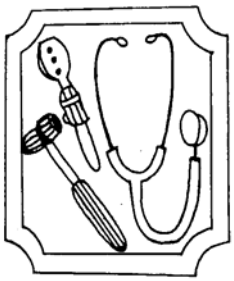

THE Original Internist

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CALENDAR OF EVENTS

March 1-2, 2008 *(Houston, TX)*
Reports, Clinical Documentations & Drug Reactions
Instructor: *Jack Kessinger, DC DABCI*

March 8-9, 2008 *(Charlotte, NC)*
Facts of Neoplastic Process & Examining the Cancer Patient
Instructor: *Jack Kessinger, DC DABCI*

March 15-16, 2008 *(Chicago, IL)*
Multi-Channel Blood Chemistries, CBC, Thyroid Panel, TSH
Instructor: *Jack Kessinger, DC DABCI*

March 28-30, 2008 *(St. Louis, MO)*
DABCI GETAWAY WEEKEND
St. Louis Airport Marriott

April 12-13, 2008 *(Charlotte, NC)*
Malignant Diseases, AIDS, & Their Management & Treatment
Instructor: *Jack Kessinger, DC DABCI*

April 19-20, 2008 *(Chicago, IL)*
Additional Blood Tests/Tumor Markers for Internal Disorder Pt.
Instructor: William Kleber, DC DABCI

April 26-27, 2008 *(Dallas, TX)*
Introduction to Chiropractic Internal Disorders
Instructor: *Jack Kessinger, DC DABCI*

May 3-4, 2008 *(Charlotte, NC)*
Upper Gastrointestinal Disease
Instructor: *Jack Kessinger, DC DABCI*

May 17-18, 2008 *(Chicago, IL)*
Blood Interpretation Workshop
Instructor: *Jack Kessinger, DC DABCI*

May 31- June 1, 2008 *(Dallas, TX)*
History Taking
Instructor: *Jack Kessinger, DC DABCI*

June 7-8, 2008 *(Charlotte, NC)*
Lower Gastrointestinal Disease
Instructor: *Frank Strehl, DC DABCI*

June 21-22, 2008 *(Chicago, IL)*
Cardiovascular Disease: Prevention / Diagnosis / Management
Instructor: *Jack Kessinger, DC DABCI*

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June 28-29, 2008 *(Dallas, TX)*
The General Examination and Associated Pathology
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July 12-13, 2008 *(Charlotte, NC)*
Reports, Clinical Documentations & Drug Reactions
Instructor: *Jack Kessinger, DC DABCI*

July 18-20, 2008 *(Cincinnati, OH)*
SYMPOSIUM
Westin Hotel

July 26-27, 2008 *(Chicago, IL)*
Electrocardiography and Photocardiography
Instructor: William Kleber, DC DABCI

July 26-27, 2008 *(Dallas, TX)*
Diseases and Exam of the Pelvis and Associated Pathology
Instructor: *Frank Strehl, DC DABCI*

August 16-17, 2008 *(Chicago, IL)*
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Instructor: *Daniel L. Richardson, MSc, DN, PhD*

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Instructor: *Jack Kessinger, DC DABCI*

September 20-21, 2008 *(Chicago, IL)*
Chronic Degenerative Disease
Instructor: *Jack Kessinger, DR DABCI*

September 27-28, 2008 *(Dallas, TX)*
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Instructor: *William Kleber, DC DABCI*

October 18-19, 2008 *(Chicago, IL)*
Pediatrics
Instructor: *Jack Kessinger, DR DABCI*

October 25-26, 2008 *(Dallas, TX)*
Blood Interpretation Workshop
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November 15-16, 2008 *(Chicago, IL)*
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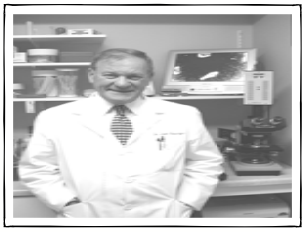
Instructor: *Jack Kessinger, DR DABCI*

November 22-23, 2008 *(Dallas, TX)*
Cardiovascular Disease: Prevention / Diagnosis / Management
Instructor: *Jack Kessinger, DC DABCI*

From the Editor's Desk



Dr. Jack Kessinger

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

When Will We Ever Learn?

Larry, the Cable Guy, states that he just simply cannot understand how anyone can allow themselves to get run over by a train. Since a train can only follow its well-established tracks, all we have to do to avoid getting run over by a train is just take three or four steps to either side of the tracks. The same philosophy can be applied to avoiding most diseases. We already know what causes most of our life-threatening diseases.

We have long been searching for the easy way out to prevent our various diseases. We keep looking for the proverbial "fountain of youth" in a magic pill or procedure. Untold amounts of money have been raised, and spent, toward this end. We have all sorts of "a-thons" — telethons, walkathons, dance-athons, etc. In addition to cardiovascular and cancer research, The National Institute of Health (NIH) provides several million dollars in the form of grants for researching any sort of health-related problems imaginable, such as alcohol and tobacco addiction or impulsive behaviors such as overeating and gambling. We have institutions that advertise for us to donate cars, boats, and other various assorted items to advance research for various health care conditions. Cardiovascular disease and cancer usually top the list of donations raised for research. Literally billions of dollars have been raised and spent on such research, and so far, nothing. No amount of money spent on research will ever result in a cure for any disease process. We already know what the cause and cure are.

Unhealthy lifestyle activities top the list of major contributing factors for almost all diseases. Poor dietary selections, tobacco use, excessive alcohol intake, and lack of adequate exercise are all well-reported risk factors of ill health. Government studies have long reported nutritional deficiencies as a single leading cause of health problems.

Unfortunately, achieving optimum health is not as simple as avoiding a train. It takes three objectives for enjoying optimum health. Knowledge is a prerequisite for health. We have to understand the hazards of unhealthy lifestyle habits, processed foods, and lack of regular exercise. Then we have to have a strong desire for good health. However, knowledge and desire alone are not enough. They must be topped off with a dogged determination. If good health were easy to obtain, everyone would be healthy.

In a well-documented study, *Malnutrition in the Elderly — A National Crisis*, commissioned by the US Administration on Aging, reports that "malnutrition in the older American represents one of the largest silent epidemics being experienced in this country, and the current healthcare paradigm must shift from the traditional rescue and repair, or sick medicine, to that of health promotion." According to the US Senate Committee on Education and Labor, 85% of older Americans have chronic diseases that could be helped by nutritional intervention. Malnutrition compromises the immune system and contributes to the development of infection, poor wound-healing, serious complications, sepsis, multi-system organ failure, disability, extended hospital stays, catastrophic health care, and death.

Overweight and obesity masks malnutrition and is associated with increased risk for diabetes mellitus, hypertension, cardiovascular disease, cancer, stroke, apnea, gout, and osteoarthritis (many of the health problems we have endless "a-thons" for). In fact, it is now reported that obesity is rapidly overtaking tobacco smoking as the number one preventable cause of premature death in the United States. According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), today, more than 65% of the population is either overweight or obese. Overweight and obese people are typically malnourished.

There are only two categories of food: whole food and processed food. A healthy diet should be primarily whole foods with restricted consumption of processed foods. It is reported that 90% of all food consumed in the US today has been processed. Processing depletes the normal nutritional value of food. No wonder we are malnourished.

There are 1,440 minutes in a day. Thirty of them should be reserved for physical activity. Regular exercise is a critical part of staying healthy. People who are active typically enjoy better health, feel better, and live longer. Exercise helps maintain a healthy weight and is essential in cardiovascular and respiratory function. It can delay or prevent diabetes, some types of cancer and heart conditions, and maintain a healthy blood pressure. Exercise will

(Continued on next page)

increase bone density. Some good examples of exercise include walking briskly, riding a bicycle, mowing the lawn, dancing, and swimming. Weight training is also a good form of exercise. Physical inactivity is also associated with many of the leading causes of death and disability in the US. Maintaining musculoskeletal mass among the elderly is critical to preventing falls, hip fractures, and disability. Exercise also builds confidence and self esteem.

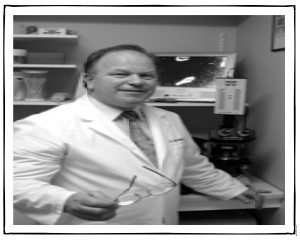
The strategy for any optimum health plan is best determined by evaluating the person's individual biochemistry, based on blood chemistries, urinalysis, lung function tests, heart and circulation studies, etc., as well as evaluating their individual diet and lifestyle. Well-documented research in leading medical journals has led to the development of the wellness model. Unfortunately, the disease-based framework continues to be the primary foundation of bio-medicine's health practice.

The World Health Organization (WHO), based in Geneva Switzerland, reports that "health is more than the absence of disease." Traditional medicine assumes that disease is mostly the result of flaws in the genetic pool, combined with an adverse lifestyle (poor dietary selections, lack of regular exercise, stress, and/or unhealthy habits such as tobacco use and excess alcohol intake). As a result, the focus of treatment is on making a diagnosis and putting a label on the disease. Then treatment targets secondary problems (symptoms) rather than the primary problem (the underlying disease). This approach primarily works well only in crisis situations, such as a heart attack, diabetic coma, infection, etc., but fails miserably in reversing or preventing chronic disease and infections. As a result, treating the symptoms by dictating to the body what you would like to have happen (rather than supporting natural mechanisms) does little more than hide the underlying causes and delay proper treatment.

A true "wellness" program addresses health from a much broader framework than the conventional approach. There are specific defects that are common to every chronic disease condition; structural misalignment (including spinal fixations and subluxations that interfere with the normal nerve flow), chronic malnutrition, chronic infections, and chronic toxicities. To actually reverse disease, it is essential for these defects to be first identified, then addressed in a particular order.

We need to guide our patients away from the train tracks! ◆

The Legacy Continues



Dr. Jay Kessinger

by A. Jay Kessinger IV, DC, ND, DABCI

My how time flies! It seems like only yesterday, or the day before, I was figuring out how old I was going to be at the turn of the century, the new millennium. I vividly recall, after some thought, arriving at the conclusion: "That's so far off I won't have to worry about that for a l---o---n---g time." In actuality, time only goes by fast if you're too busy to think about it, or you're looking back at it (I guess especially if you're like me and are older than Ward was when he was raising the Beav').

Life holds many lessons. I've read that you have to learn from others' mistakes, because there's no way you can live long enough to make them all yourself. It has been said that learning from your own mistakes is common sense, but when you can learn from others' mistakes, it's called extraordinary wisdom. My grandmother, in my opinion, used to be pretty persnickety when it came to my use of those darn slang words. She called such verbage vulgar. As I matured from childhood through adolescence even into early adulthood, my definition of vulgar was akin to nasty or obscene. When I looked it up in a small paper-bound desk dictionary, the definition given for vulgar was "common." I finally understood what Grandmother was teaching; be above common lest you be vulgar. Making a C is being the best of the worst and the worst of the best (i.e., vulgar).

Johnny's Smoke Stack, a barbecue place just up the street from our office, was sold a few years ago. The new owners had a dream and didn't want the original owners to stick around and help them through the transition. They had a dream. I watched the quality go down, the prices go up, and the business decline. I wanted to thank them for being a living example/lesson for me to excel in comprehensive cradle-to-grave natural health care as my parents, Dr. Jack & Virginia, have cultivated. This is the success formula of our clinic that I would be foolish not to follow. In conclusion, I never did talk with the new owners of Johnny's Smoke Stack and they were out of business in 11 months. The original owners have their old business back, and it's now called the Hickory Pit. Once again it's a thriving quality business providing a valuable service to our community and a personal lesson to me that money can't buy.

Living and learning, climbing and walking, working and getting ready to work, all whilst keeping our eyes wide open in observation. Times are truly changing, and even though figures don't lie, liars still figure. The advertisements for many products are so slick that no one questions their integrity until much time and money has passed. Lysterine mouth wash, as I recall, was called to the carpet for their claim of killing germs. The makers of Lysterine had to make sure they could prove their product did kill germs. As much ado as was made over this, it seemed fair to assume that it needed more ingredients added to fulfill such a claim. Lysol also came under the same rigorous scrutiny. Recently, the drug Vytorin fell short of their claims of superiority, but not before a lion's share of the gross profits from the cholesterol-lowering pharmaceutical pundits had been earned. Reportedly pharmaceutical television advertising has been banned in New Zealand in order to quell John and Jane Q. Public's desire to acquire the latest and greatest new blockbuster of the medical pharmacopia.

Modern life is composed of a world in which there is a pill for every ill; there are machines that can filtrate, oxygenate, and circulate living blood; and there are new sophisticated diagnostic and treatment facilities. There are government and private insurance plans (i.e., PPOs, HMOs, etc.) most of which are designed to keep all the money in the loop of organized and institutionalized medicine. Now that there is the diagnosis of "sleep apnea," made by spending a few nights away from home in a sleep clinic and a treatment for it (being tethered to a C-PAP machine), we're not even allowed to die in our sleep. That was the best we could hope for, according to Kenny Rogers' song, "The Gambler." But apparently, we're not allowed to die until our insurance runs out.

Before our personal time runs out, it would behoove us all to ponder much of the aforementioned with some serious thought. Our radio show's title, "A Healthy Concept," captures the essence of natural health provision. It's quality and quantity that we all desire. It is to varying degrees attainable, but once attained, it has to be maintained. Maintain your life by positive affirmations and actions toward the truth. I've read that if you do what you love, you'll never have to work a day in your life. But that can't be true … can it? ◆

The Effect of Daily Ingestion of 100 mg Iodine Combined with High Doses of Vitamins B_2 and B_3 (ATP Cofactors) in Five Subjects with Fibromyalgia

by Guy E. Abraham, MD and Jorge D. Flechas, MD

Introduction

Fibromyalgia is a common clinical syndrome of generalized musculoskeletal pain, stiffness, and chronic aching, characterized by reproducible tenderness on palpitation of specific anatomical sites, called tender points.[1] Fibromyalgia is nine times more common in middle-aged women (between the ages of 30 and 50) than in men. The association of fibromyalgia with chronic fatigue syndrome has been reported.[2]

We previously proposed that fibromyalgia is caused by deficiencies of substances needed for ATP synthesis.[3] The vitamins B_2 and B_3, as precursors of the cofactors $FADH_2$ and NADH, play a key role in ATP synthesis[4] and in the generation of intracellular hydrogen peroxide.[5] Hydrogen peroxide formation is the rate-limiting step in the oxydation of iodide to iodine by iodoperox-idases, including thyroid peroxydase (TPO). The oxydation of intrathyroidal iodide to iodine by TPO is the first and key step in the synthesis of thyroid hormones.

The role of iodine in ATP synthesis and in normal functions of striated muscles is presently unknown. In severely iodine-deficient individuals, the thyroid gland takes the lion's share of the total body iodine pool. However, in iodine-sufficient individuals, the maximum iodine content of the thyroid gland (50 mg) represents only 3% of the total body iodine of 1,500 mg[6] and striated muscles contain 33% of the total body iodine.[7]

During a study on the bioavailability of an oral dosage form of Lugol solution at 100 mg of elemental iodine a day for six weeks in six female volunteers, one of them reported significant improvement of fibromyalgia (FM) pain and associated discomfort. She decided to continue the ingestion of 50 mg iodine/day for another 40 weeks. Further evaluation of this subject revealed an inability to retain ingested iodine which was corrected with iodine supplementation at 50-100 mg/day. Further improvement of FM symptoms, including increased energy level and decreased pain post exercise, occurred following the addition of vitamin B_3 at 1000 mg/day in the form of inositol hexanicotinate for eight weeks.[8]

Further studies revealed that the potentiating effects of ATP cofactors vitamin B_2 and B_3 on orthoiodosupplementation in FM patients was not observed until the daily amounts were increased to 1,000 mg B_3 and 200 mg B_2, and that B_3 alone at 1,000 mg/day was not as effective as in combination with vitamin B_2 at 200 mg/day. In order to evaluate further the effect of iodine/iodide alone at 100 mg a day and in combination with the ATP cofactors, vitamins B_2 (riboflavin) and B_3

(Continued on next page)

Table 1

Clinical Data on 5 Female Subjects with Fibromyalgia

SS#	Age (Years)	Height (Inches)	Weight (Pounds)	BMI*	Menstrual Status	Duration of FM	Severity of FM (FIQ** Score)
1	41	53	140	28.3	Premenstrual	6 months	Moderate (54)
2	54	63	132	23.4	Postmenstrual	4 years	Severe (74)
3	47	64	204	35	Premenstrual	3 years	Severe (86)
4	43	68	227	34.5	Premenstrual	12 years	Moderate (60)
5	37	70	180	25.8	Premenstrual	8 years	Severe (83)
±	44.4	64.8	177	28			
SD	6.5	4.3	41	4.8			

* BMI = Body Mass Index

** FIQ = Fibromyalgia Impact Questionnaire: 50-60 = Moderate; 60-70 = Moderate to Marked; >70 = Severe

Table 2

Clinical Evaluation, Laboratory tests, and Questionnaires Performed on the 5 FM Subjects

Tests & Evaluation	Pre-Intervention	Post-Phase I	Post-Phase II
Physical Exam + Vital Signs	X	X	X
Body Composition	X	X	X
Ghent Score	X		X
Pressure Threshold (Dolorimetry)	X	X	X
Fibromyalgia Impact Questionnaire	X	X	X
Zung's Depression Scale	X	X	X
CBC	X	X	X
Urinalysis	X	X	X
Blood Chemistry	X	X	X
Thyroid Function Tests + TPO Ab	X	X	X
Thyroid Ultrasonometry	X		X
Serum 25-OH-D_3	X	X	X

(niacin), at daily doses of 1,000 mg B_3 and 200 mg B_2, five female subjects with FM were evaluated before treatment; after six weeks on 100 mg iodine/iodide alone (Phase I) and after six weeks of 100 mg iodine/iodide combined with the B_2 and B_3 complex (Phase II). Phase II followed Phase I without interruption. This study was performed under contract at the Flechas Family Practice Clinic and funded with a grant from Optimox Corporation.

Subjects and Methods

Female subjects with FM (criteria of reference 1 used in screening) were recruited from the private practice of one of the authors (JDF). They were ambulatory, clinically euthyroid, and off all medications one week prior to this study. Informed consent was obtained from all subjects. The clinical data on these subjects are displayed in Table 1. The self-administered questionnaires, as well as the clinical and laboratory tests performed on these subjects, are listed in Table 2. The body mass index (BMI) is the ratio of body weight divided by height squared, using the metric units of kilograms (kg) for weight and meters (m) for height. The normal range is 18.5-24.9 kg/m^2, with less than 18.5 as underweight; between 25-29.9 as over weight and 30 and above as obese. Based on this classification, one subject was within the normal range, two were overweight, and two were obese. A BioImpedance Analyzer Model 450 from BioDynamics, Seattle, WA was used to measure muscle mass, fat mass, and total body water.

After initial evaluation, each was supplied with Iodoral® 50-mg tablets and instructed to ingest two tablets a day for six weeks (Phase I) and to report any adverse effects. At their return visit at the end of Phase I, they received bottles of ATP cofactors containing 100 mg riboflavin and 500 mg niacin as inositol hexanicotinate per tablet. They were instructed to ingest two tablets daily for six weeks in addition to the 100 mg elemental iodine.

