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Dear Distinguished Colleagues,

The American Academy of Anti-Aging Medicine (A4M) welcomes you to Orlando for the Spring 2014 session of the 22nd Annual World Congress on Anti-Aging, Regenerative & Aesthetic Medicine, certification programs, workshops, and A4M Fellowships.

The A4M is proud that our 26,000 physicians, practitioners, and scientific members from 120 nations worldwide have made a lasting and palpable commitment that expands the availability of advanced biotechnologies and leading-edge preventive healthcare throughout the world. Now in its third decade of educational service, the A4M’s scientific educational programs have trained over 100,000 medical professionals worldwide.

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It is an exciting time to be involved in Integrative & Preventive Medicine. With your involvement, this medical specialty continues to expand and become more widely accessible. By attending this event, you are part of this transformation, and we applaud you for joining this fast-growing movement.

With warm regards,

Ronald Klatz, MD, DO
President, A4M

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• **Pre-Conference Specialty Workshops**
  Thursday, May 15th
  Register for topic focused workshops lead by industry leading experts in Obesity, Hair Loss Management, Stem Cells, Practice Management and Lifestyle Medicine.

• **Sponsored Evening Workshops**
  Thursday, May 15th • Friday, May 16th
  Attend free evening workshops sponsored by participating exhibitors featuring highlighted speakers discussing the latest advancements in Anti-Aging and Regenerative Medicine. (Non-CME)

• **Exhibit Hall**
  Friday, May 16th 10:00am – 6:45pm • Saturday, May 17th 10:00am – 6:00pm

• **Product Theater**
  Friday, May 16th 12:00pm – 2:00pm; 4:30 – 5:30pm • Saturday, May 17th 11:30am – 12:00pm
  Visit the Product Theater stage inside the exhibit hall where participating exhibiting companies will showcase their products & services. (Non-CME)

• **Networking Reception**
  Friday, May 16th 4:30pm – 6:45pm
  Mix and mingle with other distinguished medical professionals and exhibitors while enjoying refreshments in the exhibit hall.

• **Rolex Giveaway**
  Play the exhibit hall game and enter to win a FREE Rolex! Drawing will take place Saturday, May 17th at noon.

• **A4M Bookstore**
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**Obesity: How to Definitely Lose Weight with Efficient Dietary, Nutritional and Hormone Therapies**  
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**Sponsored Evening Workshops**

**Thursday, May 15th**

**6:15PM**  
**Topic:** How to Effectively Combine Different Modalities of Lab Testing  
**Presented by:** James LaValle, RPh, CCN  
**Location:** Sun Ballroom Level  
**Sponsored by:** AML Diagnostics

**6:15PM**  
**Topic:** The Future of Functional Medicine with OMAPREM® & PreBioPhage™ the Probiotic/Bacteriophage Combination  
**Presented by:** Sharon McQuillan, MD  
**Location:** Sun Ballroom Level  
**Sponsored by:** OMAPREM

**Friday, May 16th**

**6:45PM**  
**Topic:** In-Office Stem Cell Therapy: The Next Step in Anti-Aging Medicine  
**Presented by:** Sharon McQuillan, MD  
**Location:** Sun Ballroom Level  
**Sponsored by:** Ageless Regenerative Institute

**6:45PM**  
**Topic:** JOIN Workshop: Share the knowledge. Experience the difference. Achieve more. Listen and learn from physicians who have successfully transitioned into bioidentical hormone therapy.  
**Presented by:** Jennifer Landa, MD  
**Location:** Sun Ballroom Level  
**Sponsored by:** BodyLogicMD

**6:45PM**  
**Topic:** Accelerating the Diagnosis and Treatment of IBS  
**Presented by:** Andrea Girman, MD, MPH  
**Location:** Sun Ballroom Level  
**Sponsored by:** Genova Diagnostics

**6:45PM**  
**Topic:** Everything You Wanted to Know About CBD, But Were Afraid To Ask  
**Presented by:** John Hicks III, MD  
**Location:** Sun Ballroom Level  
**Sponsored by:** HempMedsPx

**6:45PM**  
**Topic:** The Next Generation of Scar Therapy and Patient Cases  
**Presented by:** Sara Hover, RPh  
**Location:** Sun Ballroom Level  
**Sponsored by:** PCCA
Join Us!

Networking Reception

Location: Exhibit Hall

Date: Friday, May 16th
Time: 4:30 pm – 6:45 pm

Mix & Mingle with other distinguished medical professionals and exhibitors while learning about the latest products and services available in the Anti-Aging industry.
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2. **You Must Be A Registered Conference Delegate**
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3. **The Rolex Giveaway Will Be Held On**
   Saturday, May 17th at 12:00pm in the Exhibit Hall.

4. **A W-9 Tax Form Must Be Filed Out**
   prior to prize collection.
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1. The giveaway is not open to any exhibitors or sponsors, suppliers or supplier affiliates to the 22nd Annual World Congress on Anti-Aging, Regenerative & Aesthetic Medicine.
2. Only one entry per person will be accepted.
3. This entry form must be completed fully and correctly, validated by each of the sponsors and their unique stamps in the circle above, signed and including the unique badge ID from your registration badge for verification purposes.
4. You must be present at the time of the giveaway to win.
5. The prize is not transferable or redeemable for cash.
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**Deposit The Completed Entry Form At The Rolex Booth #513**

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Elite companies in the fields of Anti-Aging, Regenerative & Aesthetic Medicine will showcase their ground-breaking products or business services via a live demonstration or presentation.

**Friday, May 16th**

**12:00 pm**
**Topic:** What’s the Buzz about CBD?
**Sponsored by:** HempMedsPx

**12:30 pm**
**Topic:** Your Practice CASH Magnet
**Presented by:** Michael Renzulli, ND
**Sponsored by:** Innovate Aesthetics/Lipo Light Pro

**1:00 pm**
**Topic:** Improving Outcomes with PCCA’s Special Micronized Progesterone in Versabase Cream
**Presented by:** Sara Hover, RPh
**Sponsored by:** PCCA

**1:30 pm**
**Topic:** Integrative Lab Solutions
**Presented by:** Peggy Watson, MD
**Sponsored by:** SpectraCell Laboratories

**4:30 pm**
**Topic:** IBS and Specialty Diagnostics
**Presented by:** Andrea Girman, MD, MPH
**Sponsored by:** Genova Diagnostics

**5:00 pm**
**Topic:** Aminos and You: Balancing Amino Acids for Better Health
**Presented by:** Frank Young, Jr.
**Sponsored by:** Young-Vitality Co.

**Saturday, May 17th**

**11:30 am**
**Topic:** Combating Age-Related Conditions with Medical Weight Loss, Bio-Identical Hormone Therapy and Men’s Health
**Presented by:** Kimball Lundahl, DC, ND
**Sponsored by:** Healthy Habits Medical Business Consultants
Maturity is the glory of years.
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Why has telomere measurement become so important?

