

Smokies Digest

Great Smokies Diagnostic Laboratory

April 2002 Volume 11, No. 1

Healthy Aging... The Odyssey Continues



FEATURES

4-5 Tools for Choosing Laboratory Assessments in an Optimal Aging Practice

By Brad Rachman, D.C., D.A.B.P.M.

6-7 The Challenge in Women's Health: Understanding the Biological Differences

By Elizabeth Lipski, Ph.D., C.C.N.

**8-9 A Marriage of Theory and Practice:
GSDL's New Individual Case Management Research Program**

By Patrick Hanaway, M.D., and John Furlong, N.D.

10-11 Case Study: Improving Estrogen Metabolism for Healthy Aging

By Kashi Rai, M.D.

12-13 Diagnosing Digestive Conditions in the Elderly

By Corene Humphreys, N.D.

16-17 Methylation: the "Linchpin" of Healthy Aging

By Mary James, N.D., with David Perlmutter, M.D.

18-19 Underlying Triggers of Inflammatory Conditions

By Russel Sher and Todd Nelson

20-21 Detox in Overdrive: Heavy Metal Exposure and Burden in Aging Patients

By Fred Harvey, M.D., and Jeff Baker, N.D.

26-27 Clinical Genomics – The Next Generation of Healthy Aging Medicine

By T. Michael Culp, N.D.

DEPARTMENTS

3 From the Founder's Desk

14-15 New Products

22-25 Book Reviews

28 ACE Clinical Genomics Training Announcement

"You mean you're comparing our lives to a sonnet? A strict form, but freedom within it?"

"Yes." Mrs. Whatsit said. "You're given the form, but you have to write the sonnet yourself. What you say is completely up to you."

Madeleine L'Engle, A Wrinkle in Time (1962)

COMING IN OUR NEXT ISSUE:

Molecular and genomic analysis uncovers new targets for modifying health.



Editor: Eddy Ball, Ph.D.

Contributing writers: Eddy Ball, Ph.D., Patrick Runkel, M.A., Scott Holmes, Elizabeth Lipski, Ph.D., Patrick Hanaway, M.D., Kashi Rai, M.D., Corene Humphreys, N.D., David Perlmutter, M.D., Todd Nelson, N.D., Fred Harvey, M.D., Jeff Baker, N.D., Russel Sher, D.C., Mary James, N.D., Brad Rachman, D.C., T. Michael Culp, N.D., John H. Furlong, N.D., DeAnna Hatch, Ph.D., Missy West, Deborah Shepard, Ph.D., Jeff Ledford

Art Director: David Barrett

Layout and Design: Paula Bishop

Cover Art: Paula Bishop

Contributing Artists: Paula Bishop, Mary Ann Lawrence, David Barrett, Merideth Lovejoy, Lisa Coin

Production Management: Rusty Cuning

Smokies Digest is produced and distributed semi-annually by Great Smokies Diagnostic Laboratory:
63 Zillicoa Street, Asheville, NC 28801-1074
1-800-522-4762 • Fax: 1-828-252-9303
cs@gSDL.com • www.gSDL.com

©2002 Great Smokies Diagnostic Laboratory

z.nl.v11n1.040402

Clinical Genomics... The Future of Medicine

Scientists from all over the world have deciphered the entire human genome. You can now download from the Internet the near-complete infrastructure for how to build and run a human body. What does this mean to you and your patients?

This spring Great Smokies mounts a bold initiative to apply innovative genetic testing in the practice of primary care medicine. We are introducing a new line of predictive diagnostic genomics tests and sponsoring a series of Clinical Genomics training. In this issue of the Digest, T. Michael Culp, N.D., offers an introduction to the concepts behind what he rightly describes as "the next-generation of healthy aging medicine."

Within the framework of Functional Medicine, genetic testing offers some exciting opportunities for primary care by enhancing practitioners' ability to predict patterns of individual biochemical response. These patterns can then be targeted by a specifically individualized treatment plan to improve patient outcomes. Advances in genetic testing now make it possible to achieve a level of diagnostic sophistication and specificity never before possible.

The one-day Clinical Genomics training series began in March and runs through June at sites throughout the country. The series has been fully approved to offer Continuing Medical Education credits to Medical Doctors and Doctors of Osteopathy and for offering Continuing Education Units to Naturopathic Doctors and Doctors of Chiropractic.

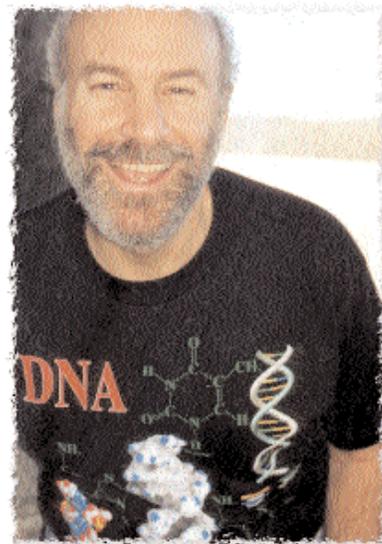
I am very proud of the exciting ground-breaking work our Genovations Research and Development team has accomplished in deciphering the clinical utility of genomics. Their innovations will provide you with unparalleled clinical decision tools.

I believe that "Genomics" will become the dominant language of this century. I invite you to join us at an ACE training session and discover for yourself how to speak it. You will also learn the ways that Clinical Genomics can make your practice of medicine more effective and rewarding.

Yours in health,



Stephen Barrie, N.D.
Founder and Chairman of the Board



*By Stephen Barrie, N.D.
Founder and Chairman of the Board*

Because Clinical Genomics is grounded in Functional Medicine concepts and backed by our commitment to total quality, practitioners can count on:

- **Practical Applications:** Test results will not merely expose a genetic predisposition. They will also point to ways that the effects of a polymorphism that is prevalent among the patient population and relevant to treatable disease conditions can be modified by nutrition and lifestyle changes to improve patient outcomes. All tests that we offer will meet these important criteria.
- **Practitioner Support:** We are sponsoring hands-on ACE training for practitioners to make certain genetic testing can be applied effectively in primary care practices. We will also provide our high level of professional support to help practitioners get every possible benefit from test results in choosing treatment interventions.

*Are you receiving the
Great Smokies Connection,
our e-mail newsletter?*

To subscribe, visit

*[http://www.gsdl.com/education
/connection/index.html](http://www.gsdl.com/education/connection/index.html)
or call 800-522-4762.*

TOOLS FOR CHOOSING LABORATORY ASSESSMENTS IN AN OPTIMAL AGING PRACTICE

By Brad Rachman, D.C., D.A.B.P.M.



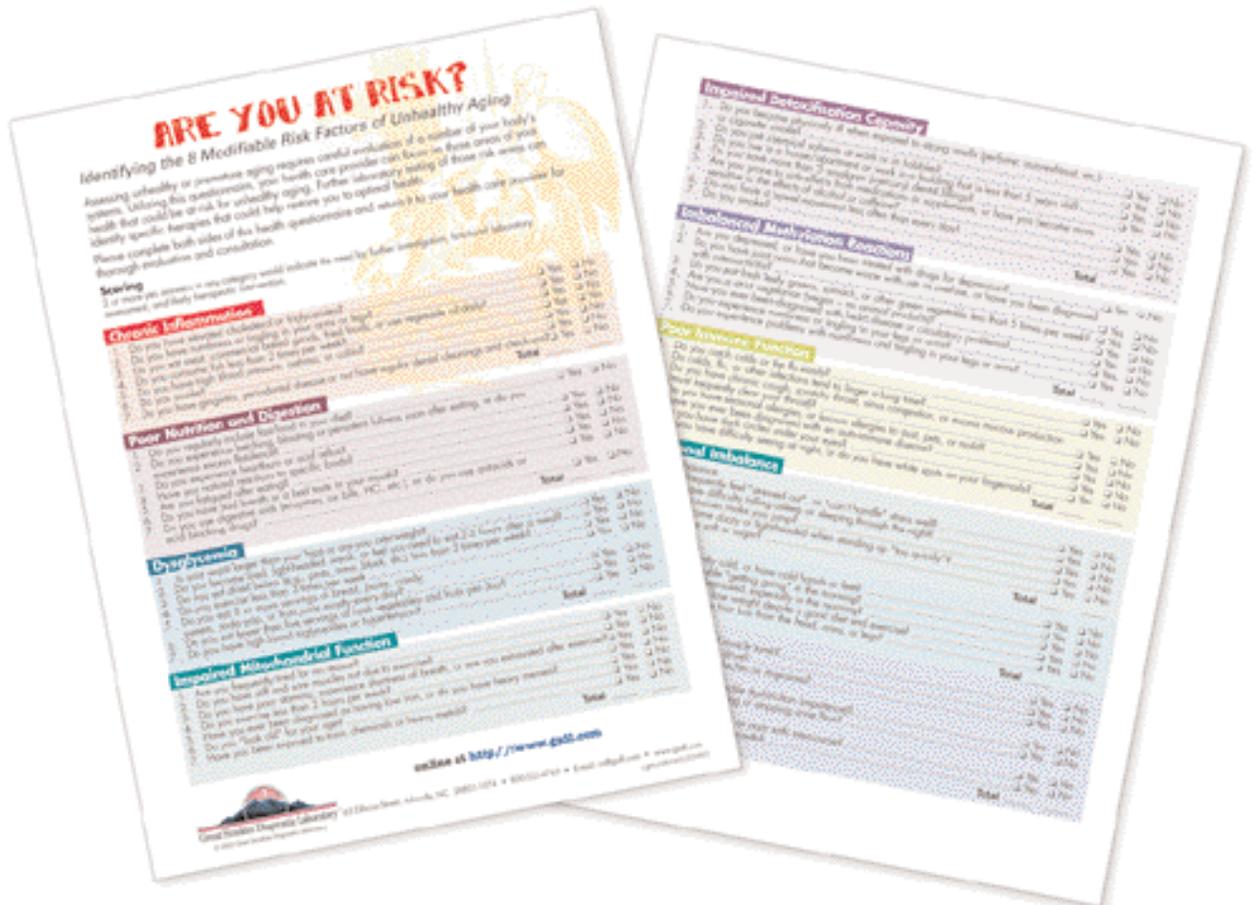
The key to successful implementation of an “optimal aging practice” is the efficient assessment of the underlying physiological imbalances in your patients.

Choosing from an increasing array of functional laboratory assessments can be a clinically daunting task. Here are three practical tools that allow a practitioner to choose appropriate functional tests relative to the eight modifiable risk factors for sub-optimal aging.

The first tool is a two-page functional assessment questionnaire. It can be administered to a new patient, to

an initial evaluation, or to a current patient, to provide more specific analysis of a condition. The questions are divided into the eight modifiable risk factors of optimal aging with yes/no answers. This format allows the practitioner to quickly pinpoint areas of highest metabolic or functional impairment that may require further investigation through laboratory assessment.

The second tool is a chart listing appropriate laboratory assessments based on the age of the patient. This is an excellent screening tool for identifying areas of physiological imbalance that tend to become more prominent at specific age intervals. It is also a good starting point for assessing patients who come to your office



THE FUNCTIONAL PERSPECTIVE

The third tool correlates common presenting symptoms with laboratory functional testing appropriate to the condition. Each correlation includes a rationale for choosing specific laboratory tests. This tool may be used most effectively for those patients coming in to a practice with a specific condition that requires clinical attention. Using this tool, each presenting condition can be assessed from an optimal aging perspective.

These tools provide the practitioner with an easy and practical system for implementing functional diagnosis relative to eight significant optimal aging parameters - a system designed to keep you on the leading edge of preventive health care.

Bradley S. Rachman, D.C., D.A.B.P.M., is a world-renowned lecturer who has developed innovative courses for patients and practitioners alike. As Director of the Department of Medical Science, Dr. Rachman is inspiring new and exciting medical education programs at GSDL.