The following clinical and laboratory evaluations were performed prior to treatment; after 6 weeks on iodine 100 mg /day (Phase I); and after 12 weeks on iodine plus six weeks on vitamins B_2 and B_3 (Phase II):

- Urine analysis was performed at the clinic with Multistix 10SG reagent strips and read on a Clinitek 100 that was calibrated daily.
- Complete blood count (CBC), the metabolicpanel,

(Continued on next page)

thyroid profile, TPO antibody titer and serum 25-OHD_3 levels were performed by Lab Corporation of America.

- Thyroid ultrasonometry was computed by a registered sonographer using a portable Biosound Esaote Megas System unit with a frequency of 7.5 MHz.

The volume of each lobe of the thyroid gland was calculated as previously described:[9] V (mL) = W (cm) x D (cm) x L (cm) x 0.52. The thyroid volume was the sum of the volumes of both lobes, taking 18 mL as the upper limit for normal thyroid volume in women living in a non-endemic goiter area.[9]

Two questionnaires were completed by the subjects before intervention, post-Phase I and post-Phase II: The FM Impact Questionnaire (FIQ)[10] and the Zung Depression Scale.[11] FIQ has been designed to measure the components of health status that are most affected by FM. A higher score indicates a greater impact of FM on the patient. The maximum score is 100. Most FM patients with mild to moderate FM scored in the 50s; with moderate to marked symptomatology in the 60s. Severely affected patients scored in the 70s and above. Klerman, *et al*,[12] reported FIQ scores of 19±5.5 in 12 healthy premenopausal American women in their 30s, compared to 71±5.0 for 10 American women with FM. Normal women from Mexico and Spain[13] scored lower on the FIQ test: 5.9±6.3 for 33 Mexican women and 1.6±2.5 for 80 Spanish women. The Zung's Depression Scale is a measure of the severity of depression with scores of 50-59 as mild to moderate depression, 60-69 as moderate to marked depression; and greater than 70 as severe depression.

During all three visits, the Pressure Tolerance of each tender point of both sides of the body was performed. The pressure tolerance meter model PTO from Pain Diagnostics and Thermography, Great Neck, New York, was used at all 18 tender points to assess the pressure threshold in kg/cm^2.[14] Pressure Threshold (PT) is the minimum force which induces pain. In seven normal women, which we used as controls, the sums of PTs of all tender points had mean ±SD of 140±30 with a 95% confidence limit of 113-168 kg/cm^2. During breast examination, the Ghent score was used to assess the severity of fibrocystic disease of the breast (FDB) in those five subjects.[15] The maximum score is 40 for both breasts. A score of 7 or less is considered normal. Paired data analysis was used to compare the mean values obtained between pre- and post-intervention within these subjects; with the SPSS software version 14.

(Continued on next page)

Table 3

Effect of Iodine/Iodide Alone or in Combination with Vitamins B_2/B_3 on Some Clinical Parameters in 5 Subjects with FM

	Pre-Intervention	Post-Phase I	Post-Phase II
	x ± SD	x ± SD	x ± SD
Systolic BP	116 ± 1.1	118 ± 11	113 ± 8*
Diastolic BP	78 ± 8	81 ± 5	74 ± 8*
Body Weight (lbs)	177 ± 41	178 ± 39	180 ± 39
Body Temp (°F)	97.8 ± 0.25	97.8 ± 0.21	98 ± 0.29*
Basal Med Rate (cal/24hrs)	1505 ± 275	1505 ± 235	1516 ± 272
Lean Mass (lbs)	107 ± 20	106 ± 17	106 ± 20
Fat Mass (lbs)	70 ± 24	71 ± 24	71 ± 22
Total Body Water	71 ± 3	70 ± 2	71 ± 3

* $0.05 < p < 0.1$

Table 4

Effects of a Daily Dose of 100 mg Iodine/Iodide with and without Vitamins B_2 and B_3 on Thyroid Function Tests in 5 Subjects with Fibromyalgia

	TSH (mIU/L)	Total T4 (µg/dl)	Free T4 (ng/dl)	Total T3 (ng/dl)	Free T3 (pg/ml)
	X ± SD	X ± SD	X ± SD	X ± SD	X ± SD
Pre-Intervention	1.35 ± 0.26	7.4 ± 2.7	1.1 ± .21	149 ± 35	3.1 ± .29
Post-Phase I	4.1 ± 1.4	6.6 ± 2.3	.93 ± .12	126 ± 24	2.9 ± .46
Post-Phase II	5.2 ± 2.1	7.1 ± 2.4	0.96 ± .18	151 ± 42	3.0 ± 0.5
Pre vs Post-Phase I p Value	<0.05	<0.05	NS	<0.05	NS
Pre vs Post-Phase II p Value	<0.05	NS	NS	NS	NS

Results

No side effects were reported by the subjects during the study period and the intervention with iodine 100 mg/day and the B_2/B_3 complex was uneventful. Comparing pre-intervention with post-Phase I and post-Phase II, no statistical significance was observed for urinalysis, blood chemistry, hematology, and body composition. The values for the above parameters were within the normal range before and after intervention. Near significance (0.1> p >0.05) for the following parameters was observed between pre-intervention and post-Phase II (See Table 3): decreased systolic and diastolic blood pressure and increased basal body temperature.

Pre-intervention, the thyroid volumes ranged from 9.0-13.3 ml with a mean of SD of 9.5±2.3 ml. Post-Phase II values ranged from 7.4-12.8 ml with a mean of SD of 10.3±2.4 ml. There was no significant difference between pre- and post-intervention mean thyroid volumes. The data on the thyroid panel are displayed in Table 4. Mean serum TSH levels increased significantly ($p<0.05$) above baseline following Phase I and Phase II interventions. The means of all four thyroid hormones decreased following Phase I, with significant differences ($p<0.05$) observed for total T4 and total T3. However, the mean levels of total T4, total T3, free T4, and free T3 increased following Phase II to reach pre-treatment levels, and there was no significant difference for the mean values of all four thyroid hormones between pre-intervention and post-Phase II.

The Ghent score for severity of FBD decreased significantly (P=0.02) post-Phase II, with mean values ± SD of 14.6±9 pre-intervention and 5.4±3.3 post-Phase II (Table 5). The means of pressure threshold of tender points (kg/cm^2) were pre-intervention — 51±3.6; post-Phase I — 63±14 (NS); and post-Phase II — 72±26 (p=0.07). There was no significant difference between pre-intervention and post-Phase I and post-Phase II for the mean values of the FIQ: pre-intervention — 74±14; post-Phase I — 70±18; post-Phase II — 65±17. The Zung Depression Scale showed a near significant decrease (p=0.08) post-Phase II. The mean ± SD were pre-intervention — 64± 14; post-Phase I — 62±7; and post-Phase II — 56±4.8.

The levels of serum 25-OH-D_3 (ng/ml) are displayed in Table 6. The mean ± SD for pre-intervention, post-Phase I and post-Phase II were respectively: 31±16; 28±15; and 19±3. There was a non-significant drop in the mean serum 25-OH-D_3 level following Phase II.

Discussion

Chronic pain is one of the most common complaints for which patients seek medical advice and FM is the most common etiology for non-localized and diffused myalgias.[14] We have evaluated five subjects who fulfill the criteria set by The American College of Rheumatology[1] for the classification of fibromyalgia. Several clinical and laboratory data were collected before intervention; post six weeks on iodine at 100 mg/day and post six weeks on at 200 mg B_2 and 1000 mg B_3 per day for six weeks concomitant with the administration of iodine 100 mg/day. Because of the small number of participants, trends were observed that

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did not reach statistical significance at P<0.05. These trends need to be confirmed with a larger group of FM sufferers.

***Clinical Response*:** The near significant decrease in systolic and diastolic blood pressure between pre-intervention and post-Phase II, combined with the near significant increase in basal body temperature, deserves further evaluation. The participants reported feeling warmer after the addition of the B vitamins to the iodine supplementation. A marked and significant (p=0.02) drop in mean Ghent score occurred following 12 weeks of supplementation. Using iodine alone, we have usually observed such a response in the Ghent score after a longer period on this supplement.

As a group, there was no significant improvement in the FIQ score, Zung's Depression Scale, and Pressure Threshold (Table 5). However, subject #5 responded extremely well (Table 7). The original pretreatment scores for depression and impact of fibromyalgia were rated as severe in this subject. Following 12 weeks on the iodine and B complex supplement, her scores improved to the level rated as mild depression and slight impact of Fibromyalgia. The FIQ score decreased markedly from a pre-intervention of 83 (severe) to a low value of 42 (mild) following 12 weeks of iodine and B vitamin supplementation. Using Klerman's FIQ scores for normal American women with mean ± SD of 19±5.5, the upper normal limit would be 19+2(5.5)=30.

Because of the marked difference in FIQ scores for normal women from different locations, upper normal limits for each FM group studied should be computed using normal women from the same population. For example, upper normal FIQ scores would be 18.5 for Mexican women, 6.6 for Spanish women,[13] and 30 for American women.[12]

The 95% confidence limits for pressure threshold in our seven normal women were 113-168 kg/ml. Pressure threshold in subject #5 improved markedly from a pre-treatment of 50 kg/cm^2 to a normal value of 119 kg/cm^2 following 12 weeks of intervention. However, as a group, the pressure threshold of five FM subjects did not reach statistical significance of p<0.05 following intervention, with a p=0.07 following Phase II. Following the end of the study, subject #5 decided to continue on the program, but she decreased the daily intake of iodine to 50 mg, while continuing the ATP cofactors. Fibromyalgia and associated discomfort returned in full force within 2 days. One day after increasing the iodine intake to 100 mg, she noticed a marked improvement of her symptoms to reach the level of well-being she experienced post-Phase II.

***Laboratory Results*:** Thyroid function tests included TSH, T4, T4, free T3, free T4, and TPO antibody titer. Serum TSH increased significantly following iodine supplementation for six weeks. This increase persisted following the addition of the B vitamins. We have observed increased TSH levels following orthoiodosupplementation, but these levels usually return to the normal range within 6-12 months.[8] There was a decrease in the main values of all thyroid hormones measured, with significance at p<0.05 for total T4 and total T3 following Phase I. However, supplementation with the B vitamins resulted in the reversal of this trend for all four thyroid hormones which

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Table 5

Pressure Threshold, Ghent's Score, and Results of 2 Self-Administered Questionnaires in 5 Female Subjects with Fibromyalgia before and after Intervention

	Pre-Intervention	Post-Phase I		Post-Phase II	
	x ± SD	x ± SD	p Value	x ± SD	p Value
Fibromyalgia Impact Questionaire	71 ± 14	70 ± 18	NS	65 ± 17	NS
Zung Depression Score	64 ± 14	62 ± 7	NS	56 ± 4.8	0.08
Pressure Threshold (kg/cm^2)	51 ± 3.6	63 ± 14	NS	72 ± 26	0.07
Ghent's Score	14.6 ± 9			5.4 ± 3.3	0.02

Table 6

Serum 25-OH-D_3 Levels (ng/ml) Pre- and Post-Intervention in 5 Female Subjects with FM

SS#	Pre-Intervention	Post-Phase I	Post-Phase II
1	25.10	35.60	24.00
2	26.30	21.60	18.20
3	15.10	16.50	16.80
4	57.20	16.50	16.40
5	29.50	51.20	19.70
X	31	28	19
SD	16	15	3
p Value		0.84	0.2

increased to pre-treatment levels following Phase II. There was no statistically significant difference between pre-supplementation and post-Phase II mean levels of thyroid hormones (Table 4). An increased organification of thyroidal iodide for the synthesis of thyroid hormones by the ATP cofactors could explain this effect on thyroid hormones.[8] Low titer of TPO antibodies were present in three subjects, ranging from 11-37. There was no increase in titer following the program. In fact, the titers decreased in all three subjects: from 11 to less then 10 in one subject; from 37 to 15; and from 25 to 16 in the other 2 subjects.

Serum 25-OH-D_3 levels pre- and post-supplementation are displayed in Table 7. According to Grant and Holick,[16] serum 25-OH-D_3 levels lower then 20 ng/ml are evidence of vitamin D deficiency; levels between 20 and 32 ng/ml are evidence of insufficiency; and 32-100 as sufficiency. Based on this classification, only subject #4 had vitamin D sufficiency at baseline. However, her serum 25-OH-D_3 levels decreased to 16.4 ng/ml post-Phase II.

Whether or not vitamin D deficiency plays a role in FM is debatable at this time.[17,18] Block and Gratwick[19] reported that out of six FM patients with serum 25-OH-D_3 levels below 10 ng/ml, who received 50,000 IU vitamin D weekly for eight weeks, only one patient believed that vitamin D therapy was helpful and the other five patients found the vitamin D therapy of no benefit for their pain. In subject #5 of our study, who showed the best response to intervention, the post-intervention serum 25-OH-D_3 was 19.7 ng/ml, a level classified as deficient vitamin D.

There was a non-significant drop of 40% in the mean serum 25-OH-D_3 levels of the five FM subjects evaluated following the addition of the ATP cofactors to iodine supplementation. The mean values were 31 ng/ml pre-supplementation; 28 ng/ml after six weeks on iodine; and 19 ng/ml post B vitamin administration. If this trend of decreasing serum 25-OH-D_3 is confirmed in a larger group of FM sufferers and becomes statistically significant, understanding its physiological significance and the mechanisms involved would require further investigation. A decrease in serum 25-OH-D_3 could be due to either decreased synthesis by the liver from vitamin D or increased metabolism of 25-OH-D_3 to calcitriol by target cells such as the kidney and other organs possessing 1-hydroxydase activity for 25-OH-D_3.

General Discussion

Based on whole body sufficiency for iodine, the US population is severely deficient in this essential element, requiring at least 100 times the RDA to achieve sufficiency.[5,9,20,21] If iodine plays a role in vitamin D metabolism and has a modulating effect on target organ response to calcitriol, the normal range of serum 25-OH-D_3 would need re-evaluation in whole body iodine sufficient individuals. Vitamin D is essentially a steroid and iodine affects receptor responsiveness to estrogens and other steroids.[22,23]

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The classification of vitamin D deficiency according to serum 25-OH-D_3 levels is based on data obtained in severely iodine-deficient individuals, consuming the very low US RDA amount of iodine. This classification will need re-evaluation following published studies looking at the effect of whole body iodine sufficiency on the conversion of 25-OH-D_3 to the active hormone calcitriol. For example, magnesium increases the 1-hydroxydase activity of the kidney.[24] Therefore adequate magnesium intake would lower the serum 25-OH-D_3 levels required for adequate calcitriol synthesis. One would expect a magnesium sufficient individual to achieve normal calcitriol levels with lower serum 25-OH-D_3 than in a magnesium deficient individual.

Standardizing the levels of serum 25-OH-D_3 would require a careful screening of subjects participating in this standardization program. Ideally, these subjects should be supplied with adequate amount of magnesium and iodine to achieve whole body sufficiency for these two important nutrients. Magnesium deficiency is common in the US population as well as the rest of the world.[25-28] Red blood cell (RBC) magnesium levels were below the normal range in all nine normally menstruating pre-menopausal American women evaluated by one of the authors (GEA) 25 years ago.[29] Vitamin B_6, at an oral daily dose of 200 mg in these nine women increased markedly the RBC magnesium with mean values more than twice the baseline levels. The B vitamins require phosphorilation to become biologically active and magnesium is required for this phosphorilation.[30] Vitamin B_6 enhances cell membrane transfer of magnesium.[29] Riboflavin is required to oxydize pyridoxine (B_6) phosphate to the active form, pyridoxal-5-phosphate.[30]

It is obvious that a complete nutritional program emphasizing magnesium instead of calcium would be required in order to standardize optimal levels of physiological parameters in optimally healthy individuals. In one of the author's (GEA) experience, megadosing with calcium (2,000-3,000 mg/day) has been the most common cause of poor response to orthoiodosupplementation. Physicians and other health care professionals need to be informed about the toxicity of excess calcium,[31] and the importance of adequate magnesium intake[31-36] for optimal health and strong bones.

The effect of a magnesium-emphasized complete nutritional program combined with orthoiodosupplementation and high doses of B_2/B_3 will be evaluated in our next study of FM sufferers. The measurement of red blood cell ATP levels, serum calcitriol, and PTH will be added to the laboratory tests in order to achieve a better understanding of the effect of the program on ATP synthesis and the interaction between the serum 25-OH-D_3 levels and the biologically active hormone calcitriol.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology, and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the Medaille d'Honneur from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980. Dr. Abraham's current research interests include the development of assays for the measurement of iodide and the other halides in biological fluids and their applications to the

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Table 7

Response of Subject #5 to Intervention

	Pre-Intervention	Post-Phase I	Post-Phase II
Ghent's Score	13		3
Fibromyalgia Impact Questionnaire	83	61	42
Zung Depression Score	75	64	55
Pressure Threshold (kg/cm^2)	53	76	119

implementation of orthoiodosupplementation in medical practice. The applications of Dr. Abraham's techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders.

Jorge D. Flechas, MD MPH, is the medical director of Flechas Family Practice in Hendersonville, North Carolina, specializing in hormonal therapy for treatment of fibromyalgia and chronic fatigue and immune dysfunction syndrome (CFIDS) since the late 1980s. He has developed a new protocol for treatment of these illnesses using oxytocin (OT), dehydroepiandrosterone (DHEA) and some natural nutrients. He feels both diseases are most likely due to a neuroendocrine /metabolic disorder with chronic hypoxia, which causes abnormalities in the biochemistry of patients. Dr. Felchas also specializes in iodine therapy for hypothyroidism and fibrocystic breast disease.

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ABSTRACTS OF INTEREST

Submitted by Emerson Ecologics

Quercetin Reduces Blood Pressure

Author: Donald Brown, ND

Reference: Edwards RL, Lyon T, Litwin SE, et al. Quercetin reduces blood pressure in hypertensive subjects. *J Nutr* 2007;137:2405–11.

Design: Randomized, double-blind, placebo-controlled, crossover trial

Participants: Males and females with either prehypertension (120–139 mm Hg systolic/80–89 mm Hg diastolic; n = 19; mean age 47.8 ± 3.5 years old) or stage 1 hypertension (140–159 mm Hg systolic/90–99 mm Hg diastolic; n = 22; mean age 49.2 ± 2.9 years old) were enrolled in the study. Subjects taking antihypertensive medications were not allowed in the study.

Study Medication and Dosage: 365 mg of quercetin aglycone b.i.d. (USANA Health Sciences, Salt Lake City, Utah) or placebo.

Duration: Four weeks of treatment with either quercetin or placebo followed by a 14-day washout phase. This was followed by cross-over and another 14 -day treatment period on either quercetin or placebo. Patients were randomized after an initial 14-day run-in period.

Outcome Measures: The change in blood pressure (BP) compared to baseline measurement was the primary outcome measure. Secondary outcomes included the effect of quercetin on measures of oxidant stress measured in the plasma and urine. Additionally, blood samples were used to measure plasma quercetin concentrations as well as blood lipid concentrations (triglycerides, LDL-C, HDL-C, VLDL-C, and total lipoprotein concentrations).

Key Findings: BP was not changed in prehypertensive patients following supplementation with quercetin nor did it change during the placebo phase of the study. In stage 1 hypertensive patients, quercetin supplementation significantly reduced systolic BP (– 7 ± 2 mm Hg; $p < 0.01$), diastolic BP (–5 ± 2 mm Hg; $p < 0.01$), and mean arterial pressures (–5 ± 2 mm Hg; $p < 0.01$). The antihypertensive effect of quercetin was independent of gender, age, and BMI in stage 1 hypertensive patients. Indices of oxidative stress in the plasma and urine were unaffected by quercetin in both groups. Also, there was no effect on blood lipid concentrations during quercetin supplementation.