The medical and public consciousness about the importance of telomeres and telomere length has exploded as the result of the 2009 Nobel Prize Award for the discovery of telomerase, the enzyme that elongates telomeres, slowing the aging process. Since then, both clinicians and the lay public have been inundated with studies correlating telomere length to diet, supplements, sleep, stress and all manner of lifestyle habits. This is on top of an even larger data base of more than 17,000 scientific publications correlating telomere length with diseases we commonly associated with aging such as cancer, heart disease (both vascular and myopathic), Alzheimer’s, arthritis (both degenerative and autoimmune) diabetes, infertility and many other age-related diseases.

As a result of the known loss of telomere length from the ends of the chromosomes with each cell division and the initial suggestion that this loss was limiting to the life span of the cell (the Hayflick Limit) the concept that telomere loss may actually cause aging arose.

The current understanding is that telomere loss will eventually limit the lifespan of cells tissues and organisms and is correlated with the aging process because it correlates well with the organism’s ability to produce new healthy cells to replace sick dead or dying cells. As the organism ages and the telomeres shorten the regenerative and repair capacity is limited by the numbers of cells that have long enough telomeres to function in healthy fashion and reproduce healthy offspring in whatever tissue is being studied.

As a result many models have been applied to try to understand just how significant telomere length is as a “key driver” of human aging versus a mere biomarker.

What we know for sure

• Telomere length and loss sets into motion at least two possible regulatory “checkpoint” outcomes that limit cell life and cell replication: senescence and apoptosis. We know that in at least certain tissues these changes lead to what is now called the “Senescent Activated Phenotype” which involves the inflammatory activation of the immune system and collateral damage to surrounding cell masses that may be neither damaged nor sick. In a very real sense, aging may accelerate aging.

• Replicative demand and stress (most commonly oxidative or nitrosative) are the two main factors in telomere loss. Importantly, both are subject to clinical interventions by the doctor and patient.

• We know that the expression of telomerase is responsible for the genomic preservation of germ line cells, part of the resistance of stem cells to oxidative damage and their enhanced longevity and that the bulk of cells in our body referred to as “somatic cells” have little or no telomerase.
expression due to telomerase repression that is not present in the aforementioned cell lines to the same degree.

- We know that longer telomere lengths appear to be protective against cancer but that in approximately 85% of human cancers high levels of telomerase are required for survival of the cancer.

- We know that in cell cultures containing healthy cells with a normal genome the normal limits of replication can be extended to what has been termed “functional immortality” with the introduction and expression of the telomerase enzyme and the obligate subsequent extension of telomere length. (Bodnar et al.)

- We know that telomerase expression may be the only realistic and viable method of mammalian life extension as was demonstrated in mice (Vera et al.).

- And finally we know that overall average telomere length does not correlate nearly as well with cellular dysfunction and aging but the presence of increased numbers of critically short telomeres does.

- The presence and degree of “critically short telomeres” as opposed to average or mean telomere length is increasingly recognized as the driver of aging and cellular dysfunction. It is also the basis for “biologic age” determination. Biologic age is how old the cell tissue or organism acts and functions as opposed to how many years it has been alive.

This information gives us a useful working definition of aging and a useful set of parameters to follow based on telomere measurements. All that remains now is to see if all of these things hold true in larger and larger human databases!

Part of the difficulty is due to the fact that initial studies involved large groups of participants and utilized the same technologies that were developed in basic science during the study of single celled organisms. This set a precedent of specific testing modalities that may actually not be all that useful in individual human testing.

Subsequently successful attempts were made to transition what was once only a basic science tool into potential use for clinical studies and eventually for the individual clinician with the interested patient. It has only been recently however that the later technology has been refined.

As is often the case with cutting edge technologies, the physician who practices Anti-Aging Medicine or some form of Age Management has become the pioneer in this and is asked by the ever more educated and discerning patient to answer the question of biologic age by utilizing telomere testing.

In a very real sense those of us who measure our patients’ telomeres will be the ones to answer this question posed above: Do all of these things hold true in larger and larger human databases?

It is imperative therefore that you understand some basic concepts:

1) The most commonly measured cell line for assessment of telomere length are the Peripheral White Blood Cell (PBMC’s) including granulocytes and/or lymphocytes. While different tissues age differently and have distinctively different telomere lengths and loss rates there is a general and useful correlation between peripheral white blood cell measurements and the general health status of the individual and their actual functional or biologic age. For example there is a well established correlation between outcomes in heart disease and WBC telomere lengths (Benetos et al.)

2) White blood cell lines are changeable with the patient’s health the patient should be in relatively “stable health” both mentally and physically since either parameter can affect numbers of cells and their telomere length. Bottom line: Do not test telomere length when your patient is (atypically) stressed or sick.

3) The actual loss or in fewer cases gain of telomere length can be best assessed by time intervals of one or more years depending on the type of telomere testing you decide to use. I cannot stress enough the need to commit to more than one telomere test at some defined time interval (such as annually) to get meaningful information.

4) Since the presence and more specifically the number or percentage of short telomeres is correlated with activating the DNA damage response that leads to cell cycle arrest or apoptosis it is the target of research focusing on differentiating biologic age from chronologic age.

5) Typical telomere attrition in PBMC’s is estimated to range between 50 to 200 base pairs (bps) per year.

6) Many test technologies have reproducibility issues and inaccuracies that exceed the actual number of base pairs lost by 2 and 3 fold, making interpretation more difficult and less meaningful. In these cases it would be better to wait several years to repeat the test.

7) At this time only there is one proprietary HT Q-FISH technology which allows for the determination of biologic age.

How we measure - currently available clinical methodologies Pro’s and Con’s

First, be aware that salivary or home salivary telomere testing is not yet available or FDA approved and is unlikely to become approved in the near future. There are essentially no scientifically validated studies around telomere length in saliva and the organism; all serious studies around telomere length in saliva and the organism; all serious
and well suited to studies with large populations of participants. It is not labor intensive and not particularly dependent on expertise and is logistically simple and scalable. It has been the standard used for large data base for comparison values and statistical machination and does not require living cells.

However, there are some very significant drawbacks. The degree of accuracy and reproducibility is listed as “undetermined” compared to other modalities. Values are extrapolated from signal intensity and not directly quantitative and it provides only average (mean) telomere length of the sample, is unable to quantify telomeres individually and therefore biologic age cannot be measured or inferred from this method.

**FLO-FISH** uses in situ hybridization technology. It is amenable to immunologic determination of lymphocyte profiles (example CD 4 and CD 8). It is more accurate, quantitative and reproducible than **Q-PCR**. However, it is more labor and time intensive and more costly. It is considered a less prominent but not insignificant research tool with good data base size. It does require live cells. But again, a major drawback is that it gives only average telomere length and not short telomere quantification or biologic age.

**HT Q-FISH**: Uses digital confocal microscopy to access large populations of individual telomeres. There is one lab which has been able to automate for high scalability while maintaining a high level of accuracy and reproducibility. This is becoming the new scientific standard as it is the only technology that can measure telomeres chromosome by chromosome and hence short telomeres which correlates to biologic age. In addition, due to greater sensitivity and accuracy, less time passage between testing is required so may be more useful for clinical interventions. Because it quantifies telomeres individually, it provides the much more useful median telomere length (although average telomere length can also be generated). It is, however, the most expensive assay currently available. It is the most expensive assay currently available. It is more accurate, quantitative and reproducible than Q-PCR. However, it is more labor and time intensive and requires a high level of expertise in the lab.