FUNCTIONAL CORNERSTONES OF HEALTHY AGING		
When	Functional Test	Rationale for Testing
Any Age	Elemental Analysis Hair, ECG, Urine Challenge	Functional Mineral Reserve Toxic Metal Burden
	Oxidative Stress	Free Radical Load Antioxidant Reserve
	Adrenal Stress	Stress Adaptation Acid-Base Balance
	Essential Fatty Acids (BCC membrane)	Inflammatory Tendency Smooth Muscle Reactivity Brain & Nerve Health
	Digestive Stool Analysis	Comprehensive Assessment of Digestion, Absorption, and the Colon's Microenvironment
	Intestinal Permeability	Leaky Gut Syndrome and Malabsorption
	By Age 40	Comprehensive Cardiovascular Assessment
Dysglycemia		Insulin Resistance Syndrome X
By Age 45	Bone Resorption	Rate of Bone Loss
	Hormone Profile	Individualize Hormone Tx Evaluate Risk of Heart Disease, Alzheimer's, Osteoporosis, and Breast Cancer
	T & Thyroid Function	Further Evaluation of Breast Cancer Risk

CONDITION-SPECIFIC FUNCTIONAL TESTING		
Symptom	Functional Test	Rationale for Testing
Fatigue	CBC with Iron Series Adrenal Stress Thyroid	Anemia Stress Adaptation Central and Peripheral Thyroid Activity & Auto-Immunity
		Mitochondrial Health Microsulfur Catabolism Citric Acid Cycle
Joint Pain		Prostaglandin, Serotonins, and Transamine Production
		Insulin Resistance, Diabetes Stomach Metabolism Food Sensitivity
Headaches		Neurotransmitter Precursors Vitamin & Mineral Cofactors DNA and Membrane Fluidity
		Androgen Levels
Heart Disease		Improved Hepatic Detoxification Phase I and Phase II
		Sufficient Androgens
Weight Gain		Growth Hormone Production Catabolism vs. Anabolism Protein Deficiency Malabsorption or Calorie Deficiency

Great Smokies Synaptic Laboratory 11200a Great Smoky, NC 28611-1074 • 800.222.4742 • Email: info@gSDL.com • www.gSDL.com
© 2008 Great Smoky Synaptic Laboratory

Need more copies of these helpful guides?

Your copy of this issue includes an insert with the materials Dr. Rachman describes. If you need additional copies, visit our web site (www.gSDL.com) where the questionnaire, the age-based laboratory assessment chart, and the condition-based laboratory assessment guide can be downloaded in PDF format.



The Challenge in Women's Health: Understanding the Biological Differences

By Elizabeth Lipski, Ph.D., C.C.N.



"Sex-specific medicine is not only about how women respond to disease and treatment differently than men. It's also about improving how health care providers respond to those differences."

Phyllis Greenberger, M.S.W., president and CEO of the Society for Women's Health Research (<http://www.womens-health.org/about/0frameset.htm>)

For much of our history, healthcare practitioners have found it tempting to discount women's treatment challenges as the consequences of

hysteria, depression, and other psychosomatic factors. Although the situation is improving, even today women's complaints aren't always taken as seriously as men's - or understood nearly as well. As a result, the quality of healthcare for women has lagged, impacting accessibility and hampering research efforts.

A new study from the Netherlands, for example, reports that women with Rheumatoid Arthritis (RA) were more likely than men to have a delay in referrals to specialists, even though disease activity was similar in both sexes. Similarly, an Austrian study reported that women take longer to access coronary angiogram than men, despite free access to services in that country's medical system.

although results were widely extrapolated for women's treatment. Despite new guidelines issued by NIH in 1990, a significant portion of non-sex-specific research still does not include women and only about 1/4 to 1/3 of recent research analyzed data or results by the sex of the subjects.

Opportunities for Improving Outcomes with Functional Assessment

In addition to hormone testing and evaluation of estrogen metabolism, there are now many functional tests available to help determine the underlying causes and triggers for chronic health conditions in women patients. Depending on the genetic, lifestyle, and environmental factors involved, each person's unique biochemistry will determine which tests are of highest priority. For example: Urinary bone resorption assessment is a useful test for early identification of bone loss and to monitor whether treatment is preventing further bone loss and development of osteoporosis. It can be used in conjunction with bone mineral density to evaluate the various factors that can contribute to bone fracture as a woman ages.

Thyroid dysfunction has been reported to be three times as high in women with rheumatoid arthritis (RA) as in women with non-inflammatory rheumatic diseases such as osteoarthritis and fibromyalgia. Some RA patients benefit from treatment of food and environmental sensitivities. And others improve after effective treatment of dysbiosis and intestinal permeability. RA has especially been linked with a genetic predisposition and Proteus bacteria as a trigger for the illness.



As recently as 1984 the National Institutes on Aging published a study using data derived only from men and called it "Normal Human Aging." Prior to 1990 women were rarely subjects for research,

There is evidence that women with cardiac conditions can present differently than men. Some 50% of women but only 17% of men who undergo diagnostic cardiac catheterization turn out to have normal coronary arteries – indicating that as much as 50% of the time chest pain in women is due to some other cause(s). Assessment of mineral status and of independent cardiovascular risk factors, such as homocysteine, fibrinogen, Lp(a), and C-reactive protein, can be used to detect other factors contributing to chest pain.

Although Chronic Fatigue Syndrome (CFS) and fibromyalgia (FM) are distinct entities, they have many common characteristics in terms of symptoms, diagnosis, and treatment. Several studies have reported a high incidence of food sensitivities, leaky gut syndrome, and thyroid autoimmunity in FM and CFS.

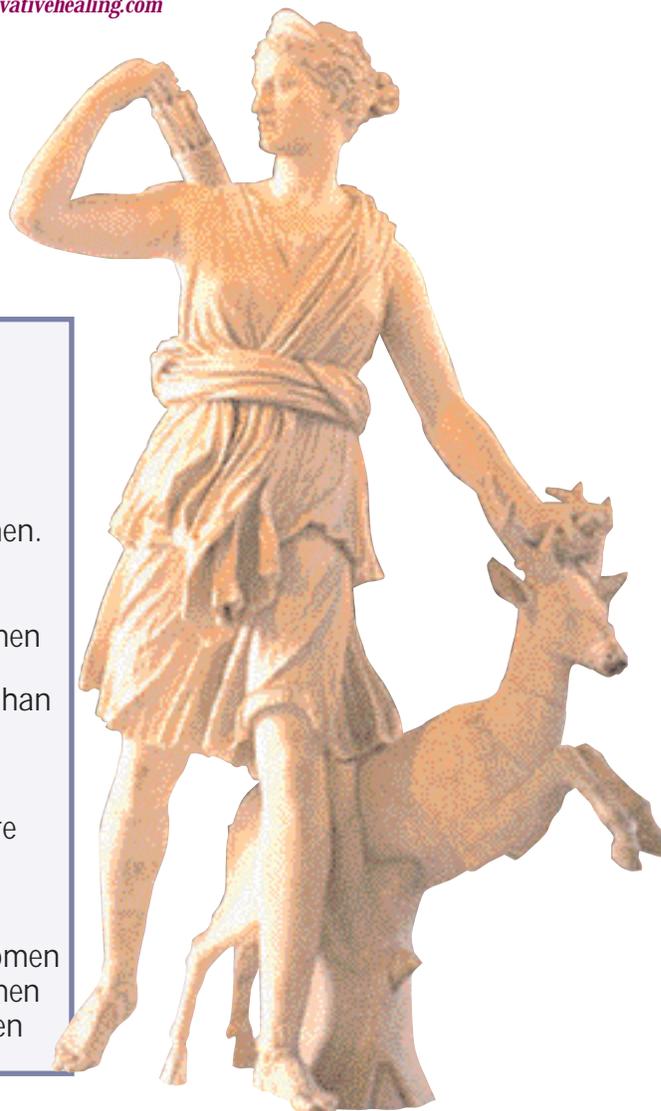
It's Worth Looking a Little Deeper

For all of these reasons, it's important to really listen to your women patients and become sensitive to the implications of sex-

specific health patterns. Women with treatment-resistant conditions are not plagued with psychosomatic illness. In fact, clues to their complaints can often be discovered by functional analysis and an integrative medicine approach to treatment. Great Smokies can greatly assist in this process with a range of functional assessments for getting to the physiological roots of women's treatment challenges.

Note: Due to space limitations, references for this article will be included with the online version at www.gsdl.com

Elizabeth Lipski, Ph.D., C.C.N., is a clinical nutritionist in practice on the island of Kauai, HI. She is the author of Digestive Wellness and Leaky Gut Syndrome. Her website: <http://www.innovativehealing.com>



Just How Different Are Women?

- 80% of the population with Osteoporosis are women.
- 75% of people with Lupus are women
- Twice as many women as men have arthritis
- Hypothyroidism is 10 times more prevalent in women than in men
- Fibromyalgia is 9 times more prevalent in women than in men
- Chronic Fatigue Syndrome is three times more common in women than in men
- Migraine headaches affect women three times more than men
- Women experience more pain with greater severity overall than men
- Interstitial cystitis is almost exclusively found in women
- Multiple sclerosis occurs more in women than in men
- Endocrine imbalance affects women more than men

A Marriage of Theory and Practice: GSDL's New Individual Case Management Research Program

By Patrick Hanaway, M.D., with John Furlong, N.D.



Comprehensive, research-oriented and user-friendly; this is the concept behind GSDL's research into functional assessment and interventions in our Individual Case Management (ICM)

Research Program. This Research Program is designed to study the impact of functional medicine approaches on illness and wellness. We provide participants with the best tools to improve their health and well-being, as we measure which biochemical parameters are modifiable and which changes lead to improvement in health status. ICM is an essential component of GSDL's ongoing commitment to improve evaluation and treatment of individuals in the clinical setting.

This integration of combined nutritional research with objective outcome measures provides important insight into effective functional medicine treatment strategies. The ICM Research Program will grow to include a number of clinical topics and participants, thus making GSDL one of only two facilities (along with the Institute of Functional Medicine in Gig Harbor, WA.) performing clinical research on combined nutritional therapies. The ICM Research Program also has the potential to enhance health benefits for GSDL employees and to provide a model for a truly prevention-based comprehensive health and wellness plan for other organizations.

Phase One: Women in Mid-Life

In our initial study, we are working with a cohort of peri-menopausal women with climacteric symptoms, who are not

currently on Hormone Replacement Therapy (HRT). These women receive a wide variety of evaluations, including: medical history and physical examination; anthropometric measurements; laboratory testing for hormone balance, cardiovascular risk, bone resorption, dysglycemia, thyroid function, toxic and nutrient elements, fatty acid profiles, and digestive health. In addition, participants complete an extensive symptom questionnaire, quality of life measure [SF-36], and computer-assisted cognitive testing.

These comprehensive measures enable GSDL doctors to develop an individualized health and metabolic 'fingerprint' for each participant. This profile is then used to determine the most important areas to address clinically. Department of Medical Science (DMS) practitioners research and consult as a group to arrive at a plan that best fits the participants' individual needs. I serve as the medical director of this innovative program, and in collaboration with DMS staff physicians, I oversee the medical concerns of each participant and determine the best intervention for that individual.

The ICM Research Program evaluates the laboratory measures and outcome measures of functional status for each participant in response to the following interventions: Diet, Vitamin/Mineral Supplementation, Exercise, Herbs, and Hormones. Recommended products are provided to the participants, who stay in close communication with staff physicians and Kay Patrick, GSDL's Clinical Research Coordinator – the "heart" of our program. Follow-up testing of all parameters is provided at appropriate intervals.

At press time, statistical analysis of the ICM data was still on-going, with a final report on the correlation of laboratory analyte values with outcome results scheduled for publication in our next issue of the Smokies Digest. The final report will include a comprehensive evaluation of the improvement of 250 analytes throughout the study period for each of the six participants.

Initial evaluation of outcome measures has already demonstrated that the treatment program was successful in producing improved outcomes for participants:

- ☛ 12% improvement in post-treatment scores on Great Smokies' proprietary Functional Medicine Index over pre-test values

- ☛ More than 6% improvement in post-treatment scores on the SF-36 Health Survey (Version 2) – 6.28% Physical Summary, 6.36% Mental Summary

- ☛ 15.3% improvement on the Kupperman Index

Evaluating Outcomes

Objective changes in laboratory testing are correlated with validated measures of each participant's functional outcome and quality-of-life. The integrated treatment plan benefits the whole person; thus we evaluate overall health and wellness as well as improvement in disease-specific symptoms. The ICM Research Program uses a prospective, clinical research design applying functional medicine testing and functional outcomes research to evaluate the efficacy of applied nutrition and botanical interventions. This research also allows GSDL to develop a database of clinical cases (while maintaining patient confidentiality) and analyze participant response to treatment.