Practice Implications: Based on the results of animal studies demonstrating the effect of quercetin on vasorelaxation and blood pressure, researchers from the University of Utah decided to see if quercetin was able to reduce BP in prehypertensive and stage 1 hypertensive human subjects. The crossover design of the study suggests that a daily dose of 730 mg of quercetin (in an aglycone form) is capable of reducing both systolic BP and diastolic BP in stage 1 hypertensive patients but not prehypertensive patients. Hopefully this study will set the stage for future dose-response studies as well as a larger placebo-controlled trial with stage 1 hypertensive patients.

N-acetylcysteine helps fight addictions

Author: Alan R. Gaby, M.D.

What do cocaine addiction and gambling addiction have in common? Three new studies suggest that both can be treated successfully with N-acetylcysteine (NAC). This research offers new hope that these highly prevalent, serious, and difficult-to-treat disorders can be better managed.

There is evidence that a subnormal concentration of glutamate in the nucleus accumbens region of the brain increases compulsive or addictive behaviors and heightens cravings. Chronic administration of cocaine to rats decreases glutamate levels in the nucleus accumbens, whereas acute administration of cocaine causes a transient increase in glutamate levels. These observations might explain the highly addictive nature of cocaine. Administration of NAC, on the other hand, has been shown to increase glutamate concentrations in the nucleus accumbens. NAC might therefore be an effective treatment for various addictions and cravings.

In a preliminary trial, 15 volunteers with cocaine addiction who were not using cocaine at the time of the study received, in double-blind fashion, 600 mg of NAC or placebo every 12 hours for a total of four doses. After a four-day washout period, each person received the alternate treatment. Compared with placebo, NAC significantly reduced the desire to use cocaine ($p < 0.05$) and significantly decreased the amount of time the participants spent viewing cocaine-related slides ($p < 0.05$).[1]

In a follow-up study by the same investigators, 23 cocaine-addicted patients who were seeking treatment for their addiction received (without randomization) 600, 1,200, or 1,800 mg of NAC twice a day for four weeks. Among the 16 patients who completed the trial, the

mean number of days of cocaine use fell from 8.1 in the 28 days prior to NAC treatment to 1.1 during the 28-day treatment period, an 86% decrease ($p = 0.001$). All three doses of NAC were well tolerated.[2]

While the prospect that a relatively nontoxic natural substance can decrease cocaine use by 86% is highly encouraging, NAC may not be as effective as the results of this study suggest. The patients in this study were selected because they were seeking treatment for their addiction and were therefore motivated to stop using cocaine. It is possible that their cocaine use would also have decreased if they had been given a placebo or no medication at all. Nevertheless, NAC deserves further study as a treatment for cocaine addiction.

Encouraging results were also reported in a study of people addicted to gambling. If no improvement was seen, the dosage was increased to 1,200 mg per day for another two weeks, and then to 1,800 mg per day for a total treatment period of eight weeks. A response to treatment was defined as a decrease of 30% or more in the score on the Yale Brown Obsessive Compulsive Scale Modified for Pathological Gambling (PG-YBOCS). After this open-label treatment, patients who responded were randomly assigned to receive, in double-blind fashion, their effective dose of NAC or placebo for an additional six weeks. During the open-label phase, the mean PG-YBOCS score decreased from 20.3 at baseline to 11.8, a 42% improvement ($p < .001$). The mean effective dose of NAC was approximately 1,500 mg per day. Sixteen subjects (59.3%) were responders, of whom 13 entered the double-blind trial. At the end of the double-blind phase, 83.3% (5 of 6) of those assigned to NAC, but only 28.6% (2 of 7) of those assigned to placebo were still considered responders ($p < 0.08$).[3]

Like earlier studies that demonstrated beneficial effects of glutamine, B vitamins, lithium, and dietary modifications in people addicted to alcohol, this new research supports the concept that there is a biochemical component to other addictions as well. Further research on ways to optimize brain chemistry will no doubt provide much-needed aid to the millions of people who claim that their spirit is willing but their flesh is weak.

Vitamin E Supplementation Reduces the Risk of Thromboembolism in a Large Blinded Trial

Author: Steve Austin, N.D.

Reference: Glynn RJ, Ridker PM, Goldhaber SZ, et al. Effects of random allocation to vitamin E supplementation on the occurrence of venous thromboembolism. Report from the Women's Health Study. *Circulation* 2007;116:1497–1503.

Design: Randomized double-blind intervention trial

Participants: 26,779 women ≥45 years of age

Study Medication and Dosage: 600 IU of apparently d-alpha tocopherol was taken every 2nd day or placebo taken every 2nd day for a median follow-up of 10 years. (The form of vitamin E was listed as "alpha-tocopherol" from the Natural Source Vitamin E Association).

Main Outcome Measures: Indices of clotting (e.g., prothrombin and factor V Leiden) were measured at baseline. During follow-up, documented cases of venous thromboemboli (VTE) including both deep vein thromboses and pulmonary emboli were recorded. VTE specifically not associated with recent surgery, cancer diagnosis, or trauma ("unprovoked VTE") were also tracked separately.

Key Findings: 269 cases of VTE occurred in the placebo group during the follow-up, versus 213 cases in the vitamin E arm of the trial--a highly statistically significant 21% reduction in risk. The reduction in risk of specifically unprovoked VTE was 27%.

The small (3%) group of subjects who had suffered a VTE before the trial experienced a statistically significant 44% reduced risk of another VTE compared with those in the placebo group. Women who had no previous history of VTE saw only an 18% reduction in risk, though even this modest difference achieved statistical significance. Those with genetic mutations rendering them susceptible to VTE (factor V Leiden or prothrombin mutations) had a dramatic highly statistically significant 49% decrease in risk if assigned to the vitamin E arm of the trial.

Practice Implications: The previous fragmentary evidence suggesting that vitamin E might antagonize vitamin K metabolism, and thus interfere with normal clotting, was apparently key to the thinking that led to the birth of this trial. While a true mechanistic understanding of what happened here must remain elusive for the present, the potential clinical ramifications are arguably clearer.

First, these data provide what may be the strongest argument for inclusion of 300 IU of vitamin E in multivitamins that has appeared in many years. (It would seem unlikely that 300 IU per day would produce different outcomes than those reported here with 600 IU given every second day.) These findings strongly suggest that anyone with a history of VTE or known to be at high risk should be taking vitamin E.

The question of whether we should interpret these findings to suggest that all adults about to take a long plane trip (which increases risk of deep vein thrombosis significantly) should be supplementing with vitamin E is

one that, for the moment will have to be answered by you, the reader. That said, the risk of a type I error (in which we would guess that vitamin E would *appear* to have a prophylactic effect that eventually would be disproven) would seem to be worth the low price of admission, given low cost and lack of toxicity. (Previously, this column discussed how the evidence purportedly showing that vitamin E supplementation "increases mortality" provided no data from specific trials at or below 400 IU/day that supported their conclusion.) These findings constitute the best day in court vitamin E has had in a very long time.

Diet Dramatically Affects the Outcome for Patients with Stage-III Colon Cancer

Author: Steve Austin, N.D.

Reference: Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. *JAMA* 2007;298:754–64.

Design: Observational prospective study

Participants: 1009 patients with stage III colon cancer (CA) who were receiving chemotherapy and consuming self-selected diets

Primary Outcome Measures: On the basis of diet diaries compiled during the time they were receiving chemotherapy and six months later, subjects were divided into those consuming a predominantly "prudent" diet and those consuming a predominantly "Western" diet. The prudent diet was characterized as being high in produce, poultry, and fish, while the Western diet was characterized as being high meat, fat, refined carbohydrate, and dessert. Disease-free survival (DFS) and overall survival (OS) were tracked for a median of 5.3 years.

Key Findings: 324 recurrences and 223 colon CA-related deaths occurred during follow-up. Those in the top quintile of adherence to the Western diet had over three times the risk of not retaining their disease-free baseline status by the end of follow-up, compared with those in the bottom quintile (hazard ratio=3.25; 95% CI, 2.0–5.2; p for trend<0.001). Similarly, the risk of dying from all causes was over twice as great in the top quintile of adherence to the Western diet versus those in the bottom quintile (hazard ratio=2.32; 95% CI, 1.35 –3.96; P for trend<0.001). Adjusting for gender, age, body mass index, exercise level, etc. did not alter these associations significantly.

Practice Implications: Much previous research has implicated meat consumption as a primary culprit in the high risk of colon CA seen in Western societies, particularly when the meat is well cooked and particularly in genetically susceptible subsets of the population. A relationship between whole grains or insoluble fiber consumption and protection against colon CA has held up in some studies but not most. This report, surprisingly in *JAMA*, takes a less reductionistic perspective by hunting for the effects of diet from a more global perspective.

Basically the more stereotypically "American" the diet was, the higher was the risk of recurrence from colon CA and death. These findings fit well with previous epidemiologic evidence showing that societies that generally eat more healthful diets than Americans do suffer less from colon CA.

However, the big news here is not the confirmation of such associations, but rather that this study focused on *secondary* prevention. That primary prevention and secondary prevention are related is accepted by most health care professionals regarding most chronic diseases. The major exception is conventional medicine's view of CA, which historically has assumed diet has little to do with survival or recurrence--at least *post diagnosis*. These new findings strongly suggest that people who are already diagnosed with colon CA (at least through stage-III disease) stand a good chance of improving their chances of survival by simply changing their diet in ways that would be obvious to most practitioners of natural medicine. These findings greatly underscore the need for colon CA patients to be working with such practitioners, as they are most unlikely to receive such advice from their oncologists.

Probiotic Combination Reduces Antibiotic-Associated Diarrhea and *C. difficile* in Older Adults

Author: Donald Brown, ND

Reference: Hickson M, D'Souza A, Muthu N, et al. Use of probiotic *Lactobacillus* preparation to prevent diarrhea associated with antibiotics: randomized double blind placebo controlled trial. *BMJ* 2007;335:80; doi:10.1136/bmj.39231.599815.55 [Epub].

Design: Randomized, double-blind, placebo-controlled trial

Participants: 135 elderly inpatients (mean age 74 years old) who were prescribed antibiotics (single or multiple antibiotics, oral or intravenous)

Study Medication and Dosage: A 100 g (97 ml) probiotic yogurt drink (Actimel, Danone, France) containing *Lactobacillus casei* DN-114 001 (1.0×10^8 cfu/ml), *Streptococcus thermophilus* (1.0×10^8 cfu/ml), and *Lactobacillus bulgaricus* (1.0×10^7 cfu/ml) b.i.d. The drink was consumed half an hour before or one to two hours after meals. The placebo group received commercial "milkshake" (Yazoo, Campina, Netherlands) that is

free of probiotics.

Duration: Participants began using the drink within 48 hours of starting antibiotic therapy and continued doing so for one week after they stopped taking antibiotics.

Outcome Measures: The primary outcome was the occurrence of diarrhea. Diarrhea was defined as more than two liquid stools per day for three or more days in quantities in excess of normal for each patient. The secondary outcome was the occurrence of *Clostridium difficile* infection, defined as an episode of diarrhea combined with the detection of toxins A or B, or both, from a stool sample. A baseline stool sample was collected to screen for asymptomatic *C. difficile* infection. Bowel movements were monitored with stool charts, which were checked every day for accuracy. When there was evidence of diarrhea, a stool sample was analyzed for *C. difficile* toxin.

Key Findings: One hundred thirteen patients completed the study (probiotic group, n = 57). The most common reason for exclusion (61%) was the likelihood of diarrhea due to causes unrelated to antibiotics. Most patients received one antibiotic, but about 40% received two. In the probiotic group, 7 of 57 participants (12%) developed diarrhea compared to 19 of 56 (34%) in the placebo group (p = 0.007). The absolute risk reduction for occurrence of antibiotic associated diarrhea was 22% (95% confidence interval, 0.07 to 0.85). Data on possible *C. difficile* was available for only 109 patients. No one in the probiotic group had *C. difficile* infection compared to 9 of 53 (17%) in the placebo group (p = 0.001). There were no adverse events related to the study drinks.

Practice Implications: While antibiotic-associated diarrhea (AAD) is a risk factor across many age groups, diarrhea secondary to *C. difficle* infection (about 15-25% of all cases of AAD) is more common in the elderly, usually within two to three weeks after cessation of antibiotic therapy. Over the past couple of years, *C. difficile* outbreaks in both Canada and the Netherlands have been associated with significant mortality in elderly hospitalized patients. This clinical trial adds the use of a *Lactobacillus* and *Streptococcus* combination to the considerations for the prevention of both AAD and *C. difficile* in elderly patients. As noted in previous reviews in this column, the best data to date on the prevention of *C. difficile* has been with *Saccharomyces boulardii* (specifically the product Florastor), typically used at a dose of 1 g/day.

More on Vitamin D, Bone Health and Cancer Prevention

Author: Tori Hudson, N.D.

Lappe JM, et al. Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial. *Am J Clin Nut* 2007; Jun;85(6):1586-1591

In a population-based study, 1180 Caucasian women older than 55, were randomized to receive a calcium supplement, a calcium supplement plus 1100 IU of vitamin D (cholecalciferol), or a daily placebo. Health status and compliance to the regimen were assessed every 6 months over 4 years and serum vitamin D was measured at baseline and annually. 1024 women completed the study. The purpose of the analysis was to determine the efficacy of calcium by itself and calcium plus vitamin D in reducing the all-cancer risk in postmenopausal women.

Fifty women developed cancers other than skin cancer. The risk for cancer in the calcium-plus vitamin-D group was less than half that in the placebo group (RR 0.4; P=0.013). The calcium-only group had no statistically significant risk reduction. Researchers adjusted for the possibility that cancers detected during the first year of the study, had been present but silent at baseline, and analyzed these separately. Relative risk for cancer in the calcium and vitamin D group was lower than in the placebo control subjects (P< 0.005), and the risk reduction for the calcium only group was not statistically significant.

Women in the calcium plus vitamin D group had higher serum vitamin D levels that correlated with lower cancer risk, both at baseline and at one year. Adherence to the study doses was 86%.

Commentary: The only other randomized trial of vitamin D and cancer was the Women's Health Initiative (WHI), which studied women with a lower baseline vitamin D status and used a lower dose of vitamin D (400 IU). The WHI reported no significant effect of the vitamin D intervention on colorectal cancer incidence but did observe a significant inverse relation between baseline vitamin D levels and cancer risk, as did this study. It's reassuring to see that the benefits of higher than recommended dosing of vitamin D is catching on. It is estimated that about 60% of women in the U.S. are vitamin D deficient, regardless of geographical location. The current adult daily recommendation for vitamin D in women between the ages of 51 and 70 is 400-800 IU per day. Intakes of up to 2000 IU per day are considered safe and to be without significant risk for adverse events. Many practitioners are advising even higher doses, but I would recommend this only after assessment for medical need, serum testing, and evaluation for risk of side effects.

Abstracts are courtesy of Emerson Ecologics.

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Water: Essential for Life

by Gregory W. Peterson, DC, DABCI, FIAMA, CCST

Introduction

Socrates is credited to have said, "Water brings life; life needs water." How right he was. Every function of the body is dependent in some way upon water. Hormones, nutrients, brain and neurotransmitters all need water for the manufacture, transportation, and utilization of nutrients in every cell, organ, and system. Without food most of us would perish in approximately 50 days if we have adequate water. Without water we might make it 10 days or so; that's about it. Only our need for air outranks water.

Our bodies need a continuous supply of pure water to maintain the delicate balance which sustains life. By weight our body is about 72% water, another 8% is a combination of chemical compounds, and the remaining 20% is bone and solid tissue. Our blood is approximately 90% water, our brains consist of 85% water. Water is vitally important to our well-being. Since our bodies are primarily water, it only makes sense that the quality of the water we consume will have a very dramatic impact on our overall state of health. Every healing and life-giving process that happens in our body needs water!

Water has numerous roles that it plays in our bodily functions:

1) Solvent: In chemistry, water is known as the universal solvent; in the body it serves the same role. It provides the basis for all the body's chemical processes.
2) Transportation: Water circulates throughout the body as blood, lymph, cerebral spinal fluid, etc. In these fluids, nutrients like oxygen, vitamins, and minerals flow to the cells while waste products like metabolites and CO_2 are carried away in water-based fluids.
3) Regulation of Temperature and pH: When the body temperature rises due to exercise or other exertion water is lost as sweat; this serves as a coolant to the body. Water also helps the body maintain delicate pH balances. The blood absolutely needs to be maintained at a pH between 7.3 and 7.4.
4) Volume and Mass: Water helps to give cells shape by providing the fluid for extracellular fluids (the fluid between cells) and intracellular fluids (fluid within the cell). The intracellular fluid accounts for approximately 40% of the total body weight.
5) Lubrication: Water acts as a lubricant in a number of different ways. For example, in a joint it forms synovial fluid; in the lungs it helps with breathing by forming surfactant.

Water and the Human Body

In 1994, a medical doctor named Batmanghelidj wrote a very thought-provoking book, *Your Body's Many Cries for Water*. In it he makes the claim that most of modern present-day diseases are the end result of dehydration or inadequate water intake. He goes on to provide dozens of case studies to support his theory quite convincingly. If you have not read the book, I encourage you to do so. It will change the way you look at your water consumption.

Many of today's ailments and illnesses can be prevented and possibly even cured with an increased intake of healthy water. According to Dr. Batmanghelidj, arthritis, asthma, back pain, fatigue, headaches, hypertension, morning sickness, and ulcers all benefit, and in many cases can be prevented, by regulating the body's natural fluid levels. Recently there has been a dramatic swing in medical theory and a long overdue realization about "healing." The best way to prevent, treat, and often cure illness is to give our body the right tools, and let it go to work. With the proper intake of healthy water and the right minerals and nutrients, our body can overcome almost anything.

How Much Water Is Needed?

How much water one should drink is open to a vast difference of opinion. There really is no iron-clad formula. For example, a 5-foot, 2-inch female working indoors is certainly going to have a different requirement than a 6-foot, 3-inch male doing construction. A basic rule of thumb: Drink pure water whenever thirsty!

The Institute of Medicine released an erroneous report a couple of years ago that stated as long as the substance contained water, it counted as water intake. However, once the chemical structure is altered such as in coffee, tea, juice, or soda pop, the water loses its ability to be used in its vital roles. Thus coffee, tea, juice, and certainly soda pop do not count as a beneficial intake to

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maintain fluid balances. Is it any wonder so many of your friends or family might be suffering from very preventable illnesses?

As a general guideline, drink two 8-ounce glasses of water before breakfast, and a glass of water about 30 minutes before lunch and supper. Drink an additional couple of glasses between meals and a glass before bed. It is advisable to increase water intake during periods of exertion, stress, or when air temperatures are warmer and drier. Pay attention to your body signals and you will become more aware of your need.

Quality of Our Water Supply

A Harris Interactive poll, published in October 2005, found that Americans rank water pollution as the number one environmental concern facing the country, topping global warming, ozone depletion, and air pollution. And yet we find a deep chasm between what people care about and what those in position to improve the situation are willing to act upon.

The 2000 EPA Toxic Release Inventory revealed that major into the water and air. Anyone care to guess how many pounds were not reported?

The causes of water contamination are numerous and range from agricultural runoff to improper use of industrial and household chemicals, and everything in between. There are currently over 100,000 different chemical compounds with potentially harmful health effects in our environment. While they have offered added convenience and perceived productivity in our lives, they have also come at a tremendous price, one being a drastic increase in degenerative diseases. In the early 1900s, before chlorine, rocket fuel, pesticides, herbicides, and the tens of thousands of other chemicals to which we have been exposed, the average person had a one in 50 chance of getting cancer. Today one in three can expect to get cancer in their lifetime, and one out of every two men can look forward to cancer.

