead to chronic low levels of DGLA (an anti-inflammatory prostaglandin), and the treatment is always to give oils containing gamma-linolenic acid (GLA), like evening primrose, borage, or black currant oil. Unfortunately, these oils can be expensive to supplement, so the test can confirm if these oils really need to be supplemented at all, often saving the patient lots of money.

2) The test measures 30 fatty acids found in the membrane, allowing very specific treatment intervention strategies. Fish oils may well be a part of that strategy, but a healthy balance among various oils is critical.

3) The EMFA test allows you to monitor amounts of specific oils and their ratios to one another. Remember each patient is biochemically individual and will have different physiological needs.

Essential fatty acids play critical roles not just in heart disease but in every type of inflammatory disorder known to humanity. To find out more information on fatty acids and health ask for the EMFA Application Guide, available from any client services representative. Call today to order your complimentary copy: 1-800-522-4762.

Michael Culp, N.D., worked as a family doctor in Seattle and taught nutritional biochemistry and other courses at Bastyr University prior to joining Great Smokies in 1998. His special interests are nutritional interventions and Essential and Metabolic Fatty Acids Analysis.

"Unfortunately, these oils can be expensive to supplement, so the test can confirm if these oils really need to be supplemented, often saving the patient lots of money."
T. Michael Culp, N.D.

Interested? Call 800-522-4762 for test kits and support materials.

NEWS AT HOME AND ABROAD

INTERNATIONAL UPDATE

Gordon Piller International, Inc. of Mississauga, Ontario is the latest example of a GSDL distributor who has entered what could be called the "next generation" of international service provision. In doing so, the firm joins colleagues in several other nations, most notably Brazil, Australia, and England, in working toward a total service model of distribution for Great Smokies' assessments.

What that means for Canadian healthcare providers is heightened visibility for complementary medicine, faster turnaround time for tests, a centralized, domestic distribution/collection base, enhanced education and support, and informed advocacy for the interests of Canadian physicians who practice complementary and functional medicine. With its volume more than tripled over the past few months to a client base of 600 physicians, Gordon Piller International plans to add a customer services representative and two sales reps (to be trained at GSDL) and implement a state-of-the-art computer system to track requisitions, shipping, and test results for clients. Among the many technical innovations expected soon is confidential delivery of test results via the worldwide web.

To improve education and support, Piller plans to attend and display at meetings of physicians interested in complementary therapies—such as the recent Second Annual Meeting of the Complementary Medical Association of Canada, where his booth and GSDL educational materials were very popular with attendees. GSDL has committed to sending its laboratory physicians and biochemists north to give presentations at future meetings, and, after training is complete, the new client services and sales representatives will be able to replicate the kind of support clients in the states enjoy.

Talk with our foreign and domestic sales representatives at 800-522-4762

Compliance Q & A

by Earlene Clark, Vice-President of Operations & Compliance Officer

Q. Why is GSDL required to file Medicare for services provided?

A. Great Smokies Diagnostic Laboratory (GSDL), as a participating provider in Medicare, is required to abide by the rules established by HCFA (Health Care Finance Administration) and other government agencies in their administration of the Medicare Program. The following policy is based on these rules.

Effective January 1, 1998, Medicare rules required all providers (participating and non-participating) to accept assignment for clinical laboratory services they furnish. Medicare pays 100% of the allowable reimbursement of these services for a Medicare beneficiary. No collection should be made from the beneficiary or any other secondary insurer unless the service is completely denied (and an advanced beneficiary notice [ABN] was obtained), is part of the patient's annual Medicare deductible, or is a screening/otherwise known non-covered procedure (for which an ABN was obtained).

Providers who repeatedly bill Medicare beneficiaries for clinical laboratory services could be subject to sanctions, such as civil money penalties and/or exclusion from the Medicare program. Moreover, if any substantial part of the patient's bill is collected before Medicare renders its determination, this may be considered a violation of the assignment agreement.

If the test is for Screening Purposes Only, known not to be Medically Necessary under Medicare guidelines, or is otherwise known to be a Non-covered test by Medicare, GSDL should not file with Medicare. An ABN should be obtained from the patient by the ordering physician's office and sent with the requisition. GSDL can then bill the physician, bill the patient's secondary insurance, or accept payment from the patient. If the patient supplies us with secondary insurance and would like us to file Medicare for denial purposes, GSDL will do that and then bill the secondary insurer after receiving the Medicare denial.

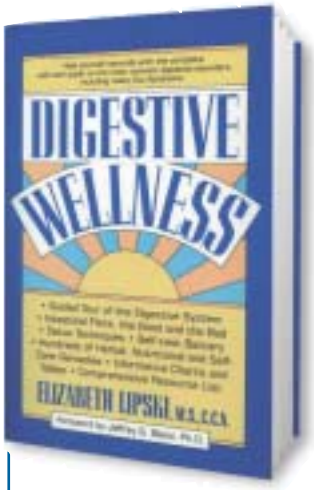
Any billing to Medicare and/or to Medicare beneficiaries that are not covered by this policy should be brought to the attention of GSDL's Compliance Officer.

Doctor's Bookshelf

DIGESTIVE WELLNESS

by Elizabeth Lipski, M.S., C.C.N.

Reviewed by Russel Sher, D.C.



How do you make sense of the plethora of information that is emerging in the field of functional medicine? *Digestive Wellness* may be the key to gaining a clear and concise understanding of the ways a Functional Medicine approach can help patients achieve optimal digestive health.