Preliminary findings after three months of treatment indicate that our targeted interventions have helped our cohort to realize improvement on several measures of health and wellness. When this phase of the research project is complete, final results will be shared through regional Achieving Clinical Excellence (ACE) Seminars and educational venues offered to clinicians across the country.

Advancing the Functional Medicine Model of Holistic Treatment

The ICM Research Program is part of GSDL's ongoing effort to provide practitioners with real-life applications of functional medicine. GSDL stands as a leader in functional medicine research and education, as we provide case histories, prospective clinical research, test refinement, controlled clinical trials, and retrospective analysis. Applying the objective results of applied nutrition and botanical medicine is a stellar example of GSDL's commitment to make the cutting edge of functional medicine available to physicians around the world.

Patrick Hanaway, M.D., a graduate of Washington University Medical School in St. Louis, Dr. Hanaway is in private practice with Family to Family in Asheville, N.C., and serves as a consultant with Great Smokies for the ACE training and ICM research programs. He is board-certified in family practice and proficient in nutrition, herbology, and several alternative and complementary therapies.

John Furlong, N.D., spent ten years in private practice prior to joining the educational staff of Great Smokies in 1996. He provides practical and technical support for our clients, especially in the areas of women's health, metabolic assessment, and elemental analysis.

"This integration of combined nutritional research with objective outcome measures provides important insight into effective functional medicine treatment strategies."

Structured Assessment Instruments for Pre- and Post-Treatment Evaluation

The Standard Form 36 (SF-36) Health Survey is a widely used multi-purpose, 36-question generic measure of physical and mental health. Its eight-scale profile of scores with physical and mental health summary measures was developed in 1988 and standardized in 1990. By 1999, it had been documented in nearly 1,500 articles and reports, including reports of nearly 200 randomized controlled trials. Ratings on the SF-36 have repeatedly been correlated to healthcare expenditures, hospitalization, and morbidity/mortality, making it a powerful tool in preventive medicine. Up-to-date information about the SF-36 is available online at www.sf-36.com

The Kupperman Index is an assessment of symptoms summarized in a menopausal index. It includes such complaints as hot flashes, sweating, sleep disturbances, nervousness, depression, irritability, vertigo, fatigue, arthralgia, headache, tachycardia, and vaginal dryness. To minimize human variability in testing, it is generally administered by the same practitioner at pre- and post-treatment. It is described in greater detail by Wiklund I et al. A new methodology for evaluating quality of life in postmenopausal women during transdermal estrogen replacement therapy. *Maturitas* 1992;14:211-24.

The Functional Medicine Index is a 300+ item health status questionnaire created by the Department of Medical science as a quality control tool for selecting participants in reference range studies.

Improving Estrogen Metabolism for Healthy Aging – One Woman's Odyssey

By Kashi Rai, M.D.

"Because of the competing nature of the 2-hydroxylation and 16 α -hydroxylation pathways, a ratio of the metabolites 2-OHEstrogen and 16 α -OHE1, 2:16 α -OHE1, has been used as a biomarker for breast cancer risk.... Recent studies showing that the ration is significantly decreased in women with breast cancer further support this hypothesis."

Haggans CJ et al. Cancer Epidemiol Biomarkers Prev 2000;9(7):719-25.



My first consultation with Rachael D. (not her real name) took place in November 2001. Rachael is a 64-year old woman of average weight who expressed

concern about symptoms of hormone imbalance, cardiovascular disease risk (based on consistently high levels of total and LDL cholesterol), elevated liver enzymes, and breast cancer risk.

She has had a long history of various hormone replacement treatments since her hysterectomy in 1968. Her mother was diagnosed with breast cancer in her seventies, which sent a strong message to Rachael about her own possible risk.

She is a long-time non-smoker, exercises moderately, and is a light drinker. She is careful about her diet and has regular consultations with a nutritional counselor in Florida, where she lives with her husband. She and her husband regularly travel to the New Orleans area, and, on the advice of family friends, she scheduled an examination and initial consultation with me during a visit with family here. At her request, her physician in Florida had sent me results of tests run earlier.

Workup

During my workup, I learned that Rachael's current HRT regimen included Biest 2.5 mg/d, 2% testosterone cream in the morning, and 50 mg/d progesterone in the evening. She was also supplementing with garlic and red rice yeast extract. Recent health problems included a root canal six months earlier and shingles the month before she saw me. She complained of hot flashes, disrupted sleep, irritability and mood swings, and night sweats.

Based on her presentation and some of the test results from Florida, I ordered routine blood chemistry, tumor marker and hepatitis titers, and liver enzymes from a reference laboratory. I also ordered Great Smokies' Women's Hormonal Health Assessment (WHHA). Because of a significantly elevated hair antimony on an earlier test, I included a Comprehensive Detoxification Profile to explore the possible connection between her symptoms and potential toxic exposure.

Results (see Figure 1) indicated that most of the markers on the WHHA were within normal range (most within Functional Physiologic Range as well). Although the markers 2-hydroxyestron (2-OHE1) and 16 α -hydroxyestron (16 α -OHE1) were "normal," the 2-OHE1:16 α -OHE1 ratio could clearly be improved.

I decided to adjust her HRT formulation, reducing her estriol and dosing every other day while maintaining the level of her estradiol, testosterone, and progesterone. I also prescribed an increase in indole-3-carbinol (found in cruciferous vegetables, such as broccoli and Brussels sprouts) to



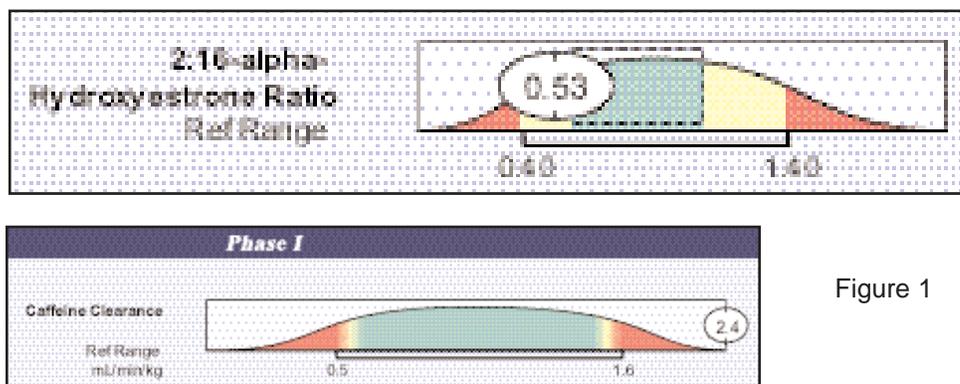


Figure 1

address both her hormone-related symptoms and improving her risk profile in regard to estrogen-dependent diseases (such as breast cancer).

Although her blood chemistry and liver markers were normal to slightly elevated, her Phase I caffeine clearance was significantly increased above the reference range (Phase II was normal). Reduced glutathione was at the lower limit of the reference range and superoxide dismutase was below reference range. I suggested that she try to avoid situations that could lead to pesticide exposures, be careful to ask about future medications that could tax her cytochrome P450 detoxification pathway, and continue taking her supplements of quercetin (500mg BID) because of its favorable affects on Phase I.

Follow-up

When Rachael returned to New Orleans in January of this year, I saw her once again and order a followup WHHA to monitor her estrogen metabolism. The treatment plan had improved her self-assessment of her symptoms. She reported feeling more “even” in her mood, sounder sleep, fewer and less severe hot flashes, and absence of night sweating. Boosting the estradiol content of her HRT had temporarily made her breasts tender, but her relatively high progesterone formulation had moderated that side effect.

Her test results (see Figure 2) showed a significant increase in 2-OHE1 levels to 448 pg/ml and a marked increase in her 2:16a-OHE1ratio to 1.28. There was little change in her 16a-OHE1 levels. Based on several clinical studies, her ratio suggests reduced risk for breast cancer.

In the future, I would like to see her increase the level of her physical activity to see how it would affect values in the future. Although I am not especially concerned about elevations in 2-OHE1 and the 2:16a-OHE1ratio, lower levels of the analytes and ratio (to within reference range values) would be preferable, ensuring optimal bone integrity metabolism.

Rachael’s persistent elevations of total and LDL cholesterol – along with lower than optimal HDL cholesterol – remain concerns. She is hardly “high-risk,” and she had normal results on homocysteine and thyroid testing, but her lifestyle and diet have not been able to influence these markers significantly.

Kashi Rai, M.D., is in private practice at For Better Health in Metairie, LA. She completed college and medical school at Louisiana State University and a residency in family practice in New Orleans. As part of a holistic approach to health, she is also concerned with helping patients achieve personal growth and self-empowerment in the course of the healing process.

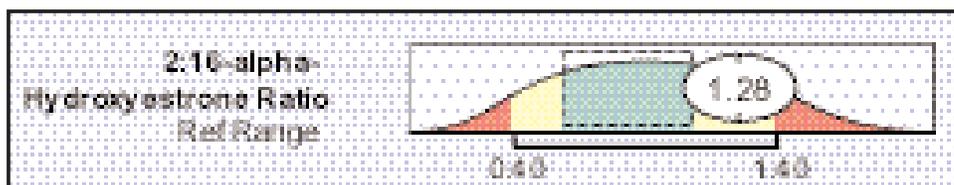


Figure 2

Diagnosing Digestive Conditions in the Elderly

By Corene Humphreys, N.D.

"The mortality attributable to gastrointestinal infection is 400-fold greater among elderly people than among younger adults."

Cusack MA et al.
Giardia in older people. Age and Aging 2001;30:419-21.



Many elderly patients present with such vague and generalized symptoms, that it can be difficult initially to determine the etiology of their complaints. Studies have found that conditions such as diarrhea, malabsorption, and parasite infestation are far more common in this age group than previously thought. Because symptoms such as anemia, low folate/B12 status, cachexia, and failure to maintain normal body weight can be due to factors other than age-related physiological changes, older patients with these conditions need to be thoroughly investigated in order to rule out underlying pathology.

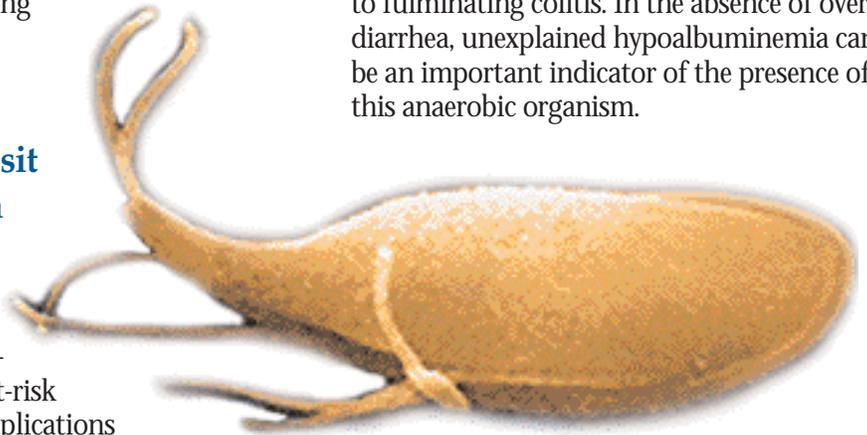
Diarrhea – Increased Transit Interferes with Digestion

Traditionally, children have been considered the major at-risk group for fatal complications from diarrheal disease. A 1999 report, however, actually found a mortality rate five times higher in patients older than 74 years of age. Charting hospital trends of gastroenteritis for 16 years, the report estimated a total of 1600 hundred fatalities a year in the elderly from diarrheal disease.

Because of understandable embarrassment about possible fecal incontinence, older patients may be reluctant to discuss their symptoms. They also may not realize that the condition may include more than the “classic” symptoms of abnormal frequency, liquidity of stools, or rectal urgency. Indeed,

experiencing three or more bowel movements a day without excess fluid can also be considered as diarrheal condition possibly linked to malabsorption or other symptoms.