In an important recent study led by the Mount Sinai School of Medicine in New York, researchers found that after testing 210 toxic chemicals, the average participant in the study group had 91 industrial compounds, chemicals, and pollutants in their urine and blood. Even the test subject with the fewest pollutants had 77 industrial pollutants in their body. Most of the people in the study did not live near major industrial polluters.

It is evident from this study that no matter how diligent we are to live in a "clean" environment, it is next to impossible to accomplish. That does not mean, however, that you need to throw in the towel and forget about striving to be healthy. That does not mean that we should not be concerned and try to push for stricter standards and a cleaner environment. We need to avoid the harmful things in life that we can while not being overly obsessive about the things we cannot change.

Quality of Tap Water

According to another Environmental Working Group report, analysis of municipal tap water from 42 states validates the public's concern about tap water. They found that between 1998 and 2003, municipal water suppliers collectively identified the following in treated tap water: 166 industrial chemicals from factory waste and consumer products; 44 pollutants that are byproducts of the water treatment process or that leach from pipes and storage tanks; 83 agricultural pollutants, including pesticides and chemicals from fertilizer- and manure-laden runoff; and 59 contaminants linked to sprawl and urban areas from polluted runoff and wastewater treatment plants.

***Industrial Chemicals in Tap Water*:** EWG's analysis of municipal water suppliers' tap water test results shows that the water was contaminated with 166 industrial pollutants including solvents, plasticizers, and propellants. This is the municipal tap water of more than 210 million people in 42 states. Fifty-six percent of those people were provided water with one or more industrial contaminants present at levels above non-enforceable, health-based limits. It is important to note that 94 of the industrial chemicals detected are unregulated, and there is no legal or health-based limit set for municipal tap water.

***Chemicals from Sprawl and Urban Areas*:** EWG's analysis shows that the water was contaminated with 59 pollutants linked to sprawl and urban areas, also including plasticizers, solvents, and propellants. This represents over 202 million people in 42 states, and 53% of those individuals were provided with water that contained one or more of these contaminants present at levels above non-enforceable, health-based limits. According to the US Council of Environmental Quality, "Cancer risk among people drinking chlorinated water is 93% higher than among those whose water does not contain chlorine." Forty-one of the urban and sprawl chemicals detected in tap water are unregulated with no legal or health-based limit set for municipal tap water.

***Agricultural Chemicals in Tap Water*:** According to EWG's analysis, 83 agricultural pollutants were found, including pesticides and fertilizer ingredients. This wa-

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ter was provided to more than 201 million people in 41 states, and 15% of those people were served water with one or more agricultural contaminants present at levels above non-enforceable, health-based limits. Fifty-four of the agricultural chemicals detected in tap water are unregulated, and there is no legal or health-based limit set for municipal tap water.

Quality of Well Water

If at you think you are safe because you have your own well, you had better think again. There are some water issues specific to wells. In a five-year national survey of nitrate and pesticides (NPS) in drinking water wells, 10 million rural domestic wells were studied. The results showed that nitrate was detected in 57%, pesticides in 4%, and both in 3%. A variety of potentially carcinogenic chemicals used in industry, business, or households could also endanger the safety of drinking water obtained from wells.

***Bacteria and Nitrates*:** These pollutants are found in human and animal wastes. Septic tanks can cause bacterial and nitrate pollution, as can large numbers of farm animals. Both septic systems and animal manure must be carefully managed to prevent pollution. Sanitary landfills and garbage dumps are also sources of contamination. Children and some adults are at extra risk when exposed to water-born bacteria. These include the elderly and people whose immune systems are weak. Nitrates cause a health threat in very young infants called "blue baby" syndrome. This condition disrupts oxygen flow in the blood.

***Concentrated Animal Feeding Operations (CAFOs)*:** The number of CAFOs, often called factory farms, is growing. On these farms, thousands of animals are raised in small spaces. The large amounts of animal waste/manure from these farms can threaten water supplies. Strict and careful manure management is needed to prevent pathogen and nutrient problems. Salts from high levels of manure can also pollute ground water.

***Heavy Metals*:** Activities such as mining and construction can release large amounts of heavy metals into nearby ground water sources. Some older fruit orchards may contain high levels of arsenic, which was once used as a pesticide. At high levels, these metals pose a health risk.

***Fertilizers and Pesticides*:** Farmers use fertilizers and pesticides to promote growth and reduce insect damage. These products are also used on golf courses, suburban lawns, and gardens. The chemicals in these products may end up in ground water. Such pollution depends on the types and amounts of chemicals used and how they are applied. Local environmental conditions (soil types, seasonal snow, and rainfall) also affect this pollution. Many fertilizers contain forms of nitrogen that can break down into harmful nitrates. Some underground agricultural drainage systems collect fertilizers and pesticides. This polluted water can pose problems to ground water, local streams, and rivers. The types of soil and the amount of water moving through the soil also play a role.

***Household Wastes*:** Improper disposal of many common products can pollute ground water. These include cleaning solvents, used motor oil, paints, and paint thinners. Even soaps and detergents can harm drinking water. These problems are often found in faulty septic tanks and septic leaching fields.

What Water Should One Drink?

"Is tap water safe to drink?" "How safe is my well water?" These are questions asked by many individuals. Unfortunately, a simple "yes" or "no" is not possible, given variables including the water source, industrial and environmental factors, and water treatment processes.

Which water is healthiest: bottled, reverse osmosis, distilled, or filtered? The choice to be made is simply which product produces the healthiest water and represents the best value for your unique situation. Quality home water filtration can offer significantly purer water than municipal, well, or bottled water.

***Bottled Water*:** According to an independent study entitled, "Bottled water: Understanding a social phenomenon," the conservation organization World Wildlife Fund (WWF) is recommending we drink tap water rather than bottled water. Their findings state that bottled water, while selling at upwards of 1,000 times the price, may be no safer or healthier than tap water in many countries. Yet, it is the fastest growing drink industry in the world and is estimated to be worth $22 billion in the US annually.

The study reveals that the bottled water market is partly fueled by concerns over the safety of municipal water and by the marketing of many brands that portray themselves as being drawn from pristine sources and healthier than tap water. However, some bottled waters only differ from tap water in the fact that they are distributed in bottles rather than through pipes. The study also finds that every year 1.5 million tons of plastic are used to bottle this water. Chemicals leaching from plastic contain-

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ers present another problem. Furthermore, toxic chemicals are released into the environment during the manufacture and disposal of the bottles.

"Bottled water isn't a long-term, sustainable solution to securing access to healthy water," said Richard Holland in the WWF bottled water article. "Clean water is a basic right. Protecting our rivers, streams, and wetlands will help ensure that tap water remains a service which delivers good quality drinking water for everyone at a fair price."

My own recommendations have changed as a result of this study. In most cases I personally believe bottled water is healthier despite the chemical leaching from the plastic. However, I am not sure that it is worth the burden it places on the environment in the manufacture and disposal of all those plastic bottles.

***Reverse Osmosis*:** Reverse osmosis was developed as a water treatment method more than 40 years ago. The process first arose as a way to make sea water drinkable. Once the method's decontaminating capabilities were recognized, reverse osmosis systems began to be commercially produced for home water purification purposes. At first, reverse osmosis units seemed like a viable option to the more costly and energy-wasteful distillation units.

Reverse osmosis is a process that uses water pressure to push water through a semi-permeable membrane with a very fine pore structure. Because most inorganic contaminants are of a larger molecular size than water, the membrane rejects certain contaminants, minerals, and a large part of the water. Municipal tap water contains contaminants such as chlorine and volatile organic chemicals (VOC). Because these contaminants are smaller in size than water, the semi-permeable membrane does not prevent them from passing through with the water; thus, they remain in drinking water. Reverse osmosis does remove some chemical components of drinking water, including fluoride.

The portion of water that passes through the membrane is stripped of inorganic compounds and trace minerals. Reverse osmosis, also, by removing alkaline mineral constituents of water, produces acidic water. Acidic water can be harmful to your body; it causes calcium and other essential minerals to be stripped from bones and teeth in order to neutralize its acidity. Because reverse osmosis units produce less than one gallon per hour, they require a way to store the water. Reverse osmosis typically wastes 2-3 gallons of water for every gallon it produces.

***Distillation*:** Although it has primarily been employed as a method of producing alcoholic beverages like whisky and vodka, distillation also works as a technique of water purification. The process of distillation has been around for a long time, and in the 1970s became a popular home water purification method.

The distillation process requires an energy-consuming heat source to vaporize the water. The object of distillation is to separate pure water molecules from the contaminants which have a higher boiling point than water. The evaporated water is captured and guided through a system of tubes to another container. Finally, when removed from the heat source, the steam condenses back into its original liquid form. Contaminants, having a higher boiling point than water, remain in the original container. This process removes most minerals, most bacteria and viruses, and any chemicals which have a higher boiling point than water from drinking water. For this reason, distillation is sometimes valued as a method of obtaining pure drinking water.

Distillation, similar to reverse osmosis, provides mineral-free water frequently used in laboratories which require mineral-free water. It removes heavy metal materials like lead, arsenic, and mercury from water as well as hardening agents like calcium and phosphorous. Distillation is often used as a water purification method in developing nations, or areas where the risk of waterborne disease is high, due to its ability to remove bacteria and viruses from drinking water.

Even though the distillation processes removes bacteria and mineral contaminants, it does not remove chlorine, chlorine byproducts, or VOCs. These chemicals, which have a lower boiling point than water, are the major contaminants of municipal water. Since most bacteria and heavy metals are removed by municipal water systems, a distillation system is unnecessary and not useful for most individuals.

Distillation, like reverse osmosis, provides mineral-free water which can be quite harmful to your health when ingested, due to its acidity. Acidic drinking water strips bones and teeth of valuable and essential mineral constituents and is also associated with increased cancer rates.

Furthermore, distillation is an incredibly wasteful process. Typically, 80% of the water is discarded with the contaminants, leaving only one gallon of purified water for every five gallons treated.

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***Filtration*:** Water filtration dates back to ancient Greece where they made a simple filter from cloth called a Hippocratic sleeve. Today's filtration methods include complex carbon blocks and multimedia water filters, which are quite efficient at reducing and removing a wide range of contaminants very cost-effectively.

The filtration process involves some type of filter media, over which water flows. Carbon block and granulated carbon filters are the most effective and popular systems. Modern filtration technology allows water filters to remove more and more contaminants through a chemical process of adsorption. In the adsorption process, contaminants are encouraged to break their bond with the water molecules and chemically adhere to the filter media.

Generally, water goes through several stages of filtration to ensure that each filter media will remove the ultimate number of contaminants including VOCs, THM, and fluoride as well as chlorine-resistant protozoa. Water normally passes through a water filter at a relatively low speed, in order to ensure adequate contact time with the filter media. Once the water has passed through the required stages of filtration, it emerges as pure drinking water, free from contamination.

Unlike reverse osmosis and distillation, water filters are not limited in the size or the type of contaminants they can remove. Thus, water filters are able to remove far more contaminants than any other purification method. Also, because they use the chemical adsorption process, water filters can selectively retain healthy trace minerals in drinking water.

Filtration is the only one of the four discussed water purification methods that is capable of removing chlorine, chlorine byproducts, fluoride and VOCs from drinking water. These are some of the most dangerous and threatening contaminants of municipally treated drinking water. Besides the removal of these dangerous chemicals, water filters also extract from drinking water the chlorine-resistant protozoa, Giardia and cryptosporidium. These protozoa have plagued the municipal water treatment industry for decades and have caused a number of epidemics of severe gastrointestinal disease contracted through drinking contaminated water.

Water filters, because they do not require the costly energy sources of reverse osmosis and distillation, provide a source of relatively inexpensive, purified water. Also, water filters waste very little water, as compared to reverse osmosis and distillation systems. Water filtration is also beneficial for private wells as they do not require high water pressure. Additional filters can be added that target nitrates, arsenic, and coliform bacteria. Water filters are therefore a good choice for private and municipal water supplies.

When considering the benefits of home water purification products over tap and bottled water, remember there are no bad systems. Any water purifier is better than no purifier. It becomes a question of how safe do you want to be, and what are you willing to spend. Once we understand the uncertainties of municipal and well water, as well as the uncertainties of bottled water, home water filtration is obviously the best choice.

Types of Filters

In recent years pitcher- and carafe-style filters have emerged as low-cost alternatives to bottled water. Keeping in mind that any filter is better than no filter, these products are by far the least effective and the most costly to use. Pitchers and carafe filters are sold on the "Polaroid principal" — sell the camera cheap and make it up on the film sales. The result is the same with the pour-through pitcher filters — lower quality at a higher price. The average pitcher filter sells for around $25 and includes one 30-gallon filter cartridge. Because of the small size of these cartridges they have a very limited level of effectiveness and a low capacity. While pour-through filters do offer a slightly improved alternative to tap water, they by no means can offer the quality.

Summary

Let me remind you of the water basics. Your primary beverage should be water. Try to have at least eight glasses of water a day, and it would be best to have the water at room temperature. The choice to be made is simply which product produces the healthiest water and represents the best value. Quality home water filtration can offer significantly purer water than tap or bottled water.

About The Author

Gregory Peterson, DC, DABCI, FIACA, FIAMA, CCST earned his doctor of chiropractic degree from Northwestern University of Health Sciences University in Bloomington, MN in 1985. He has continued intensive postgraduate studies with a number of the most prominent holistic practitioners in the US and UK. He founded the Center for Natural Medicine in Winona, MN in 1997.

He has made the pursuit of knowledge to provide the best available Care his mission. Patients from around the country seek Dr. Peterson's health recommendations for regaining and maintain health; effectively, safely and of course – naturally! ◆

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The Energy Deficit Theory of Aging And Disease

by Frank Shallenberger, MD, HMD, ABAAM

Abstract

Mitochondrial function is the single most important aspect of health, aging, and disease. Using a variation of oxygen uptake and carbon dioxide production technology, mitochondrial function can be monitored easily, reliably, and accurately in the average clinic setting.

A condition, designated as Early Onset Mitochondrial Dysfunction (EOMD) is described, which refers to a deterioration of mitochondrial function that is commonly found in young, asymptomatic, and presumably healthy subjects, and increases in incidence with age. EOMD is different from mitochondrial decay. It is reversible, and occurs long before mitochondrial decay, aging, or degenerative disease. EOMD through the combined action of increased free radical production and decreased antioxidant buffering capacity is the primary cause of mitochondrial decay, degenerative disease, aging, and all cause mortality.

A new theory of aging called the Energy Deficit Theory of Aging And Disease is discussed. This theory states that aging and degenerative disease are the results of uncorrected EOMD and that by correcting EOMD, it is possible to prevent degenerative disease and slow down the aging process.

Mitochondrial Function: The Most Important Aspect of Health, Aging, and Disease

Think about it. Can you name one reaction in the human body that is not completely dependent on the availability of ATP? Many reactions can occur in the absence of various vitamins and minerals and substrates, but nothing can happen without ATP. Life itself and ATP are synonymous. Every single aspect of life, whether it involves detoxification, elimination, digestion, reproduction, sensation, mental processes, emotions, repair mechanisms, immunity, or hormone production, is 100% dependent on enough ATP being available to accomplish the task. Couple this simple fact with the observation (discussed later) that mitochondrial function declines commonly even in young persons, and one can begin to fully realize just how important it is for health and well-being.

Healthy or Just Not Sick?

Health is one of those terms that we seem to have a pretty good understanding of until we get right down to really defining it. In fact, most persons, when asked, are hard pressed to come up with a satisfactory definition of health. They only have a sense of what it isn't. Most would agree that the presence of a disease rules out the presence of health. But on the other hand, most would also agree that health isn't simply the absence of a disease. Diseases develop over time and are present during many of those so-called healthy years before they are finally diagnosed. We have all witnessed patients who had been completely asymptomatic for years in spite of the fact that all during that time they were in the process of developing a disease.

Similarly, there is agreement that health can't be defined by the absence of symptoms, and likewise, health certainly can't be defined by the presence of normal blood testing or even normal physiological testing. How many times has a patient been declared healthy as a result of a normal examination and cardiac stress testing only to die of a heart attack the very next day? No, health cannot be determined by any of the commonly used procedures mentioned above. So how can health be determined?

Health — The Presence of Energy

Dorland's Medical Dictionary defines health as "a state of optimal physical, mental, and social well-being, and not merely the absence of disease or infirmity." In other words, health is not the absence of anything, but rather is the optimal presence of something, that something being described by Dorland as "well-being."

But the problem with this definition is that there is just no way to consistently, objectively, scientifically, or quantitatively determine "well-being," and so the definition becomes impractical from a clinical perspective. The fact that we have no effective way to measure health, whereas the measurement of disease is well established, is no doubt at the heart of why we have a disease-oriented health care system rather than a wellness oriented system. I would agree that health is the optimal presence of something, and I will speculate that that something is energy, specifically ATP production as determined by optimal mitochondrial function.

Remember that every single aspect of physical, mental, emotional, and presumably, social functioning is 100%

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dependent on ATP production. Then combine this with the fact that ATP production decreases long before any sign or symptom of either aging or disease (discussed later), and you can begin to appreciate the simple elegance of the statement that optimal health and optimal mitochondrial function are one in the same thing.

An article, which appeared in 2000, by Wilson and Tanaka entitled "Meta-analysis of the age associated decline in maximal aerobic capacity in men: Relation to training status," dramatically demonstrates the relationship between health and mitochondrial function.[1] In the article, using pulmonary gas analysis, the researchers determined optimal mitochondrial function as defined by aerobic capacity. Aerobic capacity refers to the maximum amount of ATP production that can be produced without going into lactic acidosis. Thus, aerobic capacity is a measurement of optimal mitochondrial function.

According to the authors, "Maximal aerobic capacity is an independent risk factor for cardiovascular disease, cognitive dysfunction, and all cause mortality." When they addressed the subject of aging in particular, they went on to say that although most aspects of aging could be trained away in health-conscious endurance trained men, "there continued to be a significant decline in aerobic capacity" in these very same men.

In other words, there is no better assessment of aging than of the other aspects of aging such as insulin resistance, body mass composition, bone density, cardiovascular function, etc., can be revoptimal mitochondrial function as it is determined by aerobic capacity. All erased by training, and hence are simply measurements of conditioning, not aging per se. On the other hand, mitochondrial function cannot be trained away, and therefore represents a better candidate for both health and aging measurement.

In another article, the researchers assayed the skeletal muscle mitochondrial function in 29 subjects aged 16-92 and noted a significant and consistent decline in mitochondrial function associated with age.[2] The literature is replete with studies demonstrating the integral role that decreased mitochondrial function plays in the aging process, and specifically lists cellular processes affected by decreased mitochondrial function including detoxification, repair systems, DNA replication, osmotic balance, and higher order processes such as cognitive function.[3,20]

Mitochondrial Function and Aging

There are two particular studies that have recently been published that rather dramatically identify mitochiondrial dysfunction as the primary cause of aging. In the first study mice were genetically manipulated to develop four times more mutations in their mitochondrial DNA than the control mice. This resulted in a greatly accelerated reduction in mitochondrial function over their lifespan. The genetically altered mice had a significantly reduced lifespan compared to controls. In addition, and perhaps even more to the point, they developed a premature onset of age-related phenotypes — such as lean body mass loss, alopecia, kyphosis, anemia osteoporosis, reduced fertility, and cardiomegaly. The authors concluded that the results provided a clear causative link between decreased mitochondrial function and aging.[4]

In a second study, using NMR technology, the resting mitochondrial function was determined in a cohort of mice, and the mice were followed over the course of their lifespan. A very significantly positive association between resting mitochondrial function and lifespan was noted, such that the mice in the upper quartile of resting mitochondrial function lived 36% longer than the mice in the lowest quartile.[5]

Thus, it appears that the connection between optimal mitochondrial function, health, and aging is overwhelmingly clear, and the primary goal to optimizing health and decelerating aging is to maintain optimal mitochondrial function as we grow older. It is the single most consistent and predictable marker of aging, and it can't be trained away.