In conclusion, **HT Q-FISH** is the only technology that currently measures the presence of short telomeres which appears to be the most important consideration for “biological age.”

**When you measure, now what?**

In order to address this, you need to understand the following:

1) A single isolated test of ANY KIND is of little value. Trends are established with 2 or more data points over time.

2) No one born before 2010 is likely to have any record of their telomere length at birth or any other time in life until you and they decide to measure it. Therefore you cannot ferret out who was born with long or short telomeres. The length of telomeres at birth is known to vary in healthy individuals based on many factors including parental age and ethnicity as well as transient and chronic physical and mental factors. This again stresses the importance of #1 directly above!

Be prepared for some surprises in your patient population. No matter what technology you decide on you will see “outliers” and some things that do not make sense especially with the initial measurement. More specifically you will find people who live well outside your recommendations who seem to have “good” telomere measurements and people who are highly compliant that have “bad measurements.” Address this the way you would any other biomarker in the sense of getting your patient healthier. Use the information to make your patient an ally of yours (and theirs!) and get them to take even better care of themselves. Remind them and yourself that a single isolated telomere measurement is of little value without doing another one down the road to establish a “trend”. The more data points you have the better you will be able to assign prognostic value. Remind your patient and yourself.

If a patient was gifted with long telomeres and a great anti-oxidant system they may statically do better - but why not get them to take advantage of what they were given? Similarly if a patient was born with shorter telomeres and poor defenses, it would be prudent to get them to address any factors they can to mitigate the cellular damage that is manifesting as shorter than average (or shorter median) telomeres and an increased or increasing percentage of short telomeres correlating with an older biological age than chronological age.

Analyze your patients’ telomere results reports in the context of their family history and physical. The age of their grandparents and parents on both sides at the time of death is often a telling factor. The company that uses the HT Q-FISH technology has a detailed questionnaire to help you look at known and suspected “Telomere Risk Factors”.

Above all else, follow this field and stay educated because all the signs are pointing to increased ability to intervene in a positive fashion for the overall health and wellness of your patient, and the concomitant need and importance of accurate testing!
Summary

The recent explosion of telomere based research has led to a much deeper understanding of the pivotal role telomere attrition plays in the aging process human and otherwise. The importance of longer, healthier telomeres with the concomitant reduction in critically short telomeres that activate the DNA damage response and may prematurely age cells is no longer controversial.

Many of the diseases we associate with aging can be followed and prognosticated with telomere length in addition to more commonly accepted variables.

There are typical and atypical interventions that can mitigate telomere damage and in some cases actually extend telomere length (beyond the scope of this paper), that make telomere testing more than just an interesting number. We can anticipate as the data grows and the robustness of telomere length to disease and aging becomes more widely accepted, so too will telomere testing become far more common and eventually become a standard of care.

There are several different clinical tests available each differing in many critical aspects. When you choose understand that you will want a follow up value at some defined interval to establish a trend for your patient. Similarly if you initiate any interventions in lifestyle or long term pharmaceutical management it would be wise to consider a repeat telomere test at some interval from that intervention.

Finally remember you are at the vanguard of the “Anti-Aging Revolution.” Take care of and measure your own telomeres!

About the Author

Dave Woynarowski MD is a Board certified Internist and Anti-Aging doctor who went into supplement and Nutraceutical design after 18 years of clinical medicine. He owns and operates his own website DrDave’sBest.com and has written frequent articles about Telomeres, Telomere Measurement Telomerase and TA-65. He is co-author of the book, “The Immortality Edge” with Dr Mike Fossel and Greta Blackburn and co-authored the TA-65 physician’s manual with Dr. Fossel. A nationally known expert on telomeres he has lecutured at both AMMG and A4M on the topic as well as the Longevity Now conference in Costa Mesa, California. He is currently working on a second book on the topic of Telomeres, Telomerase activation and Longevity. Currently he serves as a consultant to Life Length Inc., RD Stem Cell Inc and is conducting parallel research with stem cells and telomerase activation.

Primary References:


What a journey it’s been since I first started my fellowship training in anti-aging and preventive medicine in 2004. The fellowship training I received gave me a unique opportunity to help patients in ways I never dreamed of before. The fellowship also put me in an amazing position to start a cash-based practice and get away from the hassles of insurance billing and Medicare/HMO reimbursement rates.

A few questions I had for myself before I started my practice were, “Will I be able to make a nice living practicing this kind of medicine?” and “How will I find my patients and how will they find me?” and “How will I operate, build and market my practice AND see patients?”

Enter BodyLogicMD

When I first looked into joining BodyLogicMD, the company was fairly new with only a few practices in the network. I was nervous, yet excited, about a company that could possibly handle all the business worries I had.

First, BodyLogicMD started me off with a comprehensive business plan. What would have taken me months to develop on my own was readily available for me to implement immediately into my practice. Having a business “map” to follow when starting a new practice is key in helping any business succeed.

Still, even if it looks great on paper, how can anyone be sure it actually works?

I took the chance, and was surprised to have my practice up-and-running within a few short months. It was a partnership every step of the way; from finding an office space to negotiating the lease, from finding office furniture to gaining an office staff. I now have a virtual staff that is in charge of finding and maintaining my patient base. Many different marketing strategies are regularly incorporated on my behalf and all prospective patients contact my patient services staff (who I don’t pay for) to book their appointments. Finally!...A practice that consists of only seeing patients while not having to worry about the various business hassles.

Since opening my practice nearly six years ago, BodyLogicMD has duplicated my success for approximately 60 other physicians, while still improving their process.

Ongoing Education for Ongoing Opportunities

Other advantages of becoming a physician of the BodyLogicMD network are the numerous educational opportunities. BodyLogicMD physicians participate in educational webinars, hosted by the elite in preventive and functional medicine, as well as presentations hosted by experts in the field of technology and lab testing, which is constantly changing in the preventive arena. These free webinars are exclusive to BodyLogicMD physicians and are an invaluable resource to continuing my education beyond the fellowship.

An elite group of strategic partners also help to open doors for physicians of the BodyLogicMD network because they know we are the highest trained doctors of the most successful anti-aging network in the world.

Another tremendous benefit is the annual business retreat hosted by BodyLogicMD and their lab, pharmacy and supplement partners. There is nothing quite like spending 3-4 days networking with all of my BodyLogicMD colleagues discussing the “biology of business” and new strategies to help me grow my practice.

A Network of Experts at Your Fingertips

One aspect I have found to be very beneficial to my practice is being able to easily communicate with my BodyLogicMD colleagues. Each fellowship-trained doctor is only an email away.

We can contact one another on a daily basis to review challenging cases together or just get input from fellow physicians, who are specially-trained in different areas of medicine. Because all BodyLogicMD physicians are required to be board eligible in a field of medicine before completing the fellowship and A4M board certification, the network of physicians I work with are incredibly knowledgeable and a great resource.