When symptoms have been present less than two weeks, intestinal infection may be present - caused by bacteria, parasites, or virus. It has been estimated that up to one-third of elderly people in long-term care facilities have a positive stool assay for *Clostridium difficile*, which may be the result of increased use of antibiotic therapy, rather than age-related changes in Mucosal Associated Lymphoid Tissue (MALT), neutrophil function, and cellular immunity. Symptoms can range from asymptomatic or mild diarrhea to fulminating colitis. In the absence of overt diarrhea, unexplained hypoalbuminemia can be an important indicator of the presence of this anaerobic organism.



Infections from the parasite *Giardia* can also have highly variant clinical manifestations. The elderly may present with only vague GI symptoms, weight loss, and anemia, or they may experience acute diarrhea requiring hospitalization.

Malabsorption – Robbing the Elderly of Essential Nutrients

Although recent studies suggest that adverse changes to the small intestinal villus structure are a consequence of a disease process affecting the gut, which can occur irrespective of age, there are subtle

developments that may affect malabsorption syndromes among older patients. Changes in brush-boarder membrane integrity, for example, have been documented with advancing age. This could explain the increase in lactose intolerance that accompanies age, though the conditions may also be attributed to genetic defects in lactase production exacerbated by the changes in eating patterns or the introduction of new forms of processed foods with lactase additives.

Hypochlorhydria and achlorhydria are common in the elderly, and can lead to important nutrient deficiencies. Reduced folate conjugase activity in the intestine can occur as a consequence, as can a vitamin B12 deficiency. Low B12 levels can also occur from reduced secretion of intrinsic factor, atrophic gastritis, drugs which suppress HCL production, and small bowel overgrowth. Low serum folate and B12 levels can therefore be indicative of reduced HCL production.

Hypochlorhydria creates a favorable environment for the overgrowth of organisms in the small bowel. This can result in

nutritional deficiencies due to increased numbers of bacteria metabolizing dietary nutrients before absorption can occur. A small bowel overgrowth may also be asymptomatic in the elderly (though with severe overgrowth, diarrhea, abdominal bloating, and pain can occur).

Just Part of the Normal Aging Process, or Something More?

Not all vague symptomology in the elderly can be attributed to a physiological decline in health. As discerning physicians, we need to thoroughly investigate even the subtlest symptoms of ill health in the elderly, for they can provide vital clues as to the underlying cause of their illness. Without identifying the true cause of disease, the health and well being of the elderly may be severely compromised, which can ultimately lead to more severe pathology and steady erosion of quality of life.

Prior to joining Great Smokies' Department of Medical Science, Corene Humphreys, N.D., practiced as a Naturopath and Medical Herbalist in New Zealand. She has also received diplomas in medical laboratory technology, homeopathic medicine, and therapeutic massage.

Useful Laboratory Studies Include:

- Comprehensive Digestive Stool Analysis and Parasitology Profile (CDSA/P) can help to reveal the underlying cause of diarrhea, and includes identification of pathogenic bacteria (from direct culture), as well as Enzyme Immunosorbent Assay (EIA) testing for pathogenic organisms and parasites. The panel also includes Digestive Functional Analysis.
- Digestive Function Analysis examines the stool for the presence of meat and vegetable fibers as well as triglycerides, valerate, iso-butyrate, and chymotrypsin, reflecting pancreatic and stomach function. An additional four analytes are used to assess absorption, and include: LCFA's, Cholesterol, total cholesterol and short chain fatty acids.
- Lactose Intolerance Breath Test is a simple, non-invasive measurement of hydrogen and methane breath samples following a challenge drink of lactose to reveal impairment in the metabolism of this disaccharide.
- Bacterial Overgrowth of the Small Intestine Breath Test to detect anaerobic organisms in the small bowel is an analysis of breath samples for the presence of hydrogen and methane following a challenge drink of lactulose.

Recent Developments in

Metabolic Analysis Profile Release, Fatty Acid Enhancements

By Missy West, Product Manager

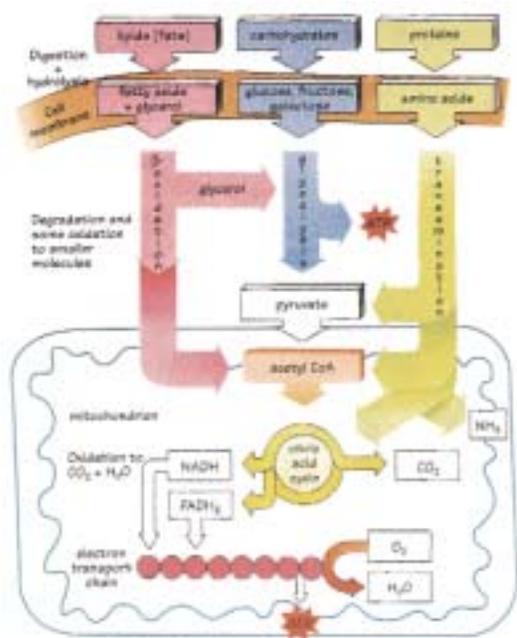


Our long-awaited panel of organic acids and related metabolites is now online with 39 analytes related to digestion, nutrient co-factor adequacy, neurotransmission, and cellular energy production. This is quite a remarkable test in that it measures downstream analytes of metabolic processes in a single urine sample. The test is thus capable of providing prima facie evidence of metabolic irregularities that may not be apparent from assessment of more conventional, proximate markers alone.

Although measurement of organic acids has long proven diagnostic for in-born errors of metabolism and for gross insults to metabolic balance, the test can also provide clinically

useful information in less acute situations, such as the chronically unwell patient with “normal” test results. For these patients, the Metabolic Analysis Profile can help practitioners finally locate the “smoking gun” responsible for a chronic condition. To provide as much clinical utility as possible, we support this test with extensive commentary, ranges for children and adults, and our unique “Interpretation at a Glance” test report.

We have also expanded the reference range and revised the test report for Essential and Metabolic Fatty Acids (EMFA) Analysis. Results have been reorganized and we’ve introduced new specialized sections and indices to clarify the clinical significance of test results. On the report, each patient’s results will also be directly related to key pathological mechanisms of inflammation, membrane fluidity, oxidative stress, enzyme activity, and insulin resistance. Moreover, the new EMFA test report is the latest of a growing number of reports offering the Functional Physiologic Range (FPR) feature to help patients and practitioners evaluate results in terms of optimal health and well-being.



Expanding Digestive Testing – Analysis of Breath Samples for Clues In IBS And IBS-like Symptoms

By Jeff Ledford, Product Manager



complaints, such as probiotic supplementation

Malabsorption syndromes can be especially difficult for patients – and for the practitioners who try to find the root causes. Some of the treatments that are often very effective for digestive

and fiber, may only make them worse. Patients may present with “textbook” Irritable Bowel Syndrome (IBS) – or with clusters of IBS-like symptoms that are no less mysterious in origin or difficult to treat.

However, the true culprits may actually be two common, but under-diagnosed conditions –small intestine bacterial overgrowth (BOSI) or

Laboratory Assessment

lactose intolerance (LI). BOSI and LI can both produce IBS-like symptoms, masking the true cause of the conditions.

BOSI is frequently a complication of parasite infection and is associated with pancreatic insufficiency secondary to chronic pancreatitis. Incidence of the condition increases with age and is possibly the major cause of clinically significant malabsorption and failure to thrive in the elderly. LI occurs in people who cannot absorb lactose or do not produce sufficient lactase, the enzyme that breaks down lactose into smaller, more easily digested molecules. These patients often experience chronic gastrointestinal symptoms and abdominal pain up to several hours after consuming foods containing lactose.

Our new tests for these conditions both involve the ingestion of a challenge sugar (lactulose for BOSI or lactose for LI) and measurement of hydrogen and methane in the breath after set intervals. This non-invasive assessment offers practitioners an attractive alternative to biopsy for diagnosis.

Work continues on additional markers for the Comprehensive Digestive Stool Analysis. Watch for announcements of specific enhancements during the next few months.



A Urine Alternative In Assessment of Estrogen Metabolism

By Deborah Shepard, Ph.D., Product Manager



Although our single-sample serum assessment of the metabolites 2- and 16alpha-hydroxyestrone (2-OHE1 and 16alpha-OHE1) has proven to be very popular, from the outset we had requests for an alternative measurement

of urine. However, not just any urine test would do. Clients who wanted the flexibility of urine to avoid blood collection in the office also wanted convenience. The conventional 24-hour collection just wouldn't do.

To satisfy this need, we've developed and fully validated an Estrogen Metabolism Assessment that assays the first urine of the day for 2-hydroxyestrone (2-OHE), of which 2-hydroxyestrone is the predominant metabolite, and 16alpha-OHE1. The analytes are referenced to creatinine to adjust for urine volume. Along with levels of the analytes and an Estrogen Metabolism Index, the test

reports the 2-OHE:16alpha-OHE1 ratio that has been associated with risk for (and, in some cases, progression of) estrogen-dependent diseases, such as breast and neck cancers, lupus, and osteoporosis.

The test can be especially useful for monitoring a patient's progress in a treatment program of nutritional and lifestyle changes to modify the ratio. Indole-3-carbinol containing vegetables, such as broccoli and Brussels sprouts, soya, flax, and exercise have been shown to influence the ratio (and disease risk) favorably.

Like our serum version, the Estrogen Metabolism Assessment, Urine can be used with both premenopausal and menopausal patients, including those using hormone replacement therapy. Our laboratory physicians recommend that the same sample be used for initial assessment and follow-up for greater ease of interpretation.



Methylation: the “Linchpin” of Healthy Aging

By Mary James, N.D., with David Perlmutter, M.D.



Methylation can be viewed as an overtaxed and under-appreciated workhorse in the body. This simple transfer of a methyl group (CH₃) from one molecule to another turns out to be one of the primary determinants

of health and disease. Indeed, almost all of the disorders common to aging are caused or exacerbated by deficiencies of the body's main methyl donor, S-adenosylmethionine (SAME), or by excess homocysteine (Hcy) resulting from impaired methylation.

Methylation is a biochemical process that begins with dietary methionine. With the help of magnesium and adenosine triphosphate, methionine is converted to SAME. When SAME donates a methyl group, it metabolizes into Hcy. Hcy is not a bad thing in or of itself. Like cholesterol, it only causes problems if allowed to accumulate. Assuming the availability of cofactors like vitamins B6, B12, folic acid, and serine, Hcy is recycled to methionine, and the cycle can then repeat itself. Betaine is an alternate cofactor that facilitates methionine recycling by donating a methyl group. Via B6, Hcy can also enter the transsulfuration pathway to become cysteine and taurine. With deficiencies of these cofactors, (common in a fast-food, meat-based diet), Hcy accumulates, with detrimental effects throughout the body.

Progression to Diseases of Aging

The link between increased blood levels of Hcy and cardiovascular disease is well documented. Levels of Hcy tend to increase with age, and as they rise, hydrogen peroxide is generated, leading to oxidation of LDL and blood vessel endothelium. Less well-known associations with high Hcy include neurological disorders.

Depression, multiple sclerosis, cognitive decline in the elderly, Alzheimer's and Parkinson's disease have all been linked to excess Hcy and alterations in B6, B12, or folate metabolism.

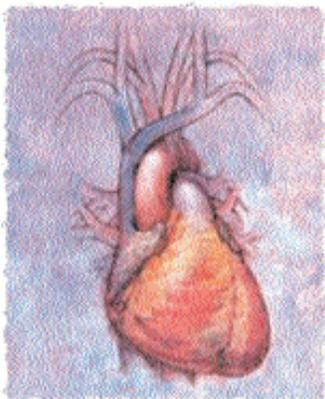
In many of these conditions, synthesis of SAME is impaired. Methylation is vital to the maintenance of the myelin sheath, to the turnover of catecholamines and neurotransmitters, and to the production of phosphatidylcholine, coenzyme Q10, and melatonin. SAME as a supplement has been successfully employed as an anti-depressant since the '70s, often outperforming tricyclic anti-depressants in studies. It is interesting to note that poor clinical response to Prozac goes hand in hand with low folate levels. In fact, researchers have suggested that folic acid might improve the effectiveness of antidepressants. But doesn't it make more sense to directly address the source of the metabolic problem?

Since the central nervous system (CNS) lacks the alternate betaine pathway to remethylate Hcy, the CNS has a reduced methylation capacity and is particularly vulnerable to Hcy's toxic effects. Hcy's neurotoxic actions are thought to result from its interaction with the N-methyl-D-aspartate receptor, resulting in excessive calcium influx, free radical production, and possible cell death. Ironically, many of the routine medications prescribed for some of these disorders only tend to exacerbate them by further raising the levels of Hcy.