Healthy for Your Age or Just Healthy?

Which brings us to the next question. What is aging? When used in the medical sense, aging is a term that refers to the progressive physical and mental deterioration that occurs as we get older. Although it certainly is associated with getting older, aging per se is a measurement of biological function, and as such, is not the same as getting older. For example, when a person goes from being 20 years old to being 30, although he is 10 years older, he is not said to have aged because he has not undergone any physical or mental deterioration. Similarly, when he becomes 40, he is still not said to have aged for the same reason. So aging and getting older are not synonymous, they are only associated because as we get older, as I will explain below, there are more and more reasons and ways to develop decreased energy production.

While ultimately aging is inevitable, the dramatic rate and extent of aging that is commonly seen today may not be. This is why monitoring a patient's mitochondrial function is so important. More than anything else, the rate and extent of aging appears to be dependent on it. Although getting older is not synonymous with aging,

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mitochondrial function is. In fact, nothing is as consistent and as predictable as the gradual, linear decline in energy production seen in all aging populations.[6] As has already been pointed out, every aspect of biological function is directly dependent on mitochondrial function, which makes mitochondrial function the most global parameter of health.

Additionally, mitochondrial function not only influences all biological function, but it is also influenced by every single biochemical and physiological event. Virtually any defect that occurs in human physiology or biochemistry will affect mitochondrial function. Thus it is also arguably the most sensitive parameter of health possible.

Thus, it seems probable that only to the extent that it is possible to initiate therapies that can successfully maintain youthful mitochondrial function in patients as they become older, is it possible to stop or slow down the aging process.

What Is a Disease?

According to the dictionary, diseases are the names that are given to various "pathological conditions of the body" in which the organs and regulating systems become dysfunctional. Study after study has demonstrated that these systems become dysfunctional as a direct result of decreased mitochondrial function. This is particularly true of the degenerative diseases of the neurological system, but is also true of liver disease, diabetes, cancer, and cardiovascular disease. So the single best way to help patients avoid degenerative disease is to initiate therapies that maximize energy production.[7-13]

One Disease — One Treatment

So, in effect, no matter whether one is dealing with aging or disease prevention, one is by necessity dealing with mitochondrial function to such a degree that it may be said, "There is only one disease — decreased mitochondrial function — and there is only one treatment — maximizing mitochondrial function." This statement reveals the potential appeal of objectively measuring a patient's mitochondrial function, because it is then possible to both diagnose the "one disease" and to monitor the "one treatment."

Majid Ali, MD, noted author, teacher, and physician, emphasizes the importance of disease prevention and has frequently commented, "I measure the efficacy of a doctor's treatment more by how the patient is five years from now than how the patient is now." In this regard, perhaps nothing is more important than monitoring each patient's mitochondrial function in order to be sure that the treatment recommended is optimizing it.

Mitochondrial Functional Analysis

Using an FDA-approved pulmonary gas analyzer, a bio-impedance body fat analyzer, a heart rate monitor, a computerized ergometer, and computer software, it is possible to determine a patient's mitochondrial efficiency. That is, how much ATP a patient's mitochondria are capable of producing and whether it is being produced from fat or glucose. The heart and soul of the testing procedure is the information received from the pulmonary gas analyzer which determines only two measurements: how much oxygen is being metabolized and how much carbon dioxide is being produced. When analyzed correctly, these two parameters can be used to determine a patient's mitochondrial functional dynamics, including:

- Total resting ATP production
- Resting ATP production from fatty acid metabolism
- Maximal ATP production from fatty acid metabolism
- Maximal aerobic ATP production (aerobic capacity)

The pulmonary gas analyzer measures the real time breath-by-breath consumption of oxygen and production of carbon dioxide, and the computer then records all the readings. Due to the effects of coughing, sighing, and other forms of irregular breathing which are virtually always encountered during any form of pulmonary testing, there are a significant number of artifacts in the recorded readings which do not accurately reflect true oxygen and carbon dioxide levels. The computer program identifies these artifacts and eliminates them. It then takes the remaining readings, averages them, and uses them to calculate ATP production using the various algorithms described in the sections below.

Measuring Aerobic ATP Production

Almost all of the oxygen that is consumed in the human body is consumed in the mitochondria to produce energy. Although a small percentage is used as part of the oxidative burst of the activated immune system and also as part of the P450 detoxification systems in the liver, as long as the subject's immune system is not actively fighting an infection, and as long as there is no acute toxicity, it can be safely assumed that in a fasting individual, all oxygen consumed is being consumed in the mitochondria. Thus, ATP can be measured as a function of oxygen uptake as follows:

$$\text{Fatty Acid} + 23\ O_2 \rightarrow 16\ CO_2 = 16\ H_2O + 130\ \text{ATP}$$

$$\text{Glucose} + 6\ O_2 \rightarrow 6\ CO_2 = 6\ H_2O + 36\ \text{ATP}$$

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Thus when fatty acids are metabolized by oxygen, there is a ratio of 5.6 (130/23) molecules of ATP produced per molecule of oxygen consumed. By measuring oxygen consumption, the amount of ATP being produced can be easily determined by multiplying this amount by 5.6. In the case of glucose, there is a ratio of six molecules of ATP being produced per molecule of oxygen being consumed (36/6). Again, simply measure oxygen consumption, and you can quickly determine ATP production by multiplying this amount by 6. Note also that glucose results in 7% more ATP production per molecule of oxygen than fat which is why glucose metabolism is said to be a more efficient form of energy production than fat metabolism.

Fat or Glucose?

The only problem with this particular scenario is that, because glucose and fat produce different amounts of ATP per O_2, in order to determine total ATP production with any degree of accuracy, it is at all times necessary to know whether the oxygen being consumed is metabolizing glucose or fatty acids. Fortunately, the above equations can also be used to solve this problem, since the substrate being metabolized by oxygen can easily be determined by the amount of carbon dioxide being simultaneously produced. For example, when glucose is being metabolized there is a 1:1 ratio of carbon dioxide produced to oxygen consumed. Since the pulmonary gas analyzer measures CO_2 production as well as O_2 consumption, it can be determined that oxygen is metabolizing exclusively glucose when the recorded ratio is one. Likewise, since when fatty acids are being metabolized, there is a ratio of .7 molecules of CO_2 produced for every molecule of O_2 being consumed, it can be determined that oxygen is metabolizing exclusively fatty acids when the ratio of CO_2 to O_2 is .7.

When the ratio of CO_2 to O_2 is between .7 and 1, an easy mathematical formula can determine the exact proportions of fat and glucose being metabolized, since the relationship between .7 and 1 turns out to be linear. Thus, when all calculations are performed, it is possible to determine with great accuracy how much ATP is being produced from each source, and hence the total amount of ATP can be accurately calculated.

Resting ATP Production

Resting ATP production can be determined in a subject by measuring the oxygen consumption and the carbon dioxide production while he is quietly resting in a relaxed, reclined position. The measurements should be made when the patient's heart rate is within five beats of his heart rate when he first wakes up from sleep, thus insuring a basal reading. Measured resting ATP production (MR-ATP) is determined using the following variation of the Lusk formula:[14]

$$MR\text{-}ATP = \{5.676(ARO_2) + 1.584(ARCO_2)\} \times C$$

In this formula ARO_2 is the average resting O_2 consumption, and $ARCO_2$ is the average resting CO_2 production, while C is a constant, relating oxygen consumed to ATP produced.

Predicted resting ATP production (PR-ATP) can be estimated using a variation of the classic Harris-Benedict formulas for basal metabolic rate. For calculating a man's PR-ATP use ((66.473 + 13.7616(weight) + 1.8496(height) – 4.6756(age)) x C)/6.95. For a women, the calculation is ((655.095 + 9.536(weight) + 1.8496(height) – 4.6756(age)) x C)/6.95. In both of these equations, C is once again a constant, relating oxygen consumed to ATP produced.

Using the above formulas, it is then possible to obtain a percent predicted determination of resting ATP production as follows:

Resting ATP production = (MR-ATP x 100)/PR-ATP

Two additional factors should come into play when making these calculations. The first is age. Since, from an anti-aging and disease prevention perspective, we are looking to maintain youthful levels of ATP production as the patient gets older, it does not make sense to evaluate energy production as a factor of age. In other words, we want our patients to be healthy, not "healthy for their age." There is general agreement in the anti-aging, exercise physiology, and longevity literature that, for all practical purposes, the effects of aging do not begin to become appreciable until after the age of forty. Hence, a reasonable benchmark for ATP production when looking to maintain youthful levels would be those levels that are typical of a forty year-old individual.

Therefore, when calculating the resting mitochondrial function of a person over the age of forty, the default age of forty is used. Thus in the case of an individual older than forty, no matter what his age is, his resting mitochondrial function will reflect what would be considered normal and expected for a forty year-old of the same sex, weight, and height. Persons younger than forty are compared to their own age group.

The second factor that must be taken into consideration for the calculation of resting mitochondrial function is percent body fat. Notice that ATP production using the above variation on the Harris-Benedict equations is positively correlated with weight. The more a person weighs, the higher the predicted ATP production.

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But excess stored fat is metabolically inert tissue. Thus, using the Harris-Benedict equations as they are classically used would result in unreasonably higher predicted levels of ATP production in persons who have an excess of body fat. This will cause them to have a falsely depressed reading for resting mitochondrial function secondary to the artifact of excessive body fat. Thus, to account for this potential inaccuracy, the weight used in determining predicted resting ATP production is corrected using a body fat analysis. The weight of overweight men is corrected to a weight based upon an ideal body fat of 18%. The weight of overweight women is corrected to an ideal body fat of 22%.

Resting ATP Production from Fatty Acids

To repeat what was already mentioned above, when glucose is being metabolized, there is a 1:1 ratio of carbon dioxide produced to oxygen consumed. When fat is being metabolized, the ratio is .7. Since the pulmonary gas analyzer measures CO_2 production as well as O_2 consumption, the percentage of fat being metabolized can be determined by examining this ratio. Based upon my own measurements and those published, a healthy person should be able to produce at least 75% of his total ATP production while at rest from fatty acids.[15-17] Less than that indicates impaired fatty acid metabolism. A calculation of resting ATP production from fatty acids (rATP-FA) is formulated which determines the percentage of ATP being produced from fatty acids in the subject while at rest. The formula for this calculation is: rATP-FA = 283.52 – (average resting CO_2/O_2 ratio) x 235.29.

An rATP-FA greater than 100 indicates that the subject is producing at least 75% of his resting ATP from fat, which points to optimal resting fat metabolism. An rATP-FA less than 100 indicates that the subject is progressively producing less than 75% of his resting ATP from fat, which points to less than optimal resting fat metabolism. An rATP-FA of 50 indicates that the subject is not producing any resting ATP at all from fat, which points to a severe impairment of resting fat metabolism.

rATP-FA and Carbohydrate Intake

There is an inverse linear relationship between carbohydrate intake as a percentage of total caloric intake and resting fatty acid metabolism.[18] The physiological reasons behind this observation are numerous but basically have to do with pre-mitochondrial factors affecting lypolysis, fatty acid mobilization, beta-oxidation of fatty acids, and fatty acid transportation into the mitochondria. These factors are separate from mitochondrial function per se, and they will be discussed in detail in a later section. In its most simple terms the finding can be explained by the reasoning that when presented with dietary carbohydrate, the body will elect to metabolize that carbohydrate rather than to store it for later use and in the meantime rely on fatty acid metabolism. Thus, the greater the intake of carbohydrate as a percentage of total calories, the lower will be the rATP-FA.

As one would expect, this inverse relationship is quite individual. There are some subjects who can have a relatively high intake of carbohydrates and yet still maintain an optimal rATP-FA, whereas my observation is that the majority of persons must maintain a very modest intake of carbohydrates in order to avoid an impaired rATP-FA. For these reasons, the clinical implications of rATP-FA primarily have to do with carbohydrate intake, and are as follows:

- A C-Factor greater than 100 indicates that the subject is eating an optimal amount of carbohydrate for his genetics and lifestyle.
- A C-Factor less than 100 indicates that the subject's intake of carbohydrates is excessive and is progressively impairing his rATP-FA.
- A C-Factor of 50 indicates that the subject's intake of carbohydrates is so excessive that it is completely suppressing his rATP-FA. In this case the subject's resting ATP production is resulting completely from glucose metabolism.

It is important to also note that besides the pre-mitochondrial effects of carbohydrate intake, rATP-FA is also influenced by factors which specifically affect mitochondrial function such as hormones, ADP availability, toxicity, specific nutrients, sleep habits, methylation, fitness, etc. However, because the demand for ATP is so minimal in a resting state, these factors usually exert a negligible effect on rATP-FA compared to the carbohydrate effect. Additionally, because these factors play a very significant role in maximal ATP production from fatty acids (see mATP-FA below) than they do in resting fat metabolism, they can be excluded as causes of a decreased rATP-FA in the event that the mATP-FA measurement is adequate.

So, in summary, a decreased rATP-FA is almost always an indicator of excessive dietary carbohydrate intake. Sometimes the amount of dietary carbohydrate required to optimize rATP-FA is quite small. In fact, after observing the rATP-FA of hundreds of patients, I can report that there are a great many people who seem to be genetically programmed such that in order to produce an optimum rATP-FA they must eat almost no

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carbohydrates at all! When both the rATP-FA and the mATP-FA are decreased, not only is dietary carbohydrate consumption in excess, but any combination of the other factors mentioned above are also at play.

Maximal ATP Production from Fatty Acids

Once the resting energy production readings have been determined, the mitochondrial function analysis protocol calls for exercising the subject on a specialized stationary bicycle called an ergometer. The resistance on the ergometer is programmed by the computer to steadily increase according to a rate that is compatible with the subject's level of strength and fitness. As the subject begins to increasingly exert, the rising energy demands cause him to metabolize increasing amounts of fat into ATP. However, since fat metabolism is not as fast and as energy efficient as glucose metabolism, as the energy demands continue to escalate, increasing amounts of glucose are mobilized into ATP. Finally, a level of exertion is arrived at wherein the maximal amount of fat that the subject is able to metabolize is reached. Beyond this point, due to the steadily increasing energy demands, the subject will metabolize progressively more glucose and less fat to meet the rising ATP needs. This point occurs when the ratio of carbon dioxide produced to oxygen consumed is .85. Thus when the CO_2/O_2 ratio reaches .85, the subject is producing the maximal amount of ATP from fat that he is capable of. Beyond this point, as exercise intensity steadily increases, the subject will be metabolizing progressively less fat and more glucose until at some point he will be metabolizing no fat at all. At this second point, all ATP production will come entirely from glucose.

Based upon my own measurements and those published, a healthy person should be able to produce at least 60% of his total aerobic ATP production from fat.[18] Less than that indicates impaired fat metabolism. This is usually a consequence of both pre-mitochondrial factors, such as excessive carbohydrate intake, impaired lypolysis, impaired fatty acid mobilization, impaired beta-oxidation of fatty acids, and impaired fatty acid transportation into the mitochondria, and mitochondrial factors such as hormone deficiencies, ADP deficiency, toxicity, nutrient deficiencies, sleep deprivation, impaired methylation, decreased fitness, etc.

Thus, mATP-FA refers to the maximal amount of ATP that the subject's mitochondria are able to produce from fatty acids, and therefore serves as a cross-check of the factors mentioned in the previous paragraph. It is a percentage calculation which compares the predicted maximal ATP production from fat in a subject with what is actually measured. The formula for mATP-FA is ((ATP Max Fat) x C x 100)/((PM-ATP) x .6). In this formula, ATP Max Fat is O_2 consumption when the ratio of CO_2 produced to O_2 consumed is .85; PM-ATP is the predicted maximal ATP production; and C is a constant, relating oxygen consumed to ATP produced. PM-ATP can be estimated using a variation of the Wasserman-Hansen-Sue formulas for predicted peak oxygen uptake. For men PM-ATP = weight x (50.72 - .372 x age) x C. For women PM-ATP = (weight + 43) x (22.78 - .17 x age) x C. Once again, C is a constant, relating oxygen consumed to ATP produced.

An mATP-FA greater than 100 indicates that the subject is able to produce at least 60% of his maximal predicted ATP production from fat. This points to optimal fat metabolism. An mATP-FA less than 100 indicates that the subject is progressively producing less than 60% of his maximal predicted ATP production from fat. This points to less than optimal fat metabolism. An mATP-FA less than 70 indicates that the subject is producing less than 30% of his maximal predicted ATP production from fat. This points to a severe impairment of fat metabolism.

Maximal Aerobic ATP Production

Maximal aerobic ATP production (maxATP) can be established by measuring O_2 consumption under exertional conditions. It is important to note here that maximal aerobic ATP refers to ATP that is produced entirely from glucose metabolism. No fat metabolism is involved at all. This is because at this maximal level of exertion it is not possible to adequately generate ATP from fat because fat cannot be mobilized as quickly as glucose and fat cannot produce as much energy per molecule of oxygen as can glucose. Therefore, at this point of exertion it is not necessary to use CO_2 production in the equations to determine fat metabolism. A percentage calculation, maxATP compares the expected or predicted maximal aerobic ATP production in a subject with what is actually measured. The formula for maxATP is simple: ((measured maximal ATP production) x 100)/(predicted maximal ATP production). Measured maximal ATP production (MM-ATP) is determined using the following formula: (average maximal O_2 consumption) x C, where C is a constant, relating oxygen consumed to ATP produced.

The additional factors of excessive body fat percentage and age, which I described above in the section on resting ATP production also come into play when determining maxATP. Therefore, in all calculations of maxATP the patient's real age is only used when he is younger than forty. When calculating the maxATP of a person over the age of forty, the default age of forty is used. Similarly, excess body fat is corrected for using

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body fat analysis.

Correcting for Anaerobic ATP Production

In a resting state, the primary fuel for oxidation in the healthy individual is fat, and the ratio of CO_2 produced to O_2 consumed is around .7. As the subject begins to increasingly exert, since fat metabolism is not as fast and as energy efficient as glucose metabolism, progressively more glucose is mobilized to meet the rising energy demands. As this occurs the ratio of CO_2 produced to O_2 consumed begins to steadily increase in a linear fashion until a level of exertion has been reached that can only be met by glucose metabolism. This point is noted when the ratio of CO_2 produced to O_2 consumed is equal to one. It represents the point at which ATP production from oxygen has reached it's maximum. Until this point has been reached, the amount of anaerobic ATP production is minimal and need not be accounted for.