The network of specially-trained physicians isn’t the only support I have for my practice. BodyLogicMD also provides me with excellent marketing support. The marketing team provides me with materials specifically designed for my practice. Many of us have been published and quoted in countless local and national magazines and newspapers, best-selling books and influential websites like Foxnews.com, Oprah.com and national television programs including Dr. Oz.

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Introduction

The process of detoxification involves the mobilization, biotransformation and elimination of toxicants of exogenous and endogenous origin. Detoxification is a vital cellular task that if lacking will lead to early morbidity and mortality. Our cells expend large amounts of energy to ensure that detoxification pathways continue to do their work. A variety of macro and micronutrients are required on a continuous basis in order to construct the multitude of enzymes for the various oxidation, reduction, hydrolysis, and conjugation pathways — as well as the provision of enzymatic cofactors, phytochemical antioxidants and fiber. Patients often request a 'detoxification program' and are surprised to learn that it is not a program that is required but a detoxification lifestyle that needs to be adopted. Components of this lifestyle include: avoidance of environmental toxicants (such as heavy metals, persistent organic pollutants and electromagnetic radiation), mobilization/elimination of toxicants via loss of excessive fat, and use of saunas, chelation therapy and exercise, optimal gastrointestinal health, excellent nutrition and hydration, attention to stress/resilience and relational health, as well as adequate sleep/relaxation. It is important for health practitioners to model the detoxification lifestyle which then encourages patients to adopt similar health practices.

Detoxification/ Biotransformation Pathways

The process of detoxification involves multiple steps in the biotransformation of primarily non-polar, lipid-soluble toxicants into polar, water-soluble and excretable derivatives — as originally postulated by Roger Williams in his 1947 monograph Detoxification Mechanisms. Since then a large body of literature has been published leading to the current understanding of how detoxification can be utilized in the prevention and treatment of disease in clinical practice. Figure 1 is an important tool that summarizes the Phase I and Phase II detoxification/biotransformation pathways which allows a conceptual framework for clinician and patient. Toxicants originate from exogenous sources such as drugs (pharmaceutical, recreational), heavy metals, chemicals (herbicides, pesticides, insecticides, food additives, household cleaners and other pollutants), microbials and so on. Toxicants also originate from endogenous sources such as bacterial endotoxins and end products of metabolism. It is important to realize that steroid hormones are also metabolized through these pathways.

Phase I Detoxification Pathways

The majority of the detoxification/biotransformation processes occur in the liver and the enterocytes which line the intestine. They are also found in many other organs such as the brain, lungs, kidneys and skin. The Phase I system is comprised of at least 57 pathways known as the cytochrome (CYP) P450 family of mixed function oxidases. Nine of the most commonly utilized CYP pathways are: 1A1, 1B1, 2A6, 2B6, 2C9, 2C19, 2D6, 2E1 and 3A4. In Phase I, toxicants are transformed to more polar, less lipid-soluble forms through the processes of oxidation, reduction or hydrolysis reactions. In order for the P450 enzymes to be present and conformationally active, one must consume high-quality, bioavailable protein as well as a host of phytonutrients, botanicals, minerals, fats and carbohydrates. These are required for epigenetic modification of transcription and production of the various CYP enzymes; enzymatic cofactors, production of energy and so on. It is understood that after going through the Phase I processes, the activated toxicants are often more toxic than their parent compounds. If these activated intermediate metabolites are not further metabolized via the Phase II conjugation pathways, they may cause damage to the cells by covalently binding to various proteins, lipids and nucleic acids within the cells. Reactive oxygen species are also a byproduct of the Phase I activity. Therefore, adequate antioxidant nutrient protection is required to quench the propagation of free radical activity with a number of plant derivatives including: the carotenes (lycopene, beta-carotene, lutein, zeaxanthin, astaxanthin), ascorbic acid, tocopherols, thios, bioflavonoids, silymarin, pycnogenol, selenium, copper, zinc and manganese (Figure 1). Other nutrients include: N-acetylcysteine, alpha lipoic acid, polyphenols (pomegranate, green tea, raspberries etc.) and curcumin.
**Detoxification Lifestyle Strategies**

Once the foundation of good nutrition has been established then other strategies are usually more effective including the optimization of gastrointestinal health, the mobilization and elimination of toxicants such as heavy metals, persistent organic pollutants via the use of chelation therapy, saunas, exercise, weight loss and so on. An important aspect of the detoxification lifestyle is the elimination of abnormal electromagnetic fields and restoration of balance in the body’s innate electromagnetic grid also known as the “living matrix.” Highly effective tools have been developed to assist the body in balancing the living matrix such as Biofeedback combined with Focused Field Stimulation.

**Case History**

This case history is a compilation of two cases supervised by Dr. John Cline MD and utilizes the Functional Medicine approach to critical thinking looking at antecedent, triggering and mediating factors. A 58-year-old G2P1A1 married woman presented with fatigue, frequent respiratory infections, nightmares with sleep disturbance for many years, anxiety, sensitivities to fumes and fragrances, symptoms of allergic rhinitis, as well as paradoxical reactions to many medications. She had been a vegetarian for several decades. Taking an environmental history revealed that she had grown up in an old house that had lead-based paint and lead water pipes. Many mercury dental amalgams were placed in her teeth as a child. Completing a degree in art/photography exposed her to many kinds of paints (containing organic chemicals and metals such as lead, cadmium, mercury, thallium etc.). Working in the dark rooms for photographic development exposed her to various chemicals in an enclosed space.

She and her husband had renovated several old houses which would have exposed her to lead-based paint, solvents, glues, lacquers, and possibly asbestos. They built a new house seven years before our meeting. There were four cordless telephones as well as wireless internet in the house. She used a cell phone several times per day holding it to her head. She noticed that with prolonged cell phone conversations she would experience a burning sensation on the same side of her head. On examination she appeared tired, nervous and her skin was dry. BP = 102/78 with pulse 72 BPM and regular. Nasal turbinates showed signs of chronic inflammation. Examination was otherwise unremarkable. Her lab work revealed normal CBC with suboptimal B12 = 328 pmol/l (N = 150 – 650 pmol/l), 25 (OH) Vitamin D suboptimal = 74 nmol/l (N = 75 – 150 nmol/l), low IgA = 0.6 g/l (N = 0.78 – 3.58 g/l) and normal Tissue Transglutaminase IgA Antibody (TTG) = < 5 units (N = < 20 units). The normal appearing TTG could have been falsely low because of the low IgA. Skin testing for inhalant allergies revealed moderate reactions to house dust mite, dog and horse danders and broom. She was advised to place dust mite covers on her pillows and mattress. She was placed on a therapeutic oral dose of pharmaceutical-grade fish oil, Vitamin D3, sublingual methylcobalamin and a B-complex.