Excess Hcy has also been linked to other disorders commonly associated with aging, including obesity, cataracts, osteoarthritis, rheumatoid arthritis, non-insulin-dependent diabetes, and cancer. Deficient SAME has been shown in animal studies to cause DNA strand breaks in certain areas of the tumor suppressor gene p53. With a defective p53 protein, certain cancer cells can grow out of control. Breast

"...there is a strong, graded association between plasma total homocysteine levels and the risk of dementia and Alzheimer's disease. An increment in the plasma homocysteine level of 5 μmol per liter increased the risk of Alzheimer's disease by 40 percent."

Seshadri S et al.
Plasma homocysteine as a risk factor for dementia and Alzheimer's disease.
N Engl J Med
2002;346(7):476-83.



cancer is also more likely to develop with undermethylation, as it is the methylation of estrogens that produces the methoxyestrogens (downstream from the 2-hydroxyestrogens) so critical to breast cancer protection. Plasma levels of Hcy tend to be higher in postmenopausal women compared with premenopausal and pregnant women, suggesting a close relationship between Hcy metabolism and estrogen status.

Targeting Pathways and Monitoring Treatment

Laboratory assessment provides an easy means of detecting hidden disruptions in methionine metabolism. Hcy is a critical marker on the Amino Acids Analysis. This profile also includes measurements of methionine, cystathionine, serine, cysteine, and taurine, whose patterns of imbalance

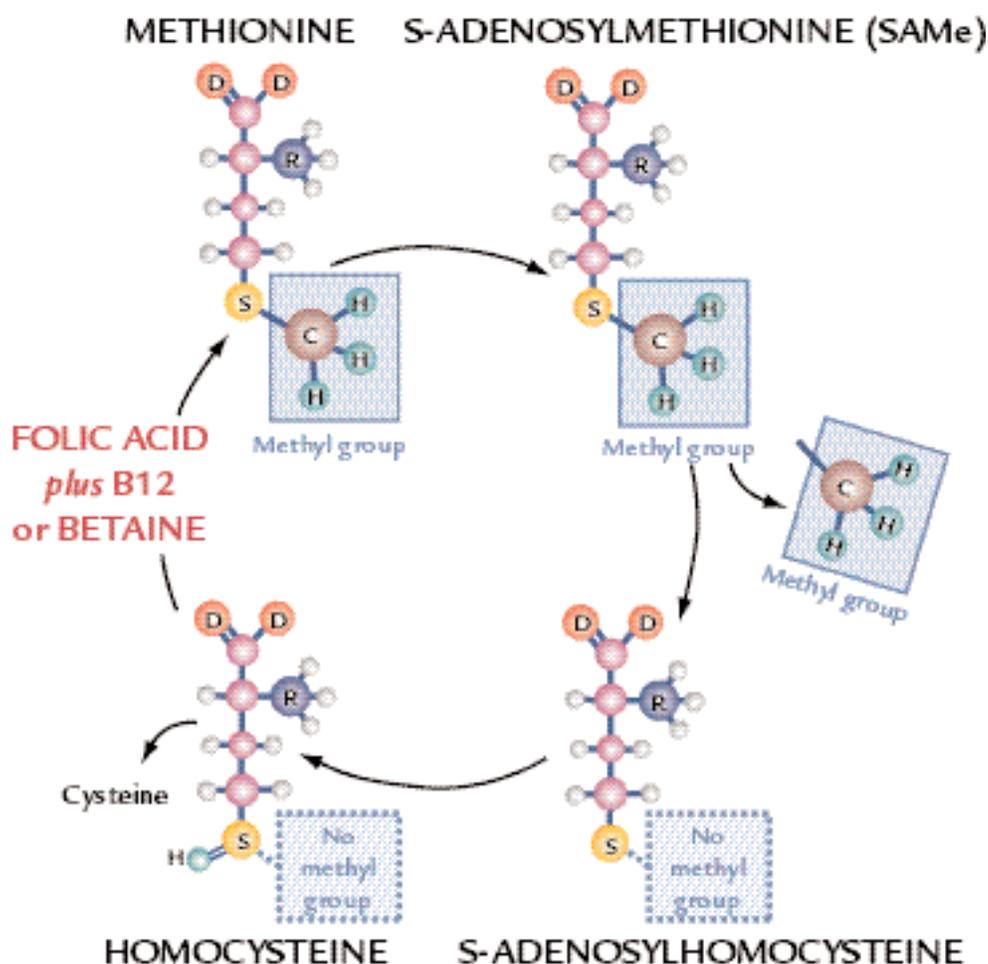
may hint at low levels of the critical nutrient cofactors. Hcy is also measured as an independent risk factor in the Comprehensive Cardiovascular Assessment. "Loading" the body with a prescribed amount of L-methionine may help to reveal impairments that might otherwise be missed.

A graduate of National College of Naturopathic Medicine, Mary James, N.D. was in private practice before becoming a nutritional consultant for a supplement manufacturer. With more than seven years experience at GSDL, she is our senior laboratory physician and has consulted with clients on thousands of test reports.

David Perlmutter, M.D., is a board-certified neurologist who practices in Naples, FL and currently serves as adjunct Professor at the Institute for Functional Medicine. In addition to his many contributions to peer-reviewed medical literature, Dr. Perlmutter has written several books, including BrainRecovery.com - Powerful Therapy for Challenging Brain Disorders.

"Researchers have suggested that folic acid might improve the effectiveness of antidepressants. But doesn't it make more sense to directly address the source of the metabolic problem?"

METHYLATION



DRUGS WHICH CAN RAISE HOMOCYSTEINE

valproic acid
 trimethoprim
 triamterene
 phenytoin
 phenobarbital
 primidone
 carbamazepine
 felbamate
 lamotrigene
 metformin
 oral contraceptives

Source: Ross Pelton, James B. LaValle, Ernest B. Hawkins. *Drug-Induced Nutrient Depletion Handbook. 2nd edition* (January 2001). Washington, DC: American Pharmaceutical Association, 2001. ISBN 091658979X

Beyond Tums® - Exploring the Underlying Triggers of Chronic Pain and Inflammation

By Todd Nelson, N.D., with Russel Sher, D.C.



Although considered normal bodily phenomena by the advertisers of various heartburn and indigestion medications, belching, burping, and bloating are actually signs of physiological imbalance that, if not addressed, may lead to further systemic imbalances and disease. An excellent example is arthritis, one of the many common chronic inflammatory illnesses that are directly affected by the state of a patient's gastric function.

Most patients with arthritis, osteo- or rheumatoid, can experience an exacerbation of pain because of low-grade infections and maldigestion in the intestine that introduce toxins into the circulation, ultimately triggering inflammatory responses in the joints. These patients commonly complain of gastric symptoms to their doctor, yet the

problem is addressed only on the level of symptomatic relief. Antacids or H2 blockers are prescribed to lessen the gastroesophageal reflux disease (GERD), bloating, or bowel disturbances they are complaining about. Unfortunately the medication is usually masking underlying problems of upper and lower intestinal dysbiosis, insufficient stomach acid, maldigestion, and malabsorption that may be contributing to arthritis pain. Add to this a leaky gut caused by chronic intake of non-steroidal anti-inflammatory drugs (NSAIDs) or steroids to relieve pain, and the intestinal environment becomes a primary contributing factor in circulat-

ing inflammatory and immune-inducing chemicals that exacerbate the disease.

All patients with chronic illness can benefit from an assessment of overall intestinal function as it relates to their condition. Adequate digestion may be assessed through several functional diagnostic tests, particularly the Comprehensive Digestive Stool Analysis (CDSA), Amino Acids Analysis, Bacterial Overgrowth of the Small Intestine Breath Test, and Lactose Intolerance Breath Test.

The CDSA reports the short chain fatty acids (SCFA's) valerate and iso-butyrate, which are produced through bacterial fermentation of protein and reflect the presence of undigested protein in the bowel. Generally these SCFA's should constitute less than 10% of the total concentration of SCFA's. Causes of these elevations may be due to deficient pancreatic proteases, hydrochloric acid (HCl), or malabsorption. Triglycerides are the major dietary component of fat. Elevations in the stool may reflect incomplete fat hydrolysis as a result of pancreatic insufficiency. Chymotrypsin is a proteolytic enzyme secreted by the pancreas, and deficiency may reflect pancreatic insufficiency.

Amino Acids Analysis is an excellent means of assessing protein digestion. Suspect incomplete proteolysis if anserine and carnosine are elevated and the essential amino acids are low, although inadequate dietary protein intake would need to be ruled out. Low stomach HCl may lead to low methionine, tyrosine, and phenylalanine. Low histidine may result in low stomach HCl since histidine converts to histamine (zinc dependent) and histamine converts to HCl. Zinc is also required for peptidase activity, and deficiency can result in low isoleucine, leucine, and valine.



In addition to directly measuring digestive markers, two breath tests can offer further indirect evidence of specific malabsorption syndromes. The Lactose Intolerance Breath Test provides evidence of malabsorption of lactose and therefore dairy products due to a deficiency in the enzyme lactase. Also assessed by breath testing, bacterial overgrowth of in the small intestine may contribute to the problem and result in symptoms of bloating, gas, reflux, diarrhea, constipation, and abdominal pain. This condition can be due to insufficient stomach HCl, slow transit time, and medications. Bacteria in the small intestine may interact with undigested matter and produce substances that can be neurotoxic, induce inflammatory and abnormal immune responses, and affect the patient systemically.

Once a thorough assessment is made, there are many natural therapeutic protocols for

restoring a normal gut environment. Individual test report commentary and interpretive guidelines (available in our *Functional Assessment Resource Manual* and online at www.gsdl.com) can provide treatment options. GSDL laboratory physicians are also available to provide consultation on test results.

Todd Nelson, N.D., director of the Tree of Life Wellness Center, has practiced holistic and integrative clinical medicine for over 18 years in the Denver/Boulder, CO area. He hosts a popular weekly radio talk show on alternative health and has co-authored books on arthritis and asthma. His special emphasis is a balanced, educational approach to self-care.

Russel H. Sher, D.C., graduated from Palmer College of Chiropractic and practiced chiropractic from a functional medicine perspective for 12 years in Colorado and his native South Africa before joining GSDL. He leads the Department of Medical Science in web-based educational development and distance learning programming.

"The immune defense system in particular is known to be adversely affected by the aging process, and there is strong evidence that a poorly functioning immune system can contribute to decreased disease resistance and reduced life expectancy in the elderly."

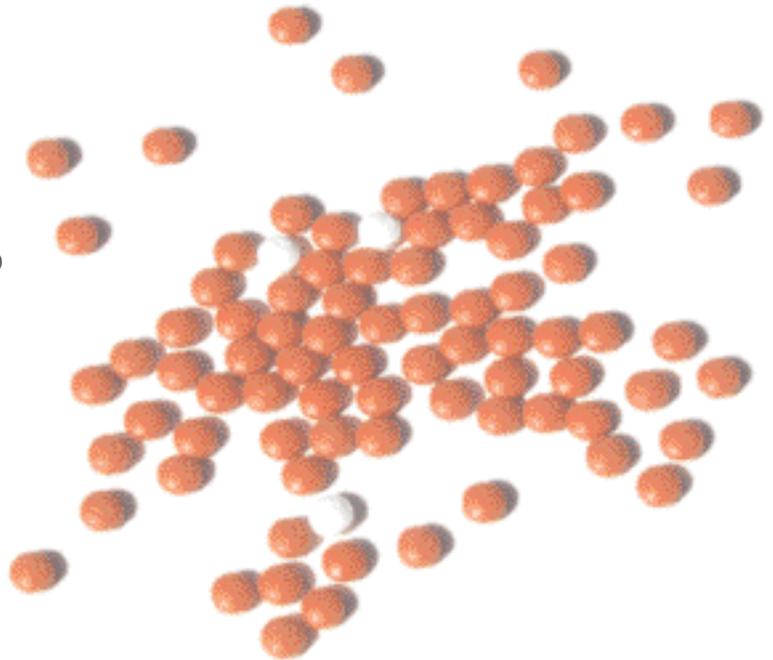
Gill HS et al.
Enhancement of immunity in the elderly by dietary supplementation with the probiotic Bifidobacterium lactis HN019. Am J Clin Nutri 2001;74:833-39.