Our modern-day epidemic of digestive illness is a timely topic, since it is estimated that one-third to one-fourth of all adults suffer from the condition. Except for the common cold, digestive illness is the leading reason people seek medical advice – and spend enormous sums on medications for its symptoms.

Lipski presents a well-researched and carefully integrated functional medicine approach to digestive health, including such causative factors as lifestyle choices, diet and quality of food, environmental pollution, food preparation, technology, irradiation, and drug use. She also includes a variety of useful questionnaires to help determine possible causes, as well as a very informative guide to the appropriate use of functional testing.

Natural therapies are reviewed and a variety of options are presented. All in all, *Digestive Wellness* is a must-read for the practitioner who is serious about uncovering the root causes of dysbiosis and restoring healthy digestion.

7-DAY DETOX MIRACLE

By Peter Bennett, N.D., and Stephen Barrie, N.D.

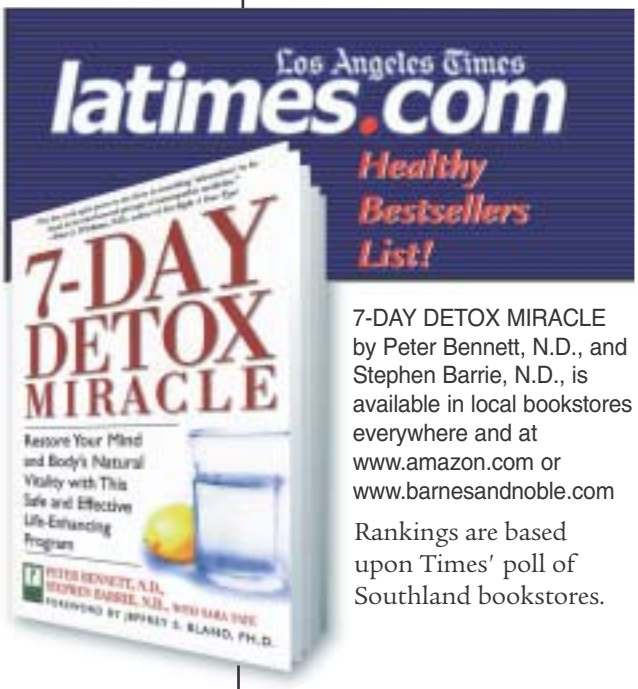
Foreword by Jeffrey Bland, Ph.D.

Reviewed by Mary James, N.D.

Detox programs are not new—shelves today are lined with products whose labels guarantee overhauls within a few days, but which sometimes aggravate. Overlooked is the fact that effective detoxification requires more than just "stirring things up." Health, in general, requires proper nutrition, assimilation, circulation, and elimination of metabolic waste. A breakdown in any one area results in toxicity that can lead to illness. Likewise, the road back to health involves a restoration of these functions—all of them.

This is what I found so refreshing about the book, *7-Day Detox Miracle*. Inside the cover is a wealth of information on the instigators of illness. The stage is set for a safe and effective cleansing program, as the same factors promoting health are those required for an effective detox program: removing obstacles to health, improving circulation, enhancing elimination, ensuring healthy GI function, stimulating the liver, and transforming stress. Toward these ends, the "EcoTox program" employs a variety of techniques, with focus on diet, supplements, and circulation.

The *7-Day Detox Miracle* provides a far-reaching education for the patient about how the body keeps itself well, and also for the clinician who desires a broader understanding of the mechanisms of detoxification. As the authors state, "The reason for an illness is more important than its name. The cure begins with the cause." This book is a great roadmap for getting there.



7-DAY DETOX MIRACLE by Peter Bennett, N.D., and Stephen Barrie, N.D., is available in local bookstores everywhere and at www.amazon.com or www.barnesandnoble.com

Rankings are based upon Times' poll of Southland bookstores.

NEW PUBLICATIONS

Book Reviews

To order Digestive Wellness by Liz Lipski, M.S., C.C.N., call Keats Publishing (a division of NTC Contemporary Publishing Group) at 800-323-4900, Ext. 147

To learn about additional titles, visit www.keats.com

Meet Sales: Decades of Service

John Evans
Sales Director

Amy McDonald
Director of International
and Special Accounts

Frank Gilreath
Functional Medicine
Consultant

Cynthia TenEyck
Adminstrative Assistant

The recent addition of new sales representatives is good news for health care providers--especially because of Great Smokies' novel concept of just what "sales" is all about. For our four-person sales department, sales means providing you with a focused educator, a vocal advocate, and a personal consultant to help you grow your practice by better meeting the needs of your patients. What emerges is a productive collaboration and two-way learning process between client and sales representative that improves the quality of health care for your patients.

Here are just a few of the benefits our sales force can bring to you:

- Free on-site training for you and your staff, directing the vast knowledge resources of the laboratory toward the specific, real-world clinical needs of your patients.

- A direct information "pipeline" to the laboratory, helping the lab's chemists, microbiologists, and consulting physicians tailor our services to your individual needs. Your input translates directly into new test innovations, improvements in educational materials and programs, development of even more informative reports.

- Valuable information about ways other practitioners have successfully integrated functional testing into their practices. With their wealth of observations from the field, our sales professionals serve as your personal consultants helping you build on the experiences of others.

With their decades of combined experience in personalized sales and service, John, Frank, Amy, and Cynthia are eager to help you take full advantage of their many talents. Give them a call at 800-522-4762 to find out how much they have to offer.

Great Smokies Diagnostic Laboratory℠
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