Genomic analysis of her phase I and phase II biotransformation/ detoxification pathways revealed single nucleotide polymorphisms (SNPs) present in phase I CYP1A1, CYP1B1 and CYP3A4 pathways.
Analysis of the phase II pathways revealed SNPs present in two of the NAT2 (N-Acetyl Transferase) slow metabolizer pathways as well as the fast metabolizer pathway. Of great significance was the complete absence of GSTM1 (Glutathione S-Transferase) which is found in the liver and kidneys. This pathway is one of the major pathways for the biotransformation/detoxification of many environmental toxicants such as solvents, herbicides, fungicides, lipid peroxides and heavy metals (mercury, cadmium lead, etc.). It was suggested that she minimize exposure to the various chemicals/metal in her environment such as cigarette smoke, herbicides, fungicides, insecticides, industrial solvents, polycyclic aromatic hydrocarbons (cigarette smoke, vehicle exhaust etc), polychlorinated biphenyls, and xenoestrogens such as organochlorines etc. Dietary advice was given in regards to the genetic SNPs that were discovered. This included eating a diet rich in antioxidants (colorful fruits and vegetables), emphasizing the cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, cabbage and kale), garlic, onions, and berries. She was advised to avoid eating charbroiled, fried foods, and red meat. She was advised to take nutritional supplements to redirect metabolism away from the 4-hydroxylation of estrogens with nutritional supplements such as diindoylmethane (DIM), indole 3-carbinol (I3C), fish oils, and rosemary. She was also encouraged to include glutathione precursors and cofactors such as methionine, N-acetylcysteine, L-glutamine, glycine, magnesium and pyridoxal-5-phosphate as well as the use of alpha-lipoic acid, milk thistle, and taurine.

She was placed on a comprehensive elimination diet and discovered that she had significant reactions to gluten and dairy. Therefore, these were eliminated from her diet. She tested her home for dirty electricity using a Graham Stetzer microsurge meter and found fields in the order of 600 – 1000 dV/dt (N = <25 dV/dt) and placed a number of Graham Stetzer filters in the plug-ins throughout her home. She exchanged her cordless telephones for land-line telephones and obtained cable internet. She observed an immediate cessation of her chronic nightmares. She was advised to avoid placing cellular telephones near her head. She went through a heavy metal detoxification program which involved dietary measures, nutritional supplements, dental work (replacing her mercury amalgams with BPA-free composites) and chelation therapy.

The treatment program resulted in renewed energy, cessation of nightmares with better quality sleep, no further anxiety, marked decrease in frequency of respiratory infections, improvement in allergic rhinitis symptoms, and diminished reactions to fumes and fragrances.

In summary, components of a detoxification lifestyle have been reviewed emphasizing the ‘food as medicine’ foundational approach recognizing that an important aspect of the detoxification lifestyle is the elimination of abnormal electromagnetic fields and restoration of balance in the body’s innate electromagnetic grid also known as the living matrix. A case study illustrating the detoxification lifestyle is presented.

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5 Eastbrook RW. A passion for P450s (remembrance of the early history of research on cytochrome P450). Drug Metab Disp. 2003;31:1461-73.

About the Author
Medical director Dr. John C. Cline is a license medical doctor in BC and certified by the International Board of Clinical Metal Toxicology. Dr. Cline is also medical director of the Oceanside Functional Medicine Research Institute. Dr. Cline is the author of the book ‘Detoxify For Life,’ a comprehensive analysis of the many toxic substances that permeate our lives. To review and purchase this book online, please visit the Detoxify For Life website. Dr. Cline holds degrees in biochemistry (1982) from the University of Calgary, where he graduated with a Medical Degree in 1985. He then completed two years of postgraduate residency in family practice at the Holy Cross Hospital in Calgary and was successful certified by the Canadian College of Family Physicians in 1997.
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There is overwhelming data to recommend a wide range of therapeutic uses for marine-derived omega-3 fatty acids (primarily EPA and DHA). Likewise, there are also an overwhelming number of different forms, sources and ways to deliver these omega-3 fatty acids; which unfortunately, has led to confusion in product selection for both clinician and patient alike. The introduction of fish oil omega-3 products as prescription pharmaceuticals in the United States has increased the debate about the appropriate product to use in clinical practice. Here are some of the issues to consider.

Dietary Supplements vs. Pharmaceutical Products
Currently there are only two approved pharmaceutical products on the market in the US. Lovaza (formerly Omacor: GlaxoSmithKline), an ethyl ester (EE) form of fish oil providing 465 mg of EPA and 375 mg of DHA (840 total) in a single softgel; and Vascepa (Amarin) which is a 1 gram capsule of an EE form of EPA-only fish oil; both indicated for severe hypertriglyceridemia (TG>500mg/dl). The rationale for Vascepa’s EPA-only approach, according to Amarin’s marketing perspective, is that the EPA does not raise LDL-C as is common with DHA (or Lovaza). Neglected in this perspective is that DHA also raises HDL-C, and dramatically increases LDL particle size which is both cardio-protective and the very reason LDL-C is increased when DHA is administered. This “anomaly” of DHA (slight increase in LDL-C) is actually a signal of a beneficial shift in lipid metabolism. Unfortunately, since the lipid-lowering guidelines are fixated on reducing LDL-C as a primary goal, the marketing of an EPA-only product for cardiovascular health will no doubt mislead many who target LDL-C alone.

Some dietary supplement companies refer to their fish oil products as “Pharmaceutical Grade.” While this term is misleading, in that no such designation exists for products which are not approved as pharmaceuticals in the US; reputable suppliers of highly concentrated fish oil dietary supplements provide products which are just as pure and effective as those approved as pharmaceuticals. In fact, as we will soon show, the “bio-identical” triglyceride form of fish oil that proves to be the best choice for clinicians is currently only available as a dietary supplement.

Fatty Acid forms & structures
When fatty acids are harvested from fish, they are typically in the form of triglycerides (TG) with some additional free fatty acids (FFA). Un-concentrated fish oil products (30% EPA/DHA as natural TG) are commonly available for increasing total omega-3 intake, although these products are rarely used in clinical trials because of their low concentration. In order to increase the concentration of EPA and DHA, the fatty acids are removed from the glycerol molecule, where the resulting free fatty acid is stabilized as an ethyl ester. In this form, the EPA and DHA can be purified from contaminants and concentrated by removing saturated fats and shorter fatty acids. Once concentrated, these ethyl esters can be used directly, or used to reassemble a triglyceride molecule (usually called a re-esterified TG). These “bio-identical” triglycerides only differ from the original molecule in that they usually contain 2 (rather than 1) EPA or DHA per triglyceride molecule. While both of the approved pharmaceutical products use the EE form, concentrated rTG and EE are available as dietary supplements in the US.

Bioavailability Studies: EE vs. TG
The efficacy of omega-3 fatty acid therapy is greatly influenced by their bioavailability. Therefore, numerous studies have been performed to compare short and long-term bioavailability in human subjects using omega-3 fatty acids from different sources and in different molecular forms. Since the creation of the ethyl ester (EE) forms of omega-3 fatty acids, many people have questioned the potential change in bioavailability of these forms, compared to the natural triglyceride forms. The early studies were small, but already these data revealed either a slightly reduced bioavailability of the EE forms (compared to TG forms, especially in the absence of additional dietary fat) or a statistically similar bioavailability between EE and TG forms. However, several larger and better designed studies have shown a superior bioavailability of the rTG forms over EE forms.