Ron – A Case Report from the Practice of Todd H. Nelson, N.D.

At age 52, Ron suffered from chronic osteoarthritis and was dependent on 10 ibuprofen tablets daily to cope with his joint pain. He was also taking an H2 blocker for GERD. Ironically, he onset of his GERD was most likely induced by his increasing amounts of ibuprofen intake. After years as a pro basketball player and referee, his joints had taken a beating, and he had already undergone one knee replacement. He entered my care to see if he could reduce his drug dependency and save his other joints.

A CDSA/Parasitology stool analysis and gut permeability study were performed and revealed a 4+ overgrowth level of *Candida albicans* and a 4+ level of the bacteria, *Klebsiella pneumoniae*. His Dysbiosis Index was 16, and his lactulose/mannitol ratio on the Intestinal Permeability Assessment indicated leaky gut.

He was put on a natural protocol to address the problems. Once the infection was cleared, normal intestinal flora restored, and digestive parameters normalized, the toxic load was lessened. Ron also adhered to the dietary, supplement, and exercise protocol outlined in my book, *Arthritis Survival* (Ivker and Nelson, Tarcher/Putnum, 2001). He is now free of joint pain, and his most recent test results indicate lowered inflammation and disappearance of gastric dysbiosis. Ron is one of many patients following a functional medicine approach who is now essentially drug-free and is functioning very well every day.



detox in overdrive: heavy metal exposure and burden in aging patients

By Fred Harvey, M.D., and Jeff Baker, N.D.



Heavy metal toxicity is thought by many to be on the decline; however, this could not be further from the truth. In fact, arsenic, lead, and mercury are listed as the top three hazardous substances respectively in the United States by the Environmental Protection Agency and the Agency for Toxic

Substances and Disease Registry (a division of the U.S. Department of Health and Human Services). Unfortunately, most of the research focuses on acute, high dose, heavy metal toxicity. Little attention has been given to low dose exposure, and its cumulative effects over time; however, mounting evidence points toward heavy metals playing an important role in many chronic illnesses.

Next to young children, older patients may be the group most affected by toxic exposure because of natural processes of aging. In addition to new exposure, aging people may be afflicted all over again by exposures that happened many decades ago – long before most people understood the dangers. Since bone is a preferred tissue site for storage of toxic elements,

men and women who are now experiencing increased bone turnover are also experiencing the release of stored toxins back into the blood stream where they can impact tissue throughout the body and overburden the body's detoxification capabilities.

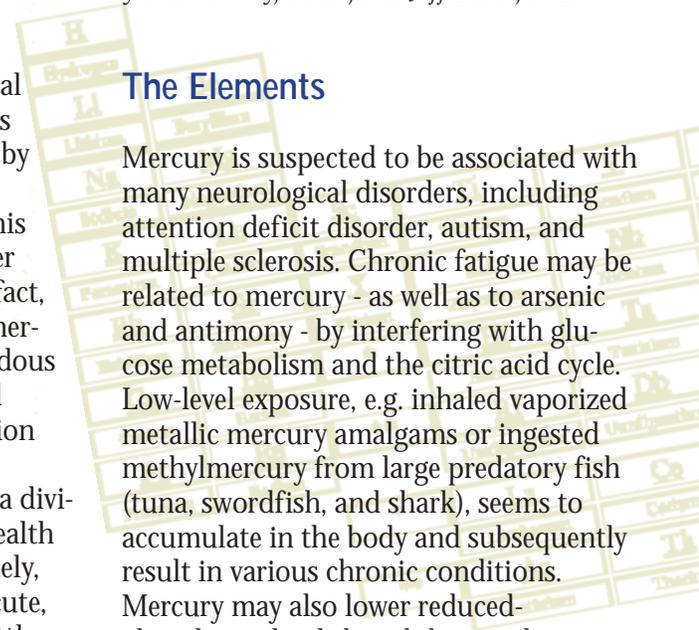
The Elements

Mercury is suspected to be associated with many neurological disorders, including attention deficit disorder, autism, and multiple sclerosis. Chronic fatigue may be related to mercury - as well as to arsenic and antimony - by interfering with glucose metabolism and the citric acid cycle. Low-level exposure, e.g. inhaled vaporized metallic mercury amalgams or ingested methylmercury from large predatory fish (tuna, swordfish, and shark), seems to accumulate in the body and subsequently result in various chronic conditions. Mercury may also lower reduced-glutathione levels by inhibiting glutathione reductase, resulting in impaired mitochondrial function, decreased detoxification capacity, and insufficient antioxidant reserves.

The main source of arsenic today is "pressure-treated" wood, where it is used as an anti-fungal and preservative. When it is liberated from the wood primarily when the wood is cut, burned, sanded, or degraded, it can then enter the air and water tables. However, low amounts may be liberated from unperturbed wood, as it is sometimes seen in families with decks. Humans can be exposed to arsenic by water, food, or air, and arsenic is considered carcinogenic to humans. Toxic effects include fatigue, immune dysfunction, vascular damage, neuropathy, and various forms of cancer (lung, skin, bladder, liver, kidney, and prostate).

Detox Challenges

In cases of chronic, low-dose exposure, heavy metals can overwhelm detoxification capacity, leading to tissue deposition.



Once deposited, toxins can interrupt normal function of those tissues and promote illness. Many times the patient notices no symptoms at the time of exposure. And it may be many years later before symptoms manifest. Unfortunately, random blood and urine testing are commonly used for heavy metal detection, which routinely miss toxicity in the tissues. As a result of these factors, many patients whose illness may be caused or compounded by heavy metal toxicity go undiagnosed.

Some people may be extremely sensitive to small amounts of heavy metal exposure, particularly mercury, which can then result in illness. These individuals may have protective nutrient insufficiencies or

genetic polymorphisms that inhibit normal elimination of these metals. In addition to Elemental Analysis of hair, blood, and urine, a Comprehensive Detoxification Profile, which includes Oxidative Stress Analysis, should be performed and used to monitor effectiveness of interventions.

Fred Harvey, M.D., holds board certification in Internal Medicine and Geriatrics. He is in private practice at the Harvey Center for Integrative Medicine in Sarasota, Florida. Dr. Harvey's focus is on preventive, integrative medicine, including nutritional and lifestyle intervention.

Jeff Baker, N.D., is a laboratory physician with GSDL and a licensed primary care physician with a doctorate from the National College of Naturopathic Medicine. Prior to joining our staff, he was in private practice in Portland, OR.

"Aging-associated release of bone lead into the circulation is, in fact, a potentially important source of soft-tissue lead exposure and toxicity.

Indeed, in U.S. population surveys, older adults have among the highest blood lead levels, second only to the peak observed in young children."

Tsaih S-W et al. Influence of bone resorption on the mobilization of lead from bone among middle-aged and elderly men: the normative aging study. Environ Health Perspect 2001;109:995-99.

Elemental Analysis: Choosing the Appropriate Panel for Your Patient

The method of testing for heavy metals should follow the basic sciences and the physiology of heavy metal detoxification. For instance, once a person is exposed to a metal, it is removed from circulation within 2-3 days. Therefore, urine, plasma, and serum will detect heavy metal exposure only within this 2-3 day time frame.

However, many metals are deposited in red blood cells after exposure. Since the lifespan of a red blood cell is approximately 120 days, RBC (Packed Erythrocyte) testing will detect metal toxicity only if the patient is tested within 120 days of the exposure. On the other hand, for testing past exposure and tissue levels, hair analysis is well supported in the literature. Hair concentrates heavy metals that are slowly liberated from tissue stores that may otherwise go undetected. Using a provocative challenge (DMSA, DMPS, EDTA, D-Penicillamine, etc.) liberates tissue stores of heavy metals that can then be measured in the urine. Therefore, choosing the appropriate method of testing is crucial for identifying all stages of heavy metal toxicity.

Test

Elemental Analysis Urine
 Toxic Element Clearance Profile
 Elemental Analysis Packed Erythrocytes
 Elemental Analysis Urine, Provocative Challenge (Pre & Post)
 Toxic Element Clearance Profile (with provocative agent)
 Elemental Analysis Hair, Toxic Element Exposure Profile

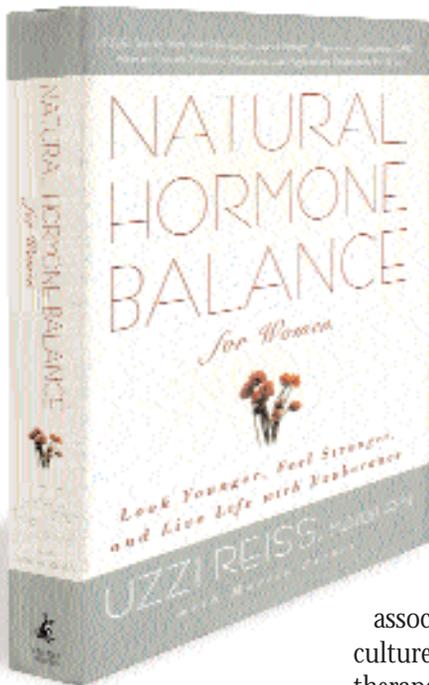
Exposure (Elapsed time since exposure)

2-3 days
 (identifies current exposure)
 up to 120 days
 Many years
 (identifies past exposure and tissue stores)
 (identifies past exposure and tissue stores)

Doctor's Bookshelf

Featured Book Review

Natural Hormone Balance for Women: Look Younger, Feel Stronger, and Live Life with Exuberance, by Uzzi Reiss M.D./OB-GYN with Martin Zucker. New York: Pocket Books, 2001. ISBN 0-7434-066506



Natural Hormone Balance for Women: Look Younger, Feel Stronger, and Live Life with Exuberance

by Uzzi Reiss M.D./OB-GYN with Martin Zucker

Reviewed by DeAnna Hatch, Ph.D.

If you were to ask women what they desire of their bodies as they grow older, they might say “youthfulness,” “energy to stay active,” “mental alertness,” “healthy skin, bones, eyes,” or simply “to feel good.” Hormone imbalance, deficiency, or excess can rob a woman of “youthfulness.” Moreover, medical science is constantly alerting women about the benefits to their hearts and bones achieved by keeping a healthy estrogen level. In a recent book by Uzzi Reiss, M.D., *Natural Hormone Balance*, the California obstetrician and gynecologist offers a guide to patients and their practitioners for helping women feel and look their best at any age.

In this thorough discussion of hormone health, Dr. Reiss reviews the changes and challenges associated with all ages, how aspects of our culture have led to these struggles, and the therapeutic advantages of using “natural” hormones – ones that are the exact chemical replicas of ones found in the body.

The book provides a list of common symptoms of hormonal imbalance and, in particular, problems of estrogen excess or

deficiency, which include fatigue, forgetfulness, depression, and insomnia. While estrogen is considered to be the target hormone in the struggle of the modern woman, there are actually several others that are also involved, including DHEA, testosterone, and melatonin. When these hormones work in harmony with one another, their healthy balance promotes the joy of youthfulness and wellbeing for women of all ages.

This book gives the practitioner tools for working with a woman as an individual. While blood, urine, or saliva hormone levels can serve as a baseline, it is imperative to realize that each woman has a distinct biochemical makeup and may react much differently to treatment. One woman might feel her best at a “high normal,” for example, while another might feel optimal with her estrogen levels in the lower part of normal.

Dr. Reiss, a board-certified obstetrician and gynecologist, conveys both the authority he has gained from years of learning and practicing and the trust he inspires as a healer who treats the whole person. His book provides the necessary details and resources, which will allow women and their practitioners to become health partners in the quest to maintain youthfulness and quality of life as women age.

Featured Book Review

The Advanced Guide to Longevity Medicine, edited by Mitchell J. Ghen, D.O., Ph.D., with contributing editors Nancy A. Corso, D.C., Herb Joiner-Bey N.D., Ronald Klitz, M.D., D.O., and Allen Kratz, Pharm. D. Landrum, SC: Partners in Wellness, 2001. ISBN 1-890694-37-1.

The Advanced Guide to Longevity Medicine

edited by Mitchell J. Ghen, D.O., Ph.D.