However, once the aerobic production of ATP has reached its maximum, as the subject continues to progressively increase his exertion level beyond this point, he will begin to produce ATP anaerobically. At this point two factors about anaerobic ATP production come into play. First, lactic acid is an essential byproduct of anaerobic ATP production. In order to produce the same amount of ATP anaerobically that is produced aerobically, 19 times as much acid is produced in the form of lactic acid. As a result of the carbonic anhydrase enzyme system, which the body uses to buffer blood pH, this excessive lactic acid is immediately converted to CO_2:

$$\text{Lactic Acid} + HCO_3 \rightarrow H_2O + CO_2$$

Therefore, the point at which the anaerobic production of ATP occurs can be determined by a sudden acceleration in the previously linear rate at which the ratio of CO_2 produced to O_2 consumed had been increasing.

When the subject eventually reaches this point, the computer determines it and ends all calculation of ATP production, and the exercise portion of the test is concluded. Therefore, the amount of ATP that is recorded does not reflect any anaerobic ATP production. It only reflects ATP produced in the mitochondria.

In mitochondrial functional analysis, anaerobic ATP production is not measured because it is produced in the cytosol of the cell and does not reflect mitochondrial production. Additionally, from the standpoint of health, aging, and disease, the ability to produce anaerobic energy is not important. Only aerobic ATP production has been shown to be correlated with degree of aging and with all cause mortality. Anaerobic ATP production has no similar correlation.

This is a very important distinction because many patients who score low maxATP values may in fact state that they exercise and feel as though they have much more energy than mitochondrial functional analysis gives them credit for. What they don't appreciate is that when they produce energy under exertion, although they may be able to produce an adequate amount of total energy, their mitochondria are not functioning optimally, and they are producing an unacceptable amount of energy anaerobically.

This shift from aerobic to anaerobic energy production is one of the primary causes of aging and chronic disease. More importantly, the shift will steadily increase over the years, often without producing any significant symptomatology until mitochondrial function has already become irreversibly compromised.

Biological Age

Using an algorithm which averages the values for resting ATP production, rATP-FA, mATP-FA, and maxATP, wherein the maxATP is double-weighted, the computer program compares the subject's overall ATP production efficiency to that predicted of sex, height, and weight matched subjects of various ages. This calculation can be used to determine the subject's "biological age" based on how efficiently he produces ATP.

Alas, aerobic ATP production steadily decreases with age. This decline results in diminished function in every single cell, tissue, and organ in the body and is the primary cause behind the symptoms and diseases of aging.[19] Since the brain, the liver, and the heart are the largest consumers of energy in the body, it is these organs that are the most affected. But no part of the body is spared.

An accurate, reliable, objective, scientifically based formulation for biological age not only reassures the treating physician that his recommended anti-aging/preventive medicine program is, in fact, really working, but it also has a tremendous motivational value for patients for long-term compliance. If the patient's biological age is less than his chronological age, he can be reassured that all the time, energy, sacrifice, and money that he has spent and continues to spend to keep strong and healthy is really doing what it's supposed to do. If the patient's biological age is greater than his chronological age, this is also reassuring. Because, instead of continuing a lifestyle or supplement program that isn't serving him well, both the patient and his physician are now armed with the information needed to make the changes that will optimize his health

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and improve his biological age. Furthermore, repeat mitochondrial functional analysis will be able to confirm that his new program is effective.

We should all remember that no matter how many candles they stick in the birthday cake, our biological age may well be the best indicator of how old we really are!

Early Onset Mitochondrial Dysfunction

In contrast to mitochondrial decay, early onset mitochondrial dysfunction (EOMD) is reversible. It is commonly found in young, asymptomatic, and presumably healthy subjects, and increases in incidence with age. It occurs long before mitochondrial decay, aging, and degenerative disease.

When I took delivery of my very first pulmonary gas analyzer, I attended a three-day seminar on oxygen consumption analysis in order to properly learn how to use the analyzer and interpret the data. During the course of those three days, I was shown many "typical" case examples of oxygen consumption rates, and after this comprehensive introduction, I was ready to go.

However, soon after I first began to use the device, I noticed a very unusual finding. Although the first patients I tested were by the usual definition "healthy" (i.e., not overtly sick), none of them were showing oxygen consumption rates that could at all be considered normal according to what I had just learned. Not to be dismayed, I moved forward and continued testing. The measurements continued to be poor for almost every patient I tested. This was even true for myself. Well, once I found myself to be lacking, I just knew there must be a problem with the equipment. After all, I took vitamins and exercised. I am a doctor specializing in anti-aging/preventive medicine with 30 years experience. These results just couldn't be accurate! I called the manufacturer of the analyzer and faxed them all my calibration and data files, and they quickly assured me that everything was working perfectly.

I then sent the test data to two experts in the field of oxygen uptake exercise testing, and the general impression from both of them was that my patients must have something wrong with them. I responded, "Something wrong with virtually every single 'healthy' patient I have tested including myself!? How can that be?" Unfortunately, they had no explanation. Worse yet, they had never seen data with characteristics quite like this before.

Then I started to become upset. Here I had spent all this money on an oxygen consumption analyzer to do some research on mitochondrial function, and the brand new equipment I was using was spewing out incorrect data. I called the equipment manufacturer back, and after much complaining, he sent out a representative to my clinic to check the whole setup. Something just had to be wrong. In fact, nothing was wrong. The representative verified that all was working well and that the testing procedure was being done correctly. He even analyzed four of the same patients, including myself, whom I had analyzed weeks before, and the results were the same. Not to be deterred, I even had the company send me an entirely different analyzer. The results were still the same. In other words, neither myself nor the majority of the so-called healthy patients I had tested had healthy values for oxygen consumption. Was there something in my clinic air? It turns out that it was more insidious than even that.

After months of going back and forth, repeatedly discussing my results with experts in oxygen uptake testing, and working feverishly to hide the fact from my wife that my $20,000 analyzer was not cooperating, something suddenly dawned on me. I started reflecting on the fact that one of these experts had spent his entire professional career looking at oxygen consumption data from world-class athletes. The other was a physician who had spent his entire career looking at the oxygen consumption data from patients with various levels of heart and lung disease. No wonder they could not understand my data files. I had been testing everyday normal people, not subjects representing the two, physiological extremes that they were used to seeing. My patients were not Olympic quality athletes, nor did they have heart or lung disease. They were not old, and they were not sick. They simply represented the general "healthy" population, and what I had discovered was that this general "healthy" population seemed to have less than optimal mitochondrial function.

Several years later, after I had developed the mitochondrial functional analysis procedure described previously, I proceeded to investigate this phenomenon to see how pervasive it really was. I selected 50 subjects as they randomly presented to one of several clinics in Carson City, Nevada; Los Angeles, California; Grand Junction, Colorado; and Singapore using mitochondrial functional analysis. Each subject selected was between the ages of 20 and 40, asymptomatic, and health-conscious enough to want to have their mitochondrial function checked for preventive reasons. The results were as follows:

- 54% (27) had normal mitochondrial function.
- 46% (23) had decreased mitochondrial function.
- 36% (18) had <90% of predicted mitochondrial function.

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- 26% (13) had <80% of predicted mitochondrial function.
- 12% (6) had <60% of predicted mitochondrial function, and fell within the diagnostic category of severe dysfunction.

The results of the study validated my earlier observations. Close to half of these healthy, asymptomatic, young, health-conscious subjects had decreased mitochondrial function. A quarter of them had less than 80% of predicted. An amazing 12% of them were in the diagnostic category of severe dysfunction, could have been diagnosed as having chronic fatigue syndrome, and were eligible for disability had they been symptomatic.[15-17]

These patients were much too young to have mitochondrial decay or any of the other effects of the aging process, and they were much too healthy to have cardiovascular or any other disease. And yet, almost half of them had evidence of mitochondrial dysfunction. This led me to my very first observation concerning mitochondrial function and health — mitochondrial decay, aging, and degenerative disease are preceded by a decrease in mitochondrial function which can often be severe and asymptomatic.

Since then, I have coined the term early onset mitochondrial dysfunction (EOMD) to refer to the condition. EOMD refers to a deterioration of mitochondrial function in the absence of true mitochondrial decay. Furthermore, while mitochondrial decay is known to be irreversible, subsequent treatment of the subjects mentioned in the above study clearly revealed that EOMD is completely reversible. While mitochondrial decay is a function of the aging process itself, EOMD is not. Although further investigation has revealed that the incidence of EOMD increases with age, it occurs even in young subjects without any evidence of aging. Could it be that EOMD is what causes mitochondrial decay? The answer to this question is discussed later on.

Decreased Fat Metabolism & EOMD

But what causes this decrease in energy production in seemingly healthy people such as myself? To answer this question I began to carefully examine the breath-by-breath data files of all of the test results to look for a pattern which occurred in all those who tested out poorly, and which did not show up in those few who tested out well. Finally, a pattern began to emerge. Every subject with EOMD also had decreased rATP-FA (resting ATP production from fatty acids) and decreased mATP-FA (maximal ATP production from fatty acids). This was markedly different from the 27 patients who had normal mitochondrial function. Of this group only 24% (12) had decreased rATP-FA, and only 7% (2) had decreased mATP-FA.

Thus the common denominator noted in 100% of the EOMD group was that they were metabolizing very little fat as an energy substrate. In fact, while I had observed that healthy, fit persons in their 20s produced at least 75% or more of their resting energy from fat, the EOMD group often produced less than 20% of their resting energy from fat. Furthermore, the less the maxATP an individual was able to produce, the lower was his percentage of ATP produced from fat, both under resting and maximal conditions.

I even found some patients with extremely low maxATPs who essentially burned no fat at all in a resting state. In contrast to this was the observation that those patients who had the highest levels of aerobic ATP production usually produced greater than 75% of their resting energy from fat. In addition, what was even more striking — in fact what amounted to 93% concordance — was the fact the really high energy producers also produced a much greater amount of ATP from fat while they were exerting, as well. The statistics were so striking that I was able to predict with 100% accuracy who would be the highest energy producers simply from examining how much ATP they produced from fat.

This, then, led me to my second observation about EOMD and energy production in general: Total aerobic ATP production (maxATP) is 100% dependent on fat metabolism, such that the more efficiently ATP is produced from fat, the higher will be the total aerobic ATP production; also, the less efficiently ATP is produced from fat, the lower will be the total aerobic ATP production. Keep in mind that total aerobic ATP production refers to aerobic capacity, which is associated with aging, degenerative disease, and all cause mortality.

What Causes EOMD?

The literature is replete with evidence to support a number of events which cause a pathological increase in free radical production leading to the irreversible mitochondrial damage referred to as mitochondrial decay.[19] It is mitochondrial decay which ultimately leads to disease and organ degeneration. In fact, there is a well-known and accepted theory of aging — the mitochondrial theory of aging — which alludes to these facts, and asserts that the very process of aging itself is simply the end result of mitochondrial decay.[2-5,20]

Pathological uncoupling leading to a proton leak across the mitochondrial membrane resulting in free radical damage to mitochondrial structures has long been

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considered the major factor leading to mitochondrial decay, but I was beginning to suspect that there was more to the story. Specifically, now that I had discovered that there was a decrease in mitochondrial function that commonly occurs long before mitochondrial decay — EOMD — I was wondering whether or not it was precisely EOMD that was one of the major factors leading to mitochondrial decay.

The answer to this question has obvious importance, because the implication is that if the EOMD which precedes mitochondrial decay is corrected in time, it just might be possible to prevent or delay mitochondrial decay altogether. So, what are the factors that can lead to EOMD? I have identified nine:

1) Decreased fat metabolism
2) Nutritional deficiencies
3) Sleep deprivation
4) Hormonal deficiencies
5) Toxicity
6) Hypoxia
7) Decreased methylation
8) Ischemia
9) Decreased fitness

EOMD Secondary to Decreased Fat Metabolism

As mentioned above, a decrease in fat metabolism, both resting and maximal, appears to be the most common single characteristic of young patients with EOMD. It is easy to understand how a decrease in fat metabolism can have such an effect, simply by recognizing that it is fat, not glucose, which is the primary substrate production in the body.

I discovered this fact quite by accident after analyzing the mitochondrial function of hundreds of patients. As I studied these patients I gradually became aware of a certain pattern. The younger, healthier, and more athletic the patient was, the more efficiently they burned fat. In fact the typical 22-year-old athlete most often obtained greater than 85-90% of his resting ATP production from fat metabolism. However, the older or sicker my patient was, the less energy they produced from fat metabolism, and the more they began to obtain their energy needs from glucose. That same 22-year-old, even if he continued to exercise and keep in shape, is very likely to be producing better than half of his resting energy from glucose by the time he reaches 55. I saw this extremely consistent shift from fat metabolism to glucose metabolism over and over again as people aged or developed illnesses.

A decrease in ATP production from fat results in a corresponding decrease in total ATP production because other than during an occasional brief period of exertion, fat is the major substrate for ATP production. The fact that fat metabolism plays the key role in mitochondrial function is emphasized in a 2002 paper demonstrating that restoration of the "key mitochondrial enzyme carnitine acetyltransferase," which is solely involved in fat metabolism, "restores mitochondrial function, thus delaying mitochondrial decay and aging."[21]

Thus, the decrease in fat metabolism such as I observed in over half of the young healthy subjects studied, plays the initiating role in all of the decreased mitochondrial function to follow. And the major cause of decreased fat metabolism, even in otherwise healthy young people, is the excessive ingestion of carbohydrates. Let me offer a very graphic case example to make my point.

A 42-year-old movie actor presented to my clinic to have his mitochondrial function analyzed. He was an avid exerciser, and took an array of supplements as part of an anti-aging/preventive medicine program. He had no complaints, and his physical and routine laboratory examination were within normal limits other than a modest elevation of his serum triglyceride levels. Indeed, on casual observation, this young man looked like the epitome of health. Looks can be deceiving however, especially in health.

When tested, this man had a greater than 40% reduction in his total aerobic ATP production. This placed him in a category of severe EOMD. Additionally, in a resting state, his ATP production from fat was zero. This remarkable shift from fat to glucose metabolism, which is so commonly seen in my young patients, is undoubtedly setting them up for metabolic syndrome. I have learned not to be too surprised by such findings, and I immediately asked him about his diet. He confessed that every day for the previous two months he had been ingesting 2-3 milk shakes blended with cookies at a popular fast food restaurant.

I asked him to continue everything he was currently doing except to avoid the milk shakes along with all other carbohydrates including grains, fruit, legumes, and sugars. In three weeks he repeated his mitochondrial functional analysis and was happy to discover that his total aerobic ATP production had now climbed to 30% greater than predicted for a man two years younger. This represented a net improvement in mitochondrial function of greater than 70% simply from decreasing dietary carbohydrate. Not surprisingly, this second test revealed that his resting ATP production from fat was now maximal. Cases such as this one form the majority of what I see on a daily basis in my clinic.

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It is important to reiterate here that excessive carbohydrate ingestion, though it is the most common cause of decreased fat metabolism, is not the only cause. Deficiencies of the thyroid hormones T4 and T3, the adrenal hormones cortisol and DHEA, and the anabolic hormones HGH, progesterone, DHEA, and testosterone also play a significant role. Other commonly encountered factors include insulin resistance, sleep deprivation, excessive dietary intake of trans fatty acids, and deficiencies of essential fats, amino acids, magnesium, B vitamins, chromium, lipoic acid, coenzyme Q10, and L-carnitine. All of these nutrients are especially likely to be deficient in patients who eat excessive amounts of carbohydrates.

So, to summarize, the evidence indicates that decreased fat metabolism resulting both from pre-mitochondrial fatty acid delivery disorders and from a deficiency of the key enzyme acetylcarnitine transferase leads to mitochondrial dysfunction. The following conditions then further intensify the dysfunction already created.

EOMD Secondary to Nutritional Deficiencies

What nutritional imbalances and deficiencies could directly result in decreased mitochondrial function? In terms of the needed cofactors in the Krebs cycle and the electron chain system, the most worrisome deficiencies would be the B vitamins, Co-Q10, magnesium, antioxidant vitamins (especially C and E), and the essential amino acids. Contrary to what is often preached, there is substantial evidence in the literature to suggest that many of our patients, especially those who are elderly, ill, or who are vegetarian commonly have less than optimal essential amino acid profiles.[22-24]

Due to their critical importance in metabolic methylation, a deficiency of the vitamins folinic acid and methylcobalamin would play a particularly important role in total ATP production because both ADP and phosphocreatine are methylation-dependent. Using genomics, researchers are discovering that very common genetic variations cause certain individuals to require much higher than normal dietary intake of these vitamins in order to maintain optimal methylation.

Dietary fats are also critical for energy production. The entire electron chain rests on the inner mitochondrial membrane, which is composed completely of unsaturated essential fats. A deficiency of the essential fats omega 3 and 6 is quite common, and has been shown to result in defective membrane transport and fluidity.[25,26] Additionally, hydrogenated and partially hydrogenated fats have been reported to act as uncoupling agents, apparently due to their negative effect on the mitochondrial membrane function.[13,27]

EOMD Secondary to Sleep Deprivation

A likely cause of EOMD is sleep deprivation, either self-inflicted or resulting from sleep disorders. In the 1950s the American Cancer Society conducted a very large study in an attempt to try and determine the major lifestyle factors that caused cancer and decreased lifespan in general. The study examined sleep habits as well as smoking, diet, cholesterol levels, blood pressure, exercise, etc. Over 1 million Americans were surveyed over a six-year interval, and the habits of those who had died during this period were identified. Out of all the factors studied, the amount of sleep time was the best predictor of mortality. The highest death rates for all ages were for those who slept four hours or less per night, and the lowest rates were for those who regularly slept eight hours.

Other investigators have published studies revealing similar outcomes. One study in particular looked at 1,600 adults aged 36-50 and found that, compared to good sleepers, poor sleepers were 6.5 times more likely to have any one of a variety of health problems.[28] Dr. William Dement, founder and director of the Stanford University Sleep Research Center and one of the original pioneers in the study of sleep, states it very clearly and succinctly in his excellent book on sleep entitled, *The Promise Of Sleep*: "Healthful sleep has been empirically proven to be the single most important factor in predicting longevity, more influential than diet, exercise, or heredity. And yet we are a sleep-sick society, ignorant of the facts of sleep and the price of sleep deprivation."

According to a 1997 article in the *New York Times Magazine*, many sleep researchers believe that sleep deprivation is reaching "crisis proportions." This is a problem not just for serious insomniacs but for the populace at large, the article said, and added: "People don't merely believe they're sleeping less; they are in fact sleeping less — perhaps as much as one and a half hours less each night than humans did at the beginning of the century — often because they choose to do so."

Although exactly how it occurs is not fully known at this time, several published studies have documented that lack of adequate sleep decreases fat metabolism, resting energy production, and exertional energy production.[29-32] Many indications are that these effects of sleep deprivation are mediated through a combination of a deficient hormone and neurotransmitter production.

EOMD Secondary to Hormone Deficiencies

What hormonal deficiencies can lead to EOMD? Since anabolic hormones, such as testosterone, progesterone, and growth hormone, stimulate the utilization of ATP for protein synthesis and other cell regulative activities,

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in so doing they increase the levels of ADP. Elevated levels of ADP are a primary stimulator of mitochondrial function. Conversely, low levels of ADP act to decrease mitochondrial function.

Catabolic hormones such as cortisol, T4, and T3 also stimulate mitochondrial function by their direct effect on the nucleus of the cell. T3 in particular is also critical for optimal functioning of physiological uncoupling, which is also responsible for the increased mitochondrial production of heat and is a major stimulant of mitochondrial function.

Finally, it should be noted that estrogen exerts a negative effect on both T3 and T4 by increasing the levels of thyroid hormone binding globulin, and hence creates a decrease in mitochondrial activity. This is precisely why women have a lower level of mitochondrial function than men, and also explains why it is so important in men to keep estrogen levels as low as possible, and in women to replace estrogen only in the smallest doses necessary to do the job.