In fact, one of the better studies performed to date compared similar doses of EPA and DHA using 5 different forms: un-concentrated triglycerides (what they called fish body oil-FBO), Cod Liver Oil (similar TG form as FBO), rTG, EE, or FFA, along with a “placebo” of corn oil (CO). In this study, 72 subjects were randomly assigned 3.3 grams per day of a blend of EPA + DHA daily as capsules for 2 weeks. Figure 1 shows the changes in serum fatty acids after 2 weeks in EPA, DHA and EPA+DHA in subjects consuming these different forms. In these subjects, the bioavailability of EPA+DHA from re-esterified triglycerides (rTG) was superior (+24%) when compared with natural fish oil (fish body oil or cod liver oil), whereas the bioavailability from ethyl esters (EE) was inferior (-27%) to the natural TG and nearly 70% less bioavailable than the rTG in these subjects. The authors suggest that the increased bioavailability of rTG over the un-concentrated TG form may be due to the fact that rTG products also contain di-glycerides along with a very small amount of mono-glycerides which act as “partially digested forms” of the natural triglyceride, potentially enhancing the bioavailability.
over the natural fish body oil. Concerning the EE form, numerous studies have shown a decreased lipase enzymatic activity when ethyl ester substrates are used, perhaps accounting for their decreased absorption when consumed away from a meal containing fat.

Ultimately, what we would like to know is whether any of these differences in bioavailability over two weeks might translate into long-term differences in fatty acid incorporation into important tissues and whether these differences can be measured in a clinically meaningful outcome. These sorts of studies have actually been carried out by researchers in Germany, where they looked at the incorporation of EPA and DHA into red blood cell membranes, commonly referred to as the omega-3 index, when individuals consumed either EE or rTG forms of fish oil.

This study looked at 150 hyper-lipidemic subjects who were also taking statin drugs. Subjects were given soft gelatin capsules containing EPA (1008 mg) and DHA (672 mg) daily in either rTG or EE forms (corn oil used in placebo group); and were followed for 6 months. Figure 2 shows the change in omega-3 index (% EPA + DHA in RBC plasma membrane). Subjects consuming the rTG form had, on average, a statistically higher omega-3 index than those consuming the EE form after three months, which was maintained even after 6 months of daily intake.

In a separate publication, the lipid lowering effects of these two therapies were revealed. What they found was that while both the EE and rTG reduced serum TG levels in these patients compared to placebo; the rTG changes were nearly double that of the EE form and the only therapy to reach statistical significance was the rTG therapy (Figure 3). So while there was a modest (but statistical) improvement in omega-3 index using the rTG form- the triglyceride lowering effects of this form, compared to the EE form, are much more substantial.

Since hypertriglyceridemia is the only approved indication for prescription omega-3 products (although there are many other uses of EPA and DHA)- this data would suggest that, for TG-lowering therapies, selecting a concentrated rTG fish oil is preferential to an EE product.
Quality control issues of fish oil
We are several decades into the regular use of fish oil derived omega-3 fatty acids as dietary supplements and pharmaceutical products worldwide. Nearly all of the quality control issues that plagued the first few years of fish oil availability, such as heavy metal contamination, pesticide residues and rancid oils are rare instances in today’s products. A number of highly reputable organizations (e.g.: GOED-Global Organization for EPA and DHA; CRN- The Council of Responsible Nutrition) have developed standards for fish oil products which set specific limits for heavy metal contamination, a wide variety of organic pollutants and oxidation limits. Most of the global fish oil providers maintain all of their products to these high standards. This is especially true of the concentrated products (rTG and EE forms); and since heavy metal and pesticide residue are virtually impossible to add during the manufacturing process, monitoring oxidation of the fatty acids is one of the critical steps in producing a high quality product.

Fish oil oxidation is measured using two methods. The first measures oxidized fatty acids directly as a peroxide value (PV or POV). Since these peroxides are transient and can form secondary oxidized molecules (like aldehydes), a second test is used to detect these oxidized compounds—the anisidine (or p-anisidine) test. When we combine these values by adding the anisidine value to twice the peroxide value (AV+2PV),- we get the TOTOX value. 5 To control combine these values by adding the anisidine value to twice the oxidized compounds—the anisidine (or p-anisidine) test. When we monitoring oxidation of the fatty acids is one of the critical steps in producing a high quality product.

Recommendations for Selecting Therapeutic Marine Omega-3 Fatty Acid

- The best therapeutic option for delivering marine omega-3 fatty acids is a concentrated “bio-identical”- rTG form of fish oil. A single softgel containing rTG fish oil can easily provide well over 700 mg of EPA and DHA and rTG forms outperforms the EE version of fish oil in terms of bioavailability and raising omega-3 index.

- Prescription pharmaceutical omega-3 fatty acids are only available in an EE form. However, in the event that a person’s insurance is willing to pay for these products upon the diagnosis of severe hypertriglyceridemia (TG > 500), these products have been shown to be safe and effective; albeit slightly less so than rTG forms available as dietary supplements. EE products should be consumed with a high-fat meal for best absorption, although it is important to instruct patients to add only healthy fats.

- Clinicians should consider having (or recommending) various blends of omega-3 products (some high in EPA, high in DHA, or a blend of EPA and DHA) to address different therapeutic targets. (see our paper addressing different therapeutic uses of EPA and DHA at www.pointinstitute.org)

- Clinicians can use blood testing (such as the omega-3 index) to determine the EPA and DHA status of patients and monitor dosage accordingly.

For a longer version of this article- including information about krill oil, manufacturing techniques, allergy concerns and more, download a free copy at: www.pointinstitute.org (whitepaper section).

References


5 For a more detailed explanation of this, a helpful summary can be found online at: http://www.oilsfats.org.nz/Oxidation%20101.pdf

About the Author: Thomas Guilliams PhD, is Director of the Point Institute of Nutraceutical Research, research arm of Ortho Molecular Products, where he serves as the VP/Director of Science and Regulatory Affairs. He is also a clinical instructor for the UW-Madison School of Pharmacy. His focus is on the evidence-based approach of Nutraceuticals.
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If you are prescribing bio-identical hormone replacement therapy, you need to consider integrating professional skin care into your practice.

Middle-aged patients are more motivated than ever to find medical options that enhance wellness and improve vitality. This includes a more vibrant and healthy looking appearance on their face and neck.

The average woman experiences a 30% loss of skin collagen in the first 5 years after menopause. This coincides with several other unwanted changes in their skin such as loss of elasticity, brown spots, dullness, and sallow looking skin. The modern woman does not accept the previous paradigm that one must have an old and tired appearance after the age of 60. This is especially true of your patients who use BHRT. As they start to feel “back to normal”, they invariably will focus on their appearance.

BHRT doctors should be recommending anti-aging skin care

The anti-aging physician is perfectly positioned to fill this need by becoming the resource for cosmeceuticals and aging skin. After all, our skin is the most visible part of us that experiences aging. If you treat patients with BHRT and nutriceuticals for internal aging, cosmeceuticals would be a natural extension of that regimen. Women feel their body changing on the inside, and see it changing on the outside. You can help them with both.