Reviewed by John H. Furlong, N.D.

I'll begin this review with a paraphrase of George Carlin: 'to some people the glass is half full; to others it's half empty... Me, I want a bigger glass!' That's exactly how I feel after completing this compilation by Dr. Ghen with contributions by over 35 specialists in the field – I'm ready for more.

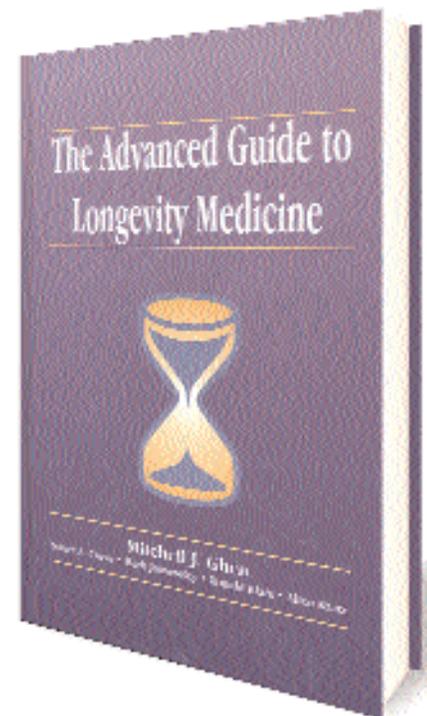
The Advanced Guide to Longevity Medicine is an exploration of ways to use the tools we've learned about over the past 100+ years of science and medicine and translate them into a new paradigm of high-function longevity. This is an ambitious undertaking, yet Dr. Ghen has enlisted leaders in numerous scientific and clinical disciplines to pull this off admirably.

Organized into a distinct chapter format, the book begins with a specific set of principles for a longevity-based practice. From cellular detoxification, nutrition, and oxygenation to inclusion of psycho-social-spiritual aspects of life, Dr. Ghen's model holds essential keys to a wide-ranging assessment. It provides a cogent model for clinicians to keep in mind as they explore an individual's health: enhancement of the dynamic genome/environment interaction to its optimal endpoint in the 21st century.

The following chapters begin with a scholarly, historical review of the basis of aging. The processes of reactive oxygen species generation, advanced glycation end-products, and redox balance are then challenged and highlighted as to those most amenable to modification. In Chapter 3 we get some intriguing images of the future from Dr. Klatz, one of the pioneers of longevity medicine and keystone workers in the American Academy of Anti-Aging Medicine.

The book's other chapters then present an in-depth look at some of the pivotal topics and interventions intrinsic to longevity medicine practice. Discussion of Biogenic medicine and new diagnostic and therapeutic methods are supported by strategies of genetic modification via diet. The concept of the CRON diet; (calorie restricted-optimal nutrition), is one to counter the epidemic of carbohydrate excess that results in our skyrocketing rates of dysglycemia and type II diabetes.

Subsequent discussions include aging and immune system changes (an excellent article by Dr. Bock), laboratory assessments, pros/cons and methods of hormone replacement therapy and homeopathic human growth hormone, as well as an exhaustive review of probiotics, enzyme therapy, and hormone monitoring. These articles are well written and contain many pearls worthy of incorporation into clinical practice.



The Ghen and Rains Physicians' Guide to Pharmaceutical Compounding

by Mitchell J. Ghen, D.O., Ph.D., and John R. Rains, Pharmacist, F.A.C.A.

Reviewed by Bob Smith

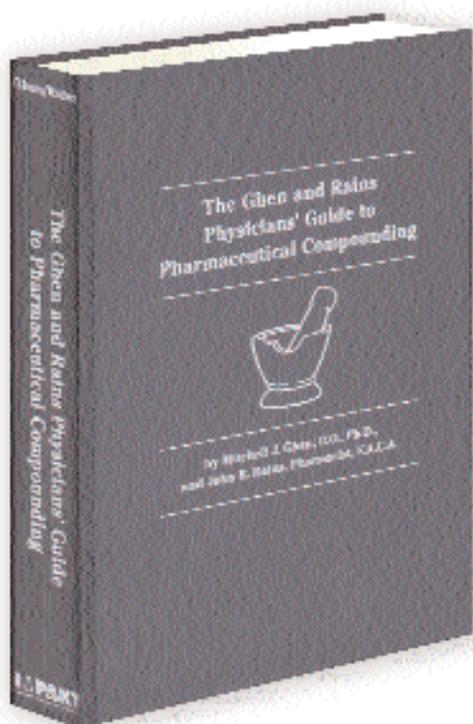
For the practitioner treating the patient rather than the disease, the compounding pharmacy offers expanded treatment

choices, ranging from specialized amino acid formulations and hormone replacement compounds to alternative delivery designs for patients with special physical or compliance requirements. Pharmaceutical compounding can serve as an effective alternative for those situations when off-the-shelf medications are not the best tools for optimal treatment of the individual patient.

Kudos to Drs. Ghen and Rains for putting together this excellent new desk reference guide. The Physicians' Guide can give practitioners the support and direction they need for understanding the art of compounding and selecting the most highly qualified professionals available. The 400+ pages are almost evenly divided between chapters on the qualifications, techniques, and the various products of the compounding pharmacy and individual monographs with over 240 unique prescriptions.

Featured Book Review

The Ghen and Rains Physicians' Guide to Pharmaceutical Compounding, by Mitchell J. Ghen, D.O., Ph.D., and John R. Rains, Pharmacist, F.A.C.A. Green Bay, WI: IMPAKT Communications, 2001. ISBN 1-890694-29-0.



Featured Book Review

Textbook of Nutritional Medicine, by Melvyn Werbach, M.D. and Jeffrey Moss, DDS, CNS, CCN. Tarzana, CA: Third Line Press, 1999. ISBN 0-9618550-9-6

Textbook of Nutritional Medicine

by Melvyn Werbach, M.D. and Jeffrey Moss, DDS, CNS, CCN

Reviewed by Russel Sher, D.C.

Drs. Melvyn Werbach and Jeffrey Moss have produced an impressive, well-organized, and well-documented textbook on nutrition. This book abstracts and analyzes thousands of research studies, providing an overview of the clinical applications of nutrition in practice as well as nutritional protocols for a wide range of clinical disorders.

The *Textbook of Nutritional Medicine* is primarily aimed at healthcare practitioners who incorporate nutritional medicine in their protocols and is of great value to those skeptics who need scientific verification of this highly validated field. This book is an extensive compilation of clinically relevant information and practical guidelines covering nutritional therapies for the most common clinical conditions. Descriptions include medical terminology that requires a basic understanding of physiology and pathology.

The book is divided into three parts; Part One: General evaluation and treatment, covering Nutrition and Integrative Medicine, Common Nutritional Deficiency Syndromes, Laboratory Testing in Nutritional Medicine, Overview of the Clinical Use of Nutritional Supplements, and How to Rule Out Food Sensitivities; Part Two: Nutritional Treatments for Specific Illnesses, detailing 105 conditions; and Part Three: Useful appendices covering essential reference information.

In Part One, the authors provide a perspective of the most common nutritionally relevant causes of chronic illness which are divided into five broad categories: Neuroendocrine imbalance, improper nutrition, chemical and/or heavy metal toxicity, compromised mucosal barriers, and

genetics. This perspective provides a contemporary approach to addressing commonly encountered clinical conditions from a nutritional and functional point of view. The section on neuroendocrine imbalances provides an impressive understanding of the stress response, describing the physiology, causative factors, clinical relevance, and clinical implications.

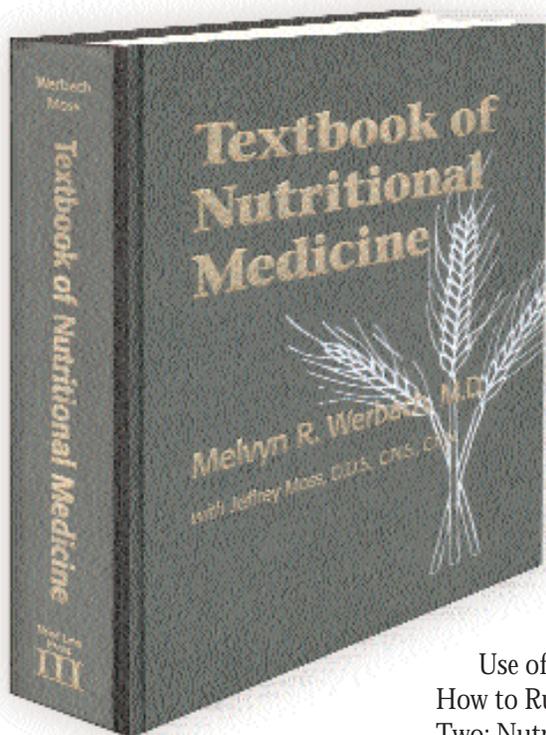
I found the chapter on Overview of the Clinical Use of Nutritional Supplements to be quite compelling. Much thought and work has gone into providing a strong argument for the use of nutritional supplementation, which is backed by current statistics comparing pharmacotherapy (including risk of toxicity) to nutrient supplementation.

One area that is sure to attract interest is the discussion on genetics (which involves the emerging arena of genomics) and includes an exceptional discussion on nutritional influences on gene expression.

The heart of the book, Nutritional Treatments for Specific Diseases covers the 105 most common presenting clinical conditions. Each chapter starts with a Nutritional Treatment Guide that lists treatments discussed in the text and rates the treatment according to efficacy. The treatment protocols are in-depth and up-to-date.

All practitioners of nutritional medicine will find this book to be a valuable and succinct resource of advanced, clinically relevant information. The insightful perspective, together with scientifically validated research, provides a meaningful education for those entering this field.

Not only is this an excellent clinical resource for the clinician, but it also provides substantial useful information for those who make presentations and require references and documentation. Overall I found this book to be an outstanding clinical resource that should be on every nutrition-oriented clinician's bookshelf.



Yeast Connection Success Stories

by William G. Crook, M.D.,

Reviewed by Corene Humphreys, N.D.

Dr. William Crook has written yet another exceptional book about systemic candida. Differing from his previous work, this book is predominantly written from the point of view of patient testimonials - both his own and that of colleagues - which reflect the importance of appreciating the body as an integrative whole, rather than as isolated parts.

The engaging testimonials reminded me, once again, of the many "faces" this insidious organism can present with. Unlike most acute infections, there is no predictable pattern of symptoms with yeast dysbiosis - clinical manifestations can affect a multitude of organs. What determines the emphasis appears to be somewhat bio-individual. This, in part, may account for the reluctance of conventional medicine practitioners to acknowledge yeast overgrowth as a clinically significant condition.

The common thread for these patients often lies in the prescribing, or over use, of antibiotic therapy. From this point many begin a slow, yet progressive, decline of health.

When conventional medicine fails to identify the etiology, or rationale, the search begins. For some, it takes many years to find the answers—a journey that ultimately brings them to the discovery of Crook's extensive research in this field.

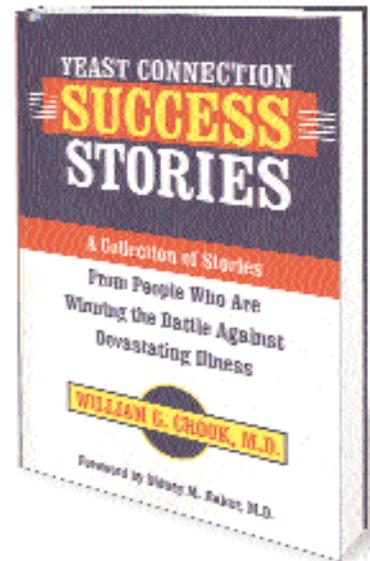
Screening for candida overgrowth is an invaluable diagnostic tool for practitioners - especially when conventional laboratory findings fail to provide any clinical explanation.

I wholly recommend this book to both the lay person and the practitioner, who can also benefit from the commentary by several practitioners included in the final chapter of the book.

The road to recovery is not an effortless one for those afflicted with systemic candida. Adhering to the protocols requires discipline and commitment. However, reading the success stories of others offers inspiration to help stay focused and a sense of camaraderie during the challenging times.

Featured Book Review

Yeast Connection Success Stories, by William G. Crook, M.D. Jackson, TN: Professional Books, 2002. ISBN 0-939478-26-7



You Are Within Normal Range

by Tammy Joseph, Reviewed by Corene Humphreys, N.D.