EOMD Secondary to Toxicity

Heavy metals and pesticides are immediately lethal in a high enough dose, but even in low doses they have two toxic effects. One is as a direct source of oxidant stress, and the other is because both of these classes of toxins have been shown to increase pathological uncoupling, which leads to a decrease in mitochondrial function. Combined with the rather well-established fact that modern man commonly has abnormally elevated levels of both pesticides and heavy metals, such as arsenic, lead, and cadmium, it is not hard to imagine that many patients with EOMD are suffering from an increased toxic burden.

In addition to the toxins mentioned above are the toxic by-products of many of the bacterial and fungal organisms that reside in the gastrointestinal tract. Some of these ferments, for example tartaric acid, have been found to block certain steps in the Krebs cycle.[33] The overgrowth of these organisms is the result of deficient and damaged immune systems combined with the overuse of industrial and medical antibiotics. The World Health Organization has established that mycotoxins are a major source of disease and disability throughout the world.

EOMD Secondary to Hypoxia

Hypoxia refers to a decreased level of oxygen in the blood, and it is much more common than is often considered. Obviously, since all mitochondrial function is oxygen dependent, hypoxia results in a significant decrease in mitochondrial function. Hypoxia is one of

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those causes of decreased mitochondrial function which can occur even in young people. Smoking, for example, results in significant hypoxia. And for those who don't smoke, there is always the issue of passive exposure.

Another source of hypoxia is even more insidious, and that is decreased ambient oxygen levels associated with pollution and the green house effect created in urban environments. In these environments ambient oxygen levels are decreased from the activity of combustion engines and not replenished due to an absence of adequate vegetation. Urban environments have been found to have significant decreases in ambient oxygen concentration in comparison to rural environments.[34] Yet another quite common and perhaps underestimated source of decreased ambient oxygen is encountered in the construction of new energy efficient homes, offices, and apartment buildings. These constructions are often so airtight that very little outside air is able to enter the building. In the larger office and apartment buildings the ambient air is often re-circulated to the point that ambient oxygen levels become deficient. This is especially an issue in colder climates wherein it is in the interest of energy conservation to minimize the amount of fresh air being introduced into the system. Many people live and work on a continuous basis in such environments. I have long been aware that sleep apnea represented a very common cause of clinical hypoxia. Sleep apnea occurs secondary to upper airway obstruction, either as a result of weight gain, alcohol, medications, or allergies. Sleep apnea can also be mediated from the central nervous system. Until I recently listened to a lecture by a dentist who had been researching the use of dental appliances to decrease upper airway obstruction I was completely unaware that hypoxia secondary to upper airway obstruction quite commonly occurs in patients even when they are awake![35]

Armed with this piece of information, I began to examine the mitochondrial function in a certain number of my patients whom I suspected might have daytime hypoxia secondary to upper airway obstruction. In these cases I performed a mitochondrial functional analysis using a mask air intake device, which left their airway in their normal position, and compared it to measurements using a mouthpiece which has the effect of opening an obstructed airway. Low and behold, I noticed that in many of these patients mitochondrial function measured with the mouthpiece far exceeded that obtained with the mask. These results have led me to believe that daytime hypoxia secondary to upper airway obstruction is a very real, and probably common, phenomenon.

One more often overlooked source of hypoxia comes from low-level carbon monoxide exposure. The legal limit for occupational carbon dioxide exposure over a 40-hour work week has been set at 9 ppm, but based on the amount of individual variation in hemoglobin structure, this amount may be excessive for many. Additionally, many homes, especially those in colder climates, have ventilation/pressure issues that actually draw carbon monoxide into the home, often resulting in clinical carbon monoxide poisoning.[36-38] I am aware of one case in particular of a 15-year-old girl who developed symptoms that were diagnosed as lupus. For two years she was treated for this condition by her physicians, only to have it resolved when, quite accidentally, it was discovered that her home had excessive ambient levels of carbon monoxide. The most interesting aspect of the case was that the other members of her household did not seem to be affected.

Asthma is a disorder that has demonstrated a consistently increasing incidence for many years now. Moreover, studies have shown that sub-clinical reactive airway with mild bronchoconstriction is often not diagnosed, especially in those who don't exercise. I routinely assess the O_2 saturation of my patients, and I often find O_2 sats less than 93% in patients who were not complaining of dyspnea on exertion and were not aware that they had a pulmonary disorder. This has led me to believe that yet another source of hypoxia is undiagnosed, sub-clinical reactive airway disorder stemming from allergic reactions to molds, pesticides, food additives, petrochemical out-gassing, etc.

Contributing to this problem is the ever-increasing amount of elemental mercury being discovered in the environment. Elemental mercury is a known immune adjuvant, which means that it potentiates the immune response to an antigen. This is why it is routinely used in the production of vaccines. Unfortunately, because it is such a strong immune adjuvant, environmental mercury may result in hyper-reactive immune responses to everyday allergens and be a major contributor to reactive airway disorder.

Last is the issue of decreased oxygen dissociation. In this condition, oxygen fails to be released from the hemoglobin molecule, and as a result, even though it is being delivered to the capillary bed, it fails to be taken up by the mitochondria and metabolized into energy. Two factors initiate the release of oxygen from hemoglobin. The first is an acid pH. Because acid in the forms of CO_2 and lactate are the byproducts of our everyday metabolism, as oxygen demands increase with

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exertion and/or stress, more acid is produced. This results in a decreasing pH in the capillary environment, which is beneficial since hemoglobin loses its affinity for oxygen in a low pH environment, and a lowered pH stimulates the release of more O_2 from hemoglobin to satisfy the increased demands.

Unfortunately however, this mechanism can be adversely affected by alkaline salts, which act to prevent the physiological decrease in the capillary pH that occurs with increasing energy requirements. Although the infrequent use of such salts cannot be considered much of a problem, chronic usage, such as occurs in persons routinely taking antacids, may lead to decreased mitochondrial function. I am also referring to the current health fad of constantly drinking alkaline water to supposedly "remove the acid from the body." Although it can be very therapeutic during the initial phase of treatment in a person with advanced mesenchymal acidosis, the constant intake of unphysiological alkaline beverages and minerals, such as coral calcium, etc., may have the ironic long-term effect of actually increasing mesenchymal acidosis. By decreasing oxygen dissociation, such unphysiologically alkaline blood will only serve to force the body to meet more and more of its energy demands anaerobically, ultimately resulting in the formation of 19 times more acid per molecule of ATP produced.

The second factor that results in decreased oxygen dissociation may be even more pervasive, and that is a decrease in the molecule 2,3,di-phoshoglycerate (2,3-DPG). 2,3-DPG is produced in the red cell in the pentose phosphate pathway as a result of glucose being metabolized to lactate. This reaction is catalyzed by oxidation, and therefore the levels of 2,3-DPG are typically much lower in persons who do not regularly exercise. 2,3-DPG acts to displace oxygen from hemoglobin because hemoglobin has a much higher affinity for 2,3-DPG than for oxygen. Studies have shown that stored blood, due to its complete lack of oxidation has negligible levels of 2,3-DPG. However when the same blood is exposed to an oxidant such as ozone, the levels of 2,3-DPG dramatically increase to normal.[39]

The other group with documented low levels of 2,3-DPG are diabetics. Even though the physiology texts proclaim that insulin is not required for glucose to enter red blood cells, I am quite sure that this is only true during exertion and not in a resting state. The increased production of 2,3-DPG is undoubtedly one of the reasons that diabetics do so much better when glucose intolerance is improved. It also helps to explain why regular exercise is so crucial for adequate mitochondrial function in the diabetic patient.

EOMD Secondary to Decreased Methylation

There are three sources of ATP in the body. Two of them have already been discussed (i.e., ATP derived aerobically in the mitochondria and ATP derived anaerobically in the cytosol). The third source is from a molecule called phosphocreatine. Phosphocreatine is formed in the cytosol when ATP transfers high energy phosphate to creatine. Phosphocreatine is able to store this high-energy phosphate until an energy demand is created, at which time it will transfer it back to ADP to form ATP. This process results in the reformation of creatine. Thus, during the initial minutes of exercise, until it becomes exhausted, phosphocreatine serves as a third source of ATP. It turns out that the amount of phosphocreatine present in the body can be determined by examining the level of CO_2 in respiratory gas.

Phosphocreatine is a relatively strong acid, whereas creatine has a neutral pH. When phosphocreatine is converted to creatine as ADP is converted to ATP, the pH in the tissues is shifted toward an alkaline state. This alkaline shift causes the enzyme carbonic anhydrase to convert CO_2 to HCO_3, thus lowering the level of CO_2. The decrease in CO_2 is readily detected by examining the concentration of CO_2 in the exhaled respiratory gas.[18]

Because of the contribution of phosphocreatine to the production of ATP in the first few minutes of exercise, the concentration of CO_2 in the expired breath decreases even as the concentration of O_2 being utilized increases. The net effect is a decrease in the CO_2/O_2 ratio. This decrease will be maintained until the stores of phosphocreatine are exhausted, at which time the ratio will begin to climb in a linear fashion. By measuring the length of time of this initial depression of the CO_2/O_2 ratio, it is possible to quantify phosphocreatine. But why is this important?

Creatine is synthesized when the amino acid S-adenosylmethionine (SAM) methylates guanidinoacetate to form creatine and S-adenosylhomocysteine. About 70% of all methylation in the body is devoted to this critical reaction to create creatine, because without creatine there will be no phosphocreatine, and without phosphocreatine there will be a shortage of available ATP.[40] Therefore, the amount of phosphocreatine in the body directly correlates with the critical process of methylation. To the extent that there is a phosphocreatine deficiency in the body, one can safely assume that there is a concomitant methylation deficiency.

But methylation is not only critical for the formation of ATP through the above-mentioned reaction. It is equally

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critical in energy production because of its importance in adenosine production. Adenosine is the base from which ATP (adenosine triphoshate) is produced. Adenosine is produced when S-adenosylhomocysteine is hydrolisated to adenosine and homocysteine. Note that unless SAM is converted to S-adenosylhomocysteine through the methylation of guanidinoacetate to form creatine, no adenosine will be formed. Such a deficiency of adenosine will result in a depletion of ADP, ultimately resulting in the kind of pathological mitochondrial uncoupling that shuts down and eventually destroys the mitochondria.

But these observations are not just interesting academic perusings, they are, in fact, clinically useful. I have named the initial depression of the CO_2/O_2 ratio that is seen on exercise testing, as I have described above, the "methylation curve." What is uniformly observed is that subjects with the highest maxATP are also those with the longest and deepest methylation curves, indicating an optimally functioning methylation process. Likewise, the subjects with lower levels of maxATP unvaryingly demonstrate little to no methylation curve, indicating both sub-optimal methylation and an inability to produce phosphocreatine secondary to deficient ATP production.

Those who are familiar with methylation disorders will recognize that they often occur as a result of mercury toxicity, casein allergy, and genetic predisposition. Furthermore, methylation disorders can often be corrected with the orthomolecular administration of folinic acid, trimethylglycine, pyridoxine, and methycobalamin. It is interesting to note that when subjects with a decreased maxATP, along with a depressed or absent methylation curve, are given these substances, they often rather dramatically show a substantial improvement in both measurements.

EOMD Secondary to Ischemia

Ischemia refers to a decrease in the delivery of blood to the capillary bed. Obviously, due to decreased oxygen availability, a decrease in blood flow will cause the same kind of decrease in energy production observed with hypoxia. Ischemia, however, has a much greater negative effect on mitochondrial function than hypoxia because ischemia not only decreases the delivery of oxygen to the tissues, but it decreases all the cofactors of oxygen metabolism, as well as the removal of carbon dioxide.

Perhaps the single most common cause of ischemia in today's society is from decreased cardiac output secondary to sedentary lifestyle. Using pulmonary gas analysis, it is possible to estimate cardiac output with some precision. I perform this measurement routinely whenever I am assessing mitochondrial function, and I rarely find that a subject with decreased mitochondrial function has a normal cardiac output.

A much more significant cause for ischemia would be stress, and the resultant increase in vasoconstriction from increased sympathetic tone. I am not aware of any published studies on the effects of stress on systemic vasoconstriction, but there is an abundance of published data on the vasoconstricitve effects of stress on the myocardial circulation and in Raynaud's phenomenon.[41-44] These studies clearly verify that perceived stress such as simply hearing bad news can immediately create detectable ischemia in both myocardial and finger tissues. Similarly, the stress from chronic pain or other stressful symptoms can equally create ischemia.

When discussing ischemia, certainly atherosclerosis and loss of arterial elasticity must be considered. The level of atherosclerosis can be quite considerable in patients over the age of 40, even in the absence of clinical symptoms such as claudication or angina. In most cases, ischemia due to atherosclerosis will be subclinical and will only be picked up by stress testing such as occurs with mitochondrial functional analysis.

Another cause of systemic ischemia in many patients comes secondary to an immune system activation of the coagulation cascade as described in a brilliant paper by David Berg, LH Berg, and J. Couvaras entitled, "Is CFS/FM due to an undefined hypercoagulable state brought on by immune activation of coagulation?"[45] In this paper Dr. Berg directly describes cases of chronic fatigue being reversed using the anti-coagulant heparin. I routinely examine the blood of my patients using a dark-field microscope and have noticed that the majority of the patients I examine have a noticeable precipitation of fibrin deposits detectable on this simple examination. I have also performed several investigations on patients with dark-field evidence of abnormal coagulation-wherein I examined the results of mitochondrial functional analysis before and after the administration of heparin. In every case, these patients had a noticeable improvement in mitochondrial function from the administration of heparin. From these observations, I have deduced that ischemia from abnormal coagulation is a very commonly occurring cause of decreased mitochondrial function.

Ischemia can also be caused by decreased endothelial function at the level of the capillary wall. The decreased function of the endothelial cells which make up the capillary wall results in edema of these cells with a resultant decrease in circulation and perfusion. This condition has been well-described and popularized by Manfred von Ardenne is his book, *Oxygen Multi-Step*

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Therapy. According to Dr. von Ardenne, decreased endothelial function as a cause for decreased mitochondrial function is altogether common in many presumably healthy people.[46] Not surprisingly, I have often found that the mitochondrial dysfunction in patients whom I suspected had this disorder improves significantly using Dr. von Ardenne's stepped oxygen exercise protocol.

Lastly, please reflect on the fact that many of the same conditions that create hypoxia can also result in ischemia. Thus, it is not unreasonable to assume that in many patients the two conditions coexist and act synergistically to appreciably impair energy production.

EOMD Secondary to Decreased Fitness

Many people mistakenly assume that early onset decreases in mitochondrial function are simply a matter of decreased fitness resulting in decreased cardiac output and decreased lung function. While fitness level is certainly a factor in the EOMD so commonly detected in the individual who is over 50 years old, it can hardly explain the EOMD observed in the young and health-conscious. It should also be noted that a significant number of my patients of all ages who demonstrate EOMD are already regularly exercising.

A recent publication helps to illustrate the point that EOMD is not simply a function of fitness. The authors performed a meta-analysis of mitochondrial function studies in aging men and compared the incidence of EOMD in exercisers with highly trained marathon runners. The authors underlined the increasing frequency of EOMD in men as they became older. They also pointed out that EOMD "is an independent risk factor for cardiovascular disease, cognitive dysfunction, and all cause mortality." Additionally, they demonstrated that even highly trained marathon runners consistently had significant EOMD, clearly indicating that there are other factors affecting mitochondrial function than fitness.[1]

The above caveat having been expressed, there is certainly no doubt that exercise does indeed play a major role in mitochondrial function. Irrcher, *et al*, in a 2003 article on the subject, point out that a program of regular endurance exercise improves mitochondrial function, induces mitochondrial generation (biogenesis), and delays the progression of aging.[47] Other studies document the beneficial role of exercise in the heart and the brain.[48-50] But not all exercise is equivalent. Statistical studies are repeatedly showing that moderate exercise seems to have a more beneficial effect than intense exercise, secondary to the excessive free radical activity induced when subjects with EOMD exercise beyond their aerobic capacity.[51] I have already published one paper on this subject which demonstrated that due to the commonality of EOMD, the majority of persons exercising today are doing so at levels which exceed their mitochondrial capacity.[52]

Nevertheless, when properly performed, exercise improves mitochondrial function, increases antioxidant buffering capacity, decreases oxidant stress, and increases longevity in both humans and animals.[53]

EOMD: The Primary Cause of Mitochondrial Decay, Aging, and Degenerative Disease

Mitochondrial decay induced by excessive free radical activity is known to be the intrinsic cause of aging and degenerative disease. This forms the central basis for the Free Radical Theory of Aging.[2-5,19,54] EOMD occurs in the young before any signs or evidence of mitochondrial decay. The evidence is strong that EOMD is the primary cause of mitochondrial decay and, hence, the ultimate cause of aging and degenerative disease. The implication of this statement is important because EOMD is preventable and even reversible, and if EOMD causes mitochondrial decay, then mitochondrial decay, aging, and degenerative disease can be minimized by measuring and treating EOMD.

EOMD causes mitochondrial decay by initiating a vicious cycle of chain reactions as follows: 1) a decline in mitochondrial function caused by the nine factors mentioned previously; 2) a resultant increase in the production of free radicals as a result of the "functional hypoxia" induced by #1; 3) an accumulation of mitochondrial DNA mutations; 4) a further increase in the oxidative damage to DNA, protein, and lipids (particularly the inner mitochondrial membrane, which houses the entire electron transport chain); 5) a subsequent decrease in the capacities of oxidatively damaged proteins and other critical macromolecules further impairing mitochondrial function; 6) an increase in the turnover rate of antioxidant buffering enzymes as a result of increased free radical production combined with a decrease in the production of these enzymes as a result of impaired mitochondrial function. The result of this cycle of events is a simultaneous increase in free radical production with a decrease in free radical buffering capacity.[55]

This vicious cycle is really brought home in an article entitled, "Oxidative damage and mutation to mitochondrial DNA and age-dependent decline of mitochondrial respiratory function." In this article the authors are depicting EOMD when they describe the "gradual impairment of respiratory function" which increases with age. They go on to state, "An immediate consequence of

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such gradual impairment of the respiratory function is the increase in the production of the reactive oxygen species (ROS) and free radicals in the mitochondria through the increased electron leak of the electron transport chain. Moreover, the intracellular levels of antioxidants and free radical buffering enzymes are gradually altered. These two compounding factors lead to an age-dependent increase in the fraction of the ROS and free radical that may escape the defense mechanism and cause oxidative damage to various biomolecules in tissue cells." They conclude by stating that it is these two processes, decreased oxidant buffering capacity and increased ROS production, which are responsible for the age-dependent process of mitochondrial decay.[56]

It is important to note here that the ROS mentioned above are formed in direct proportion to the proton gradient formed across the mitochondrial membrane as part of the function of the electron transfer chain. The greater the gradient, the more ROS are formed. Of course, one very obvious way to decrease the gradient and to thereby limit the production of ROS is to allow the protons to re-enter the mitochondria through complex five, which converts ADP to ATP. As long as there is a significant amount of ADP, complex five will function very well in this manner. However, four of the factors leading to EOMD mentioned previously — methylation disorders, nutritional deficiencies, hormonal deficiencies, and decreased levels of fitness — also result in the decrease of available ADP, resulting in greater ROS formation.