Unfortunately, in my experience as a pharmacist, many wellness doctors are not offering professional options for aging skin. This is not just a missed opportunity for your patients but also your practice. Prices of high-end cosmeceuticals can exceed $150 for one bottle. This revenue should stay within your practice instead of going to a department store or med-spa down the street. The BHRT physician needs to be addressing anti-aging skin care as an adjunct to wellness and preventative medicine.

Understand the basics of skin aging

Before recommending professional skin care, it is important to have a basic knowledge of the biological process of skin aging. Although a natural improvement may occur from BHRT alone, other ingredients are necessary to address the many factors of aging.

In general, skin aging is determined by three factors: chronology, hormonal decline, and environmental damage. The most significant extrinsic factor is photo-damage.

Free radicals have both direct and indirect effects on the skin. They oxidize cellular components and promote the expression of genes that accelerate aging. Most notably, collagen-producing fibroblasts become less prevalent while matrix metallo-proteinases (MMP’s) become more prevalent. There is also an indirect but significant pathway triggered from pro-inflammatory cytokines.

These pathways act in concert to create dramatic and rapid clinical changes in the skin. Most superficial skin care brands are woefully inadequate to produce significant and lasting transformation.
Cosmeceuticals use proven ingredients and avoid hype

Probably the most confusing aspect of recommending skin care is keeping up with all of the new products. There are endless fads and marketing campaigns that are enticing for both consumers and professionals. The best way to maintain consistent results with your patients is to stick to a few ingredients or formulas that can be trusted to bring results for your patients.

The following two ingredients have been utilized for decades and have numerous clinical studies that prove their effectiveness.

Retinoids at night

These Vitamin A derivatives are the most important and arguably most effective ingredients for photo-aging. They have been proven over a period of decades to make histological changes in aging skin and ameliorate common signs of aging.

There are other cosmetic forms of retinoids that have demonstrated efficacy with less incidence of side effects. The most notable form is retinol.

Tucker-Samaras et al. conducted a double blind, randomized study comparing stabilized 0.1% retinol moisturizer to a vehicle control. A total of 64 patients were randomized and applied the product to a designated half side of the face. After 8 weeks of use, the retinol group experienced a significant improvement in wrinkles, pigmentation, elasticity, and firmness.

Other clinical studies point to similar efficacy and low side effect potential with concentrations ranging from 0.1% to 0.4%

Vitamin C in a daytime moisturizer

Topical vitamin C is an important ingredient for maintaining healthy and vibrant looking skin. It has several biological functions in skin tissue that are vital for skin cell protection and dermal rejuvenation.

L-ascorbic acid is the skin’s most important aqueous phase antioxidant. It is a scavenger of radical oxygen species (ROS) and an essential enzymatic cofactor in collagen synthesis. There is evidence that it also suppresses the expression of nuclear factor kappa beta (NFkB), a factor involved in the pro-inflammatory cytokine cascade.

The downside of L-ascorbic acid is extreme instability due to oxidation. Other stable derivatives of Vitamin C are often used, such as lipid-soluble Tetrahexyldecyl Ascorbate and Ethyl Ascorbic acid.

The amazing clinical benefit of Vitamin C is demonstrated in several clinical studies.

Humbert et al. performed a study of topical Vitamin C 5% in postmenopausal women. As with retinoids, Vitamin C displayed significant histological and clinical improvements in photo-aged skin after 6 months of use. An increase in mRNA of procollagen I and III was observed as well as a decrease in matrix metallo-proteinase-I (MMP-I).

Fitzpatrick et al. studied a combination of Tetrahexyldecyl Ascorbate 7% with L-ascorbic acid 10% in a double-blind, half-face trial for 12 weeks. Researchers found the treatment side had a statistically significant improvement in overall facial appearance at the end of the trial.

Based on guidance from clinical evidence, Vitamin C should be formulated with a potency of 5-15%.

The most powerful proof for good skin care

Explaining the science and ingredients to your patients is important, but there is one piece of evidence that outweighs all others and that is your own personal testimony.

Most patients will inevitably ask, “What do you use for your own skin?”

If products are good enough to recommend, they should be good enough for your own skin as well. Become a firm believer in your skin care regimens through personal experience. You will be surprised at how much credibility that will provide to your patients.

In my experience, almost all BHRT practitioners who have successfully integrated skin care in their practice have started with themselves. The wellness industry should champion results over marketing hype, and speaking from experience is one of the most powerful ways to do that.

Lastly, ask your patients about skin care during their wellness consultation. Educate them on the biological process of skin aging and what they can do about it. The 60 year-old patient does not desire to look 30 again, but she does want to look vibrant in every phase of life, including menopause.

Integrating anti-aging skin care should not be considered an issue of mere aesthetics, but a justified extension of the holistic approach to wellness.

References


About the Author

Rick Rhoads, Pharm.D. is a compounding pharmacist at University Compounding Pharmacy and the founder of BioRenew Skincare Inc. He has been helping doctors provide better skin care and boost revenues for the past 5 years.

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September 20-21, 2014
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Keynote Presenters

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Leonard Guarante, PhD
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Introduction

When steroid hormones are applied to the skin in a cream or gel, some body fluids (saliva and capillary blood) reveal striking and high uptake of the hormone, while others (serum and urine) show little to no hormone uptake\(^{(1-5)}\). This holds true for all estrogens, progestogens, and androgens delivered topically. While this is widely recognized by practitioners who use topical hormones, few attempts to explain this odd paradox have been offered until recently\(^{(1-3)}\), other than to say the hormone absorbs poorly through the skin.

Endogenous Sex Hormone Production and Levels in Serum, Capillary Blood, Saliva and Urine

To better understand why topically delivered hormones show up in saliva and capillary blood, but proportionately much less in serum or urine, it is important to appreciate first how the sex-steroids distribute into these four body fluids (venous serum, urine, saliva, fingertip capillary blood) when they are produced endogenously.

In premenopausal women at the peak of their reproductive years the ovaries produce about 100-200 µg of estradiol, 10-30 mg of progesterone, and 0.25-0.5 mg of testosterone during the peak of the luteal phase\(^{(6)}\). This results in a serum or capillary blood level of about 70-150 pg/ml of estradiol, 10-30 ng/mL (10,000-30,000 pg/mL) of progesterone, and 20-100 ng/dL of testosterone. The optimal Pg/E2 ratio in both saliva and serum is about 100-300 when estradiol is within optimal physiological range (see Table 1). Venipuncture serum and capillary whole blood levels obtained by finger stick are near identical when the sex hormones are produced endogenously\(^{(7)}\).

Salivary estradiol, progesterone, and testosterone levels are about 1-2% of the serum values, with luteal estradiol in the 1.5-3 pg/mL range, progesterone in the 100-300 pg/mL range and testosterone about 20-50 pg/mL (ZRT Laboratory data). The optimal Pg/E2 ratio in saliva is about 100-300, which is about the same ratio as that seen in serum and capillary blood, when estradiol levels are in the normal range during the mid-luteal phase of the menstrual cycle.

Analysis of urinary steroid metabolites in our laboratory, using gas chromatography/tandem mass spectrometry (GC-MS/MS), reveals that the urinary estradiol and progesterone metabolites peak during the luteal phase, following the pattern of endogenous hormone production reflected in serum, capillary blood, and saliva levels (see Figures 1 and 2). The ratio of PgDio/E2 metabolites can vary somewhat (optimally between about 900:1 and 3000:1), which is higher than the ratios seen in saliva and blood (serum and capillary).