"What can I eat on a yeast free diet?" This is a common question posed by many patients when embarking on an anti-candida regime. Tammy Joseph offers practical advice on how to remove yeast-promoting foods from the diet, a vital step in overcoming systemic fungal infection.

The author speaks from first-hand experience, having successfully eradicated the organism, predominantly through dietary intervention. Like many people plagued by overgrowth of *Candida*, she suffered a cluster of vague, but very real symptoms. Also like so many people who are hosting this unwelcome visitor, she found no relief from conventional approaches to her symptoms. "Doctor after doctor performed expensive tests, then bestowed a similar verdict, telling me, 'You're clearly ill, but your tests are within the normal range.'"

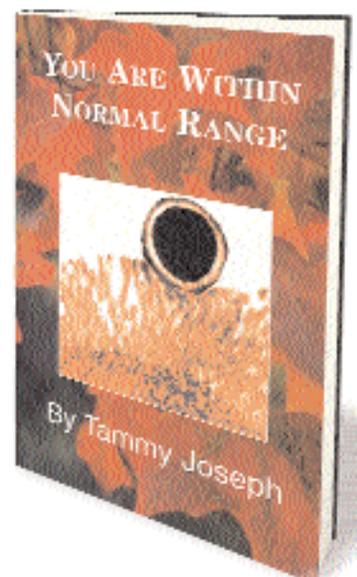
A chance encounter with a specialist in metabolic and nutritional disorders, Ron Rosedale, M.D., marked the beginning of her turn-around. His nutritional advice sparked her recovery and inspired her book.

Inside *You Are Within Normal Range* is a comprehensive list of foods to avoid, those recommended, as well as handy shopping and dining out tips. Numerous recipes are provided, along with companies that can supply the ingredients - all invaluable information when initially modifying the diet.

Targeted for the layperson, the book also outlines the symptoms of yeast overgrowth, along with diagnostic profiles to assist in identification. *You Are Within Normal Range* an ideal book for practitioners to offer patients, once they have been diagnosed with a systemic yeast infection.

Featured Book Review

You Are Within Normal Range, by Tammy Joseph. Self Published: www.youarewithinnormal-range.com, 2001.



Clinical Genomics – The Next Generation of Healthy Aging Medicine

By T. Michael Culp, N.D.

"Virtually all human diseases result from the interaction of genetic susceptibility factors and modifiable environmental factors, broadly defined to include infectious, chemical, physical, nutritional, and behavioral factors."

Office of Genetics and Disease Prevention of the Centers for Disease Control and Prevention (CDC).



The concept of 'biochemical individuality' was first proposed by Roger Williams in 1956 to explain variability in disease susceptibility, nutrient needs, and drug responsiveness among otherwise seemingly healthy people. It is only in the wake of the ongoing genomic revolution, however, that predictive genetic testing has become available to allow us to assess true biochemical individuality. For the first time, physicians can gauge with increasing precision who is more likely to develop specific diseases, who will respond favorably (or react adversely) to a particular drug or supplement therapy,

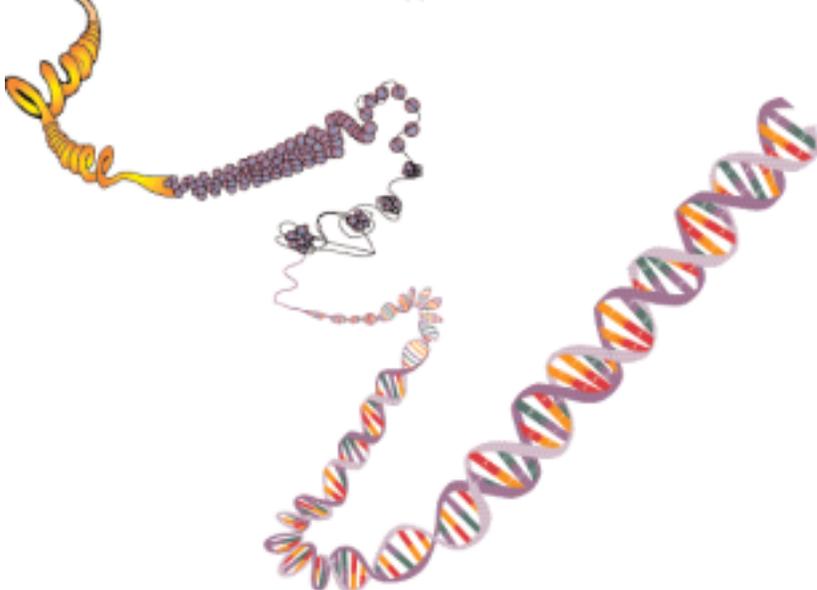
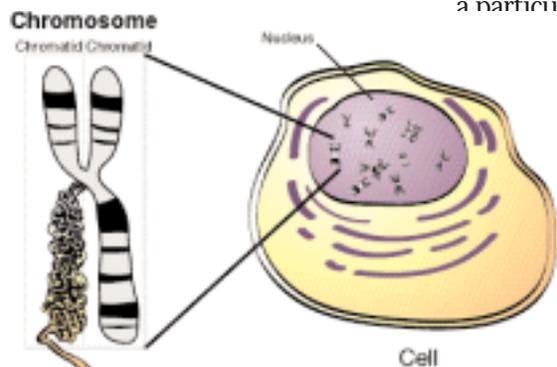
of the entire human genome was published in April 2001, almost exactly one hundred years after the rediscovery of Mendel's "Laws of Heredity." The human genome consists of slightly more than 3 billion nucleotides (give or take a hundred million) and it codes for every protein and every enzyme made by the human body. Some 30,000 to 40,000 genes are thought to exist in the human genome, yet we know the function of slightly less than half of them.

New Directions in Primary Care

As primary care practitioners, we stand at a critical crossroads where increases in availability of DNA-based testing and demand by patients for genetic information and advice necessitate our need to become both genetically literate and genomically competent. The power to read and understand the genetic code of individuals will prove to be every bit as great an advance in clinical diagnostics as when Robert Hooke's improvements to the microscope allowed scientists to discover that living organisms were made up of "cells."

New methods of investigating the genome are now being aimed at better understanding the multifactorial etiology of the most prevalent and debilitating health conditions that humans face - opening up the potential for astounding clinical applications.

Director of Curriculum Development T. Michael Culp, M.A., N.D., received his doctoral degree from Bastyr University. In addition to his particular expertise in therapeutic and orthomolecular nutrition, Dr. Culp has taught graduate courses at Bastyr University and Atlantic University of Chinese Medicine.



optimal for health and

You're Dealt

ific study of a time. of genomes, f a single he laws of

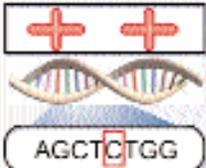
a flexible, mic system e, interact- id influenc- emical hysiology.

Project is encing of the e first draft

Key Concepts

- Virtually all human diseases result from the interaction of genetic susceptibility and modifiable environmental factors, broadly defined to include infectious, chemical, physical, nutritional, and behavioral factors.
- Slight variations in genetic makeup called Single Nucleotide Polymorphisms (SNPs - pronounced “snips”) are associated with almost all diseases.
- Genetic variations themselves do not cause disease but rather influence a person’s susceptibility to specific environmental interactions that increase disease risk.
- GENOVATIONS™ offers a unique line of Predictive Genomic Diagnostic Profiles. Each profile focuses on a carefully selected set of SNPs associated with a particular disease or physiologic imbalance (e.g. cardiovascular, bone metabolism, detoxification, immune surveillance, etc.).

Inflammation Immune Dysfunction

<p>Interleukin 1 Receptor Antagonist</p> <p style="text-align: center;">IL-1RN Chromosome 2 2q14.2</p> <div style="text-align: center;">  <p style="font-size: small; color: blue;">www.gsdl.com/IL1RN</p> </div>	<p>HEALTH IMPLICATIONS: Interleukin-1 receptor agonist (IL-1RA) is a naturally occurring competitive inhibitor of IL-1α and IL-1β-induced pro-inflammatory activity. A defect in the IL-1RA gene can contribute to a more prolonged and severe inflammatory response and has been associated with increased risk for chronic inflammatory conditions like atherosclerosis, osteoporosis, rheumatoid arthritis, lupus, colitis, and Crohn's disease. However, the IL-1RA SNP also confers benefit when fighting infections or cancer through amplified immune vigilance.</p> <p>MINIMIZING RISKS: Eat a diet rich in anti-oxidants (colorful fruits and vegetables), increase consumption of cold-water fish, like salmon, and reduce intake of vegetable oil and fatty meat. Fish oil supplementation, silymarin (milk thistle) directly inhibit IL-1 production. Nicotinamide and other anti-inflammatory botanicals like boswellia (frankincense), glycyrrhiza (licorice), and curcumin (turmeric) may mediate the pro-inflammatory effects of increased IL-1. Compounds in cannabis have also been shown to suppress IL-1 levels. Corticosteroids and cyclosporin A inhibit IL-1 production but with significant immune suppression and numerous other side-effects. Experimental IL-1RA therapy is showing promise in treating rheumatoid arthritis, as is leflunomide.</p> <p>FURTHER EVALUATION: IL-1RA defects lead to increased inflammatory tendencies throughout the body. Consider laboratory evaluation of cardiovascular health (lipids, C-reactive protein, etc.), for bone resorption (deoxydysidolmic), and for digestive health (bowel microbiology, food antibodies, etc.). The physician should be cognizant that there is also an increased risk of auto-immunity in this patient.</p>
---	--

Touchstones for Genomics Testing

Though many SNPs can be related to a particular disease or function, not all are clinically useful. To assure clinical value, the Genovations™ line of CardioGenomicSM, OsteoGenomicSM, and ImmunoGenomicSM Profiles assess only SNPs that meet four critical requirements:

Relevant- GENOVATIONS™ SNPs are carefully selected based on their direct influence over specific biochemical imbalances which create known symptom clusters or diseases.

Prevalent- GENOVATIONS™ SNPs carry clinically significant population prevalence. These are relatively common genetic predispositions associated with extremely prevalent conditions.

Modifiable- GENOVATIONS™ profiles focus on genetic variations whose expression is influenced by environmental factors. Each profile contains intervention options based on the patient’s genomic pattern.

Measurable- For each SNP, GENOVATIONS™ profiles provide recommendations for follow-up functional laboratory testing. These functional assessments evaluate and monitor phenotypic expression of genetic tendency, functional integrity, and metabolic reserve.

in Primary Care Medicine

A One-Day Achieving Clinical Excellence Seminar

Earn while you learn – you may qualify for up to 6 hours of CME or CEU credit

Master effective ways to use insight into genetic variation to transform your practice of medicine

Help patients avoid chronic diseases, including:

- **Cardiovascular disease**
- **Osteoporosis**
- **Detoxification and oxidative stress defects**
- **Immune system, GALT defects, and chronic inflammation**

Registration is ongoing for sessions in 11 major U.S. cities – Call **888-201-2185** or enroll online at www.gsdl.com

Denver, CO
Saturday, April 20, 2002

Chicago, IL
Saturday, April 27, 2002

Dallas, TX
Sunday, April 28, 2002

Philadelphia, PA
Saturday, May 4, 2002

Boston, MA
Sunday, May 5, 2002

Orlando, FL
Saturday, June 8, 2002

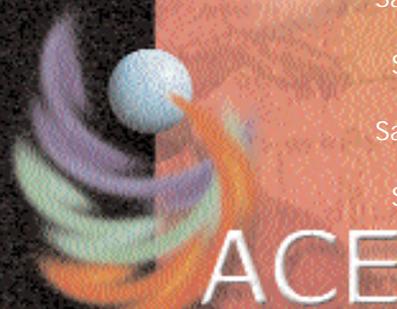
Atlanta, GA
Sunday, June 9, 2002

Washington, DC
Saturday, June 15, 2002

Westbrook, CT
Sunday, June 16, 2002

Portland, OR
Saturday, June 22, 2002

San Francisco, CA
Sunday, June 23, 2002



63 Zillicoa St. • Asheville, North Carolina 28801-1074

Return Service Requested

PRSR STD
U.S. POSTAGE
PAID
PERMIT NO. 104
HICKORY, NC