Another way to reduce the proton gradient, and thus decrease ROS formation, is through uncoupling proteins. These are proteins that are on the mitochondrial membrane which allow protons to re-enter the mitochondria without the need for ADP. The most active of these uncoupling proteins is activated by the thyroid hormone triiodothyronine, and it is via this method of decreasing the mitochondrial proton gradient that this critical thyroid hormone serves to prevent mitochondrial decay. The point here is that many of my patients with EOMD, even those with values for serum TSH, T3, and T4, which are in range, show a decrease in their resting ATP production as well as a decrease in maximal ATP production.

The most common cause for decreased resting ATP production is hypothyroidism. Additionally, hypothyroidism is also a cause of decreased maximal ATP production. This observation has made me believe that sub-clinical hypothyroidism is much more common than it is currently thought to be, and may be a particularly onerous component of EOMD. It also serves to explain why one recently published animal study demonstrated that mice in the upper quartile of resting ATP production lived 36% longer than those in the lowest quartile.[5]

Levine and Kidd, in their classic text *Antioxidant Adaptation – Its Role In Free Radical Pathology*, emphasize that free radical pathology is an inherent result of hypoxia. On page 133 they state, "An oxygen deficit can be toxic to the cell by exacerbating free radical generation in membranes housing electron transfer assemblies." This free radical generation destroys the mitochondrial membranes housing the electron transfer assemblies, which decreases mitochondrial function, while at the same time increasing the electron leak through the membranes. The increased electron leak leads to a further increase in free radical generation, all of which ultimately results in mitochondrial decay.

They go on further to state, "The patterns of cellular damage from ischemic/hypoxic insult, which have been well studied, parallel those seen following inhibition of cellular ATP production ..." Inhibition of cellular ATP production is what we are seeing in EOMD, and Levine and Kidd state that, from a pathological perspective, it is tantamount to classical hypoxia. On page 136 they further clarify this inhibited state of ATP production when they equate classical hypoxia to impaired oxygen utilization using the term "functional hypoxia": "Cellular hypoxia can result from deficiency of oxygen delivery (ischemia/hypoxia) or impaired oxygen utilization (functional hypoxia)."[57]

In essence, the terms "impaired oxygen utilization," "functional hypoxia," and "EOMD" are identical in implication. They all describe the same pathological mechanisms that exist in classical hypoxia, all of which lead to mitochondrial decay. The proposed mechanism by which EOMD causes mitochondrial decay, aging, and degenerative disease is pictured in Figure 1.

Energy Deficit Theory of Aging and Disease

After reflecting on the above observations, I made the following postulations, which I have called the Energy Deficit Theory of Aging and Disease:

1) Degenerative disease and aging are preceded by early onset mitochondrial dysfunction (EOMD), which occurs long before actual mitochondrial decay, and commonly occurs in the young and asymptomatic. The presence and extent of EOMD can be determined by mitochondrial functional testing.
2) EOMD results from two commonly occurring states: 1) decreased pre-mitochondrial fat metabolism, which leads to 2) decreased

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mitochondrial function, which is further compromised by ischemia, hypoxia, toxicity, sleep deprivation, methylation disorders, nutritional deficiencies, hormonal deficiencies, decreased fitness.

3) EOMD creates a state of "functional hypoxia," which, through the combined action of increased free radical formation and decreased antioxidant buffering capacity, is the primary cause of mitochondrial decay, aging, and degenerative disease.

4) The processes causing EOMD, and hence the processes causing aging and degenerative disease, can be decelerated and even reversed by altering these two states to improve mitochondrial function. The degree of success or failure in this endeavor can be documented using mitochondrial functional testing.

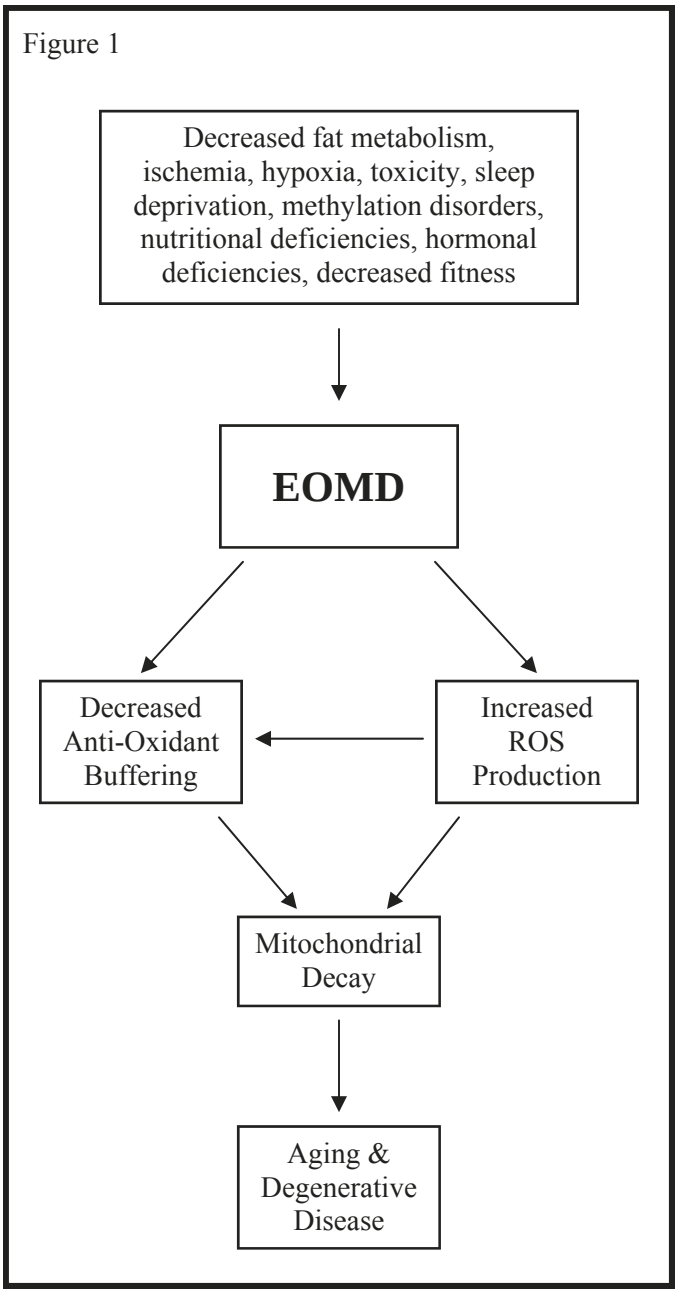
Energy Deficit Theory Is Not Mitochondrial Theory

The Energy Deficit Theory is not just the Mitochondrial Theory repackaged into different terminology. The Mitochondrial Theory looks at energy deficit states exclusively in terms of mitochondrial decay as a result of oxidative damage to mitochondrial DNA. The Mitochondrial Theory states that aging occurs as a result of mitochondrial decay and as such is not reversible. The Energy Deficit Theory offers a unique slant on how this happens and what comes first.

Like the Energy Deficit Theory, the Mitochondrial Theory recognizes that there is a steady, linear, and predictable decrease in energy production associated with aging. But unlike the Energy Deficit Theory, the Mitochondrial Theory assumes that this decrease in energy production is purely a result of aging, and as such is after the fact. The Energy Deficit Theory states that the observed decrease occurs long before aging has occurred and, therefore, is the root cause of aging. More importantly, the Energy Deficit Theory identifies the factors causing this decrease in energy production and what can be done to retard and reverse it.

For the past 3,000 years, the Chinese have utilized a system of medicine that determines energy production by a subjective evaluation of pulses and physical findings. They use the word "chi" to refer to energy production. They hypothesized that all disease proceeds from a decrease in chi and that health is best maintained over time by increasing chi through various exercises, acupuncture, dietary protocols, and medications. The Energy Deficit Theory is directly allied to this basic concept, and further describes in scientific terms the factors that lead to a decrease in chi.

Figure 1



DEDICATION

In every person's life there are certain people whom through courage, honesty, commitment to excellence, tireless example, and humble encouragement inspire us to look deeper into our lives and move closer to our potential. Such a person for me has been Richard Kunin, MD. Dr. Kunin is well-known to all biologically minded physicians who have an appreciation for the radical concept that our bodies were built to heal themselves when given the right nutrients and lifestyle. Much of the "new" information discussed in this paper regarding the dangerous effects of our modern high carbohydrate diets only serves to solidify the same concepts that Dr. Kunin was espousing a mere 50 years

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ago. It's tough to be so far ahead of your time, and it serves us well to be often reminded that we all owe Dr. Kunin and the other pioneers like him a great deal of gratitude. I am proud to call Richard Kunin a friend of mine and to dedicate this article to him.

ACKNOWLEDGMENTS

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Book Review

by Barry S. Kendler, PhD, CNS, FACN

Sick and Tired? Reclaim Your Inner Terrain

by Robert O. Young, PhD, DSc
Woodland Publishing, Pleasant Grove, UT, 2001
ISBN: 1-58054-056-2

Do not allow the prosaic title to deter you from reading this book! Though intended for lay readers, it is more suitable for professionals familiar with the biological and nutritional sciences. However, do not read the book unless you are willing to have your conceptual framework of fundamental biological principles seriously challenged. The author, a conventionally trained research microbiologist, presents his unconventional findings based on the study of live blood, i.e., unstained blood examined using dark-field, phase-contrast microscopy, capable of magnification of up to 28,000 times. Use of this technique has enabled him to view bacteria, yeast, molds, crystallized toxins and cholesterol, undigested fats, and many other forms in the blood.

Microzymas and Their Transformations

Young maintains that microorganisms emerge from red and white blood cells. Even more remarkable is his claim that the doctrine of pleomorphism, introduced by Antoine Bechamp over a century ago, is valid. According to this doctrine, minute particles, which Bechamp named microzymas, meaning small ferments, are independently living elements that inhabit cells, interstitial fluid, blood, and lymph. Microzymas are capable of fermenting sugars.

In health, microzymas organize and construct body cells; they are the precursors to all living matter. However, in disease, microzymas become disorganized and alter both their form and function. In fact, they evolve into bacteria and other microorganisms. Only the terrain, that is, the condition of the body's environment, determines whether the microzymas will function normally or will evolve into microorganisms that cause symptoms of disease.

An acid-forming diet and nutritional deficiencies are among the factors that can disrupt body chemistry, triggering transformation of microzymas into bacteria, then into fungi, i.e., yeasts and/or molds. The latter infest blood and other tissues, resulting in disease through production of mycotoxins, mostly waste products of fungal metabolism. Bacteria don't always evolve into fungi and can also produce disease symptomatology from exo- and endotoxins.

The reason that microzymas undergo deleterious transformation into bacteria, and then fungi, is that they receive chemical signals from an acidic environment that the organism is dead or disorganized. A vicious cycle is created where mycotoxicosis exacerbates the acidity of the body.

Young asserts that the live blood analysis reflects favorable changes in the diet, lifestyle, and even emotions. After instituting these changes, the symptomatic microforms diminish in number or completely disappear.

The Primary Role of the Immune System

Young offers a novel concept of the immune system. Rather than being primarily an anti-infectious mechanism, it serves mainly as an "elegant janitorial service," picking up and discarding filth, including metabolic waste products and remnants of the half billion cells that die daily. Infectious immunity is merely a backup system and, by itself, cannot create freedom from disease.

The current emphasis on immunity and stimulation of immune function is a result of belief in the germ theory of disease. This belief fosters over-reliance on the immune system, ignoring its primary function in disease prevention. By the time the system is activated, the terrain has already been compromised.

Mycotoxins

Most mycotoxins are unsuitable for use as antibiotics because of their toxicities. A common mycotoxin that is especially problematic is acetaldehyde. Not only its effects are detrimental, but so are those of its metabolites, oxalic, lactic, and uric acid, in addition to alcohol. Uric acid and oxalic acid promote gout and kidney stones, respectively. Lactic acid promotes cancer development, as will be explained below. Acetaldehyde promotes hepatic production of low density lipoprotein, which is used to bind and deactivate this and other mycotoxins. However, the product of this binding can become oxidized and result in atherosclerosis.

Acetaldehyde exhibits some other detrimental properties. Among these are destruction of neurotransmitters, damage to DNA, and binding to red blood cells which

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interferes with their entry and progression through capillaries, resulting in oxygen deprivation. DNA damage can culminate in pancreatitis, cardiomyopathy, brain atrophy, stomach ulceration, esophageal varicosity, cirrhosis, enlarged spleen, and a multitude of other disorders.

Cancer

Young has an entirely different view of this disease — one, which he claims, responds favorably to dietary intervention. Cancer results from disorganization of microzymas and their subsequent evolution to bacteria and fungi with concomittant production of exotoxins and mycotoxins, respectively. Uric acid and acetaldehyde production by fungi promote mineral-depleting responses by the body in an effort to neutralize their effects. For example, the cells are depleted of magnesium, potassium, and sulfur by the effects of acetaldehyde and are depleted of potassium, magnesium, sodium, zinc, and calcium by uric acid. Reduced oxygenation by red blood cells, as described above, results in more alcohol formation and symptoms of intoxication, such as disorientation, confusion, and dizziness.

In response, the immune system releases large amounts of reactive oxygen species to counteract the fungi. This release of free radicals is referred to as microzymian oxidative buffering species or MOBS. If there is an excessive accumulation of debris, the janitorial action of the immune system is overwhelmed. Eventually, cells may be converted from oxidative metabolism to abnormal anaerobic metabolism. The latter cells may travel through the bloodstream and initiate fermentation of other cells via fungal penetration or poisoning.

Young says that although fungi and/or lactic acid are found in autopsies of cancer victims, scientists have not considered that they could play a causative role.

Intestinal Dysbiosis

A term used to refer to an imbalance of the intestinal flora, intestinal dysbiosis is a condition that leads to fungal overgrowth and ultimately penetration of the intestinal wall, causing "leaky gut" syndrome. Upon entry into the bloodstream, fungal mycotoxins deplete the body of nutrients and oxygen, increase acidity, and may invade body tissues and organs. The causes of intestinal dysbiosis are many and include diet, inappropriate food combinations, mental or emotional stress, environmental toxins, and medication, especially antibiotics.

According to Young, the colon becomes loaded with debris and filled with thick and sticky mucus from engulfing toxins; this he terms mucoid. Many foods cause the intestines to produce mucus to trap toxins, especially dairy products, other animal proteins, white flour and other processed foods. Vegetables, he claims, are not mucoid-forming.

Inappropriate food combination is said to be a major cause of mucoid production. Protein digestion begins in the acid environment of the stomach but starch digestion requires a mildly alkaline environment. Consequently, each of these foods interferes with the digestion of the other. Accordingly, these foods should not be eaten at the same meal. Two other inappropriate food combinations are foods high in sugar and high in starch and foods high in sugar and high in protein.

Among the digestive disturbances that occur as a result of intestinal dysbiosis are putrefaction, fermentation, heatburn, gas, bloated stomach, ulcers, gastritis, and constipation. The mucoid material adheres to the colon wall and this serves as a habitat for destructive, toxin-releasing microorganisms. Dysbiosis can also result from diets containing 50% or more carbohydrate from grains, legumes, and foods high in sugar content. Fungi also cover sections of the small intestine, interfering with absorption.

The author attributes many disorders to fungal infection, including allergy, environmental hypersensitivity, fatigue, neurological imbalance, hypoglycemia, diabetes, and overweight.

Nutritional Support for a Compromised Internal Environment

The remedies for a compromised internal environment begin with restoration of the body's normal balance, a process that involves alkalinization, hydration, oxygenation, mineralization, and nutritional supplementation. This protocol involves the consumption of large quantities of fresh vegetable juices and a formula made up of powdered, dried green vegetables for a week. This is followed by a mild laxative or a botanical formulation that includes aloe vera. A total of 14 nutritional items is recommended, including caprylic, undecylenic, butyric, alpha-lipoic and essential fatty acids, olive leaf, garlic, bromelain, organic germanium, rare metals, and N-acetyl cysteine.

Dietary guidelines for those who have intestinal dysbiosis or other symptoms of a compromised internal environment include avoidance of junk food, fruit, foods from animal sources, commercially stored grains, yeast-containing foods, dairy products, condiments, edible mushrooms, peanuts, corn, heated oils, microwaved

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food, alcohol, caffeine, and smoking and chewing tobacco.

Recommended are dark green and yellow vegetables, sprouts, unstored grains, legumes, soy products, fresh herbs, seeds, some nuts, fresh freshwater fish, lots of pure water, and multiple vitamin-mineral supplements. A food guide pyramid is presented with dark green and yellow vegetables at the base, followed by sprouted grains and legumes, seeds and some nuts, omega-3 and omega-6 polyunsaturated acids, and low sugar fruits, in that order.

Appendices
A series of appendices, which exceed the text in length by about three-fifths (110 pages vs.169 pages), includes instructions for juicing and sprouting and recipes. Also appended are references to alternative medical modalities, a wellness protocol, testimonials, and case histories, including AIDS and cancer patients. Photographs of live blood analyses accompany the latter. There is an appendix on technical essays that examines the pivotal roles of Bechamp and other pioneers in pleomorphic hypotheses, a discussion of mineral colloids and the mycotoxic/oxidative stress test and 13 tables diagramming pathological processes in the form of flow charts. Finally, there is a discussion of viruses, including HIV, and vaccines, based on the pleomorphic hypothesis. Over 200 references from biomedical literature are also provided.

Commentary
The book is somewhat disorganized and redundant. For example, he discusses Bechamp and Pasteur in both the text and appendices. He also makes derogatory statements about the integrity of the federal Food and Drug Administration and the pharmaceutical industry, statements that are both unsupported and pointless. His claims about inappropriate food combinations and pH balance are undocumented. He strongly advises against consumption of peanuts and corn, claiming that both foods are infested with fungi, although documentation of this comes from Asian sources. He makes unfounded and ludicrous statements about the origin of pancreatic cancer in the Carter family as possibly being due to peanut consumption.

However, Young's revolutionary and novel perspectives on the orgin of disease cannot easily be dismissed as nonsense, although the traditional scientist or physician is likely to try to do so. However, he has impeccable scientific credentials and has conducted thousands of hours of careful microscopic observations. Young is not the first to make such claims, and he gives full credit to Antoine Bechamp and other scientists in this context.

Thus, Young cannot easily be dismissed as a fraud, despite the fact that, if true, his findings would necessitate the rewriting of all microbiology and pathology textbooks. Moreover, he has documented the recovery of numerous patients with advanced cancer that have followed his protocol.

This book ultimately challenges open-minded biomedical professionals in all relevant disciplines to test his hypotheses and protocols to determine their validity or lack thereof. Considering that treatment of advanced solid tumor malignancies, AIDS, and other diseases have not been advanced in the past decades, there is ample reason for considering novel approaches, whether or not they are in accord with conventional scientific knowledge. ◆

Message from the ACA CDID

New Clinical Message Board

The council on Diagnosis and Internal Disorders of the ACA has established a clinical message board for DABCI's, DABCI students and practitioners of functional medicine. We invite all interested parties to participate. Our clinical message board will be in a new Yahoo! Group format.

Topics of discussion will include:
- Diagnostic questions
- Case Studies
- Current Research
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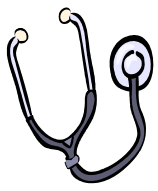

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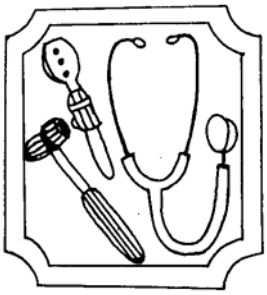

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