**Table 1. Expected premenopausal luteal phase blood levels of estradiol and progesterone, and their ratio.**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Estradiol (pg/mL)</td>
<td>43-180</td>
<td>-</td>
</tr>
<tr>
<td>Progesterone (ng/mL)</td>
<td>3.3-22.5</td>
<td>2.0-20</td>
</tr>
<tr>
<td>Pg/E2 ratio*</td>
<td>100-225</td>
<td>-</td>
</tr>
</tbody>
</table>

*Based on optimal estradiol median levels during the luteal phase of 100 pg/mL and optimal progesterone at 10 ng/mL to the high end of the range.
Topical Dosing with Physiological Levels of Sex Hormones

When sex hormones are delivered topically as a bolus dose, their levels rise dramatically and peak within about 3-6 hrs in saliva and capillary whole blood derived from the finger(1). The level of increase is directly proportional to the dose. Figures 3 and 4 are examples of salivary and blood spot testosterone values following different topical doses of testosterone, and Figure 5 shows salivary estradiol levels following different topical doses of estradiol. Once the peak is reached, the level of supplemented hormone in these body fluids begins to decline and reaches baseline about 36-48 hrs after dosing, but this depends on individual differences in metabolism and clearance. Ranges generally are established on values at 12-24 hrs following hormone supplementation, as it is more convenient for the patient to collect a sample first thing in the morning following a morning and/or night hormone dose the previous day. This also provides a more accurate representation of steady state levels, as earlier time points may be subject to erratic fluctuations as levels stabilize depending on the application site. With physiological dosing, salivary hormones increase within about 3-6 hrs to supraphysiological/pharmacological levels, while steady-state values are achieved at 12-24 hrs. For example, 30 mg topical progesterone, which represents the peak luteal daily production of progesterone, results in salivary progesterone levels ranging from about 500-3000 pg/mL at 12-24 hrs after application, but up to 10 times higher levels at shorter time intervals of 3-6 hrs(1); physiological luteal phase salivary progesterone levels, however, are only about 50-300 pg/mL. This has created quite a lot of confusion because physiological dosing (i.e. the same amount of hormone as that released from the ovaries on a daily basis) results in a 10-fold higher hormone range in saliva, but very little increase in serum progesterone(1-4,8). Because physiological topical dosing with 15-30 mg of progesterone has been shown in numerous studies to be clinically effective without causing adverse side effects in most individuals(9-11), the saliva range for topically administered progesterone is clinically more relevant when it is reset 10x higher; otherwise, practitioners may assume the dosing is excessive, and reduce dose to an amount that is less likely to be clinically effective. Some saliva testing labs have failed to recognize this issue and opt to just have the patient not use the topical hormone for more than three days before testing. This is problematic since it only reassesses near-baseline levels and is not truly representative of either supplemented or baseline saliva levels during active dosing.

Data from ZRT Laboratory show that, like saliva, capillary blood levels of topically delivered hormones peak at about 3-6 hrs, reach a more steady-state from about 8-24 hr, and levels are directly proportional to dosing(1). Unlike saliva, however, a physiological dosing (e.g. 15-30 mg of topical progesterone) generally results in a physiological level of progesterone in capillary blood (about 20-40 ng/mL), which is well within the optimal range known to protect against the cell proliferation-promoting effects of estrogens in target tissues such as the breasts and uterus(9-11).

In sharp contrast to the dramatic increase in progesterone seen in saliva and capillary blood following 30 mg of topical progesterone, serum levels of progesterone rise only to about 1-3 ng/mL(1,5,8), which is much lower than luteal range. For those practitioners accepting serum values as representative of systemic tissue levels, the 1-3 ng/mL results from serum testing have been interpreted to mean that progesterone is poorly absorbed and not capable of achieving levels that counter the growth-promoting effects of estrogens in the uterus and breasts(4). Topical dosing with progesterone even in the pharmacological 50-300 mg range does not raise serum progesterone to luteal levels(1). This is true also for topically delivered estrogens(12), progestogens(5), and androgens(13) and has, unfortunately, resulted in the use of very high topical dosing in an attempt to raise serum levels to a physiological range. This rarely, if ever, happens with topical delivery of sex-hormones(1).

Overall, what is seen with physiological topical dosing of all sex steroids in various combinations of compounded and FDA-approved hormone creams and gels is that the serum levels are much lower
than the levels seen in capillary blood or saliva. This paradox has been difficult to reconcile because venous and capillary blood levels of sex steroids are near-identical when produced endogenously, or delivered as a troche, i.m./s.c. injection, or s.c. pellet, but are remarkably different (as much as 100-fold with topical progesterone) when estrogens, progestogens, and androgens are delivered topically. Clearly, something is uniquely different about the way topically applied hormones absorb through the skin and reach tissues systemically\(^{1(10,11)}\).

Because salivary and capillary blood levels of progesterone and other steroids delivered topically increase so dramatically relative to serum, the obvious question to ask is why and how this happens, and are tissues other than the salivary gland and capillary beds of the finger-tip exposed to the higher levels of hormones? Based solely on serum testing one would surmise that progesterone is poorly absorbed and, not having reached physiological luteal levels, would be ineffective for countering the growth-promoting effects of estrogens on target tissues such as the breast and uterus. On the other hand, capillary blood progesterone results show that progesterone is very efficiently absorbed and achieves luteal levels that effectively counter estrogen stimulation. In fact, studies with breast biopsies of women using physiological topical progesterone therapy, with the exception of the topical preparations listed.

In developing urine testing of steroid hormones by GC-MS/MS at ZRT Laboratory it became apparent that the problems with detecting urinary progesterone metabolites (e.g. pregnanediol) at levels much higher than that seen during the luteal phase of the menstrual cycle, when the ovaries produce about 10-30 mg of progesterone daily (Figure 2). Because 100-300 mg of oral progesterone is necessary for an optimal clinical effect, and raises urine pregnanediol higher than luteal range, it is also necessary to reset the expected optimal urinary pregnanediol range to a higher value to avoid confusion and potential under-dosing to achieve an endogenous luteal pregnanediol range. In fact, ranges should be reset for all orally delivered hormones, particularly estrogens like conjugated estrogens, estradiol (see Figure 1), and estril, which are commonly used as oral replacement therapies.

In summary, serum and urine testing for topically delivered hormones grossly underestimate systemic delivery of hormones to target tissues and should be used with caution when designing appropriate dosing for optimal clinical response. As shown in Table 2, all body fluids (serum, saliva, capillary blood spot, urine) can be used to assess accurately endogenous hormone levels and exogenous hormone therapy.

### References


### Table 2. A guide to steroid hormone testing in different body fluids, without hormone supplementation and following different routes of hormone administration.

<table>
<thead>
<tr>
<th>Body fluid tested</th>
<th>Endogenous steroids – no supplementation</th>
<th>Oral steroids</th>
<th>Topical steroids</th>
<th>Vaginal steroids</th>
<th>Troche/sub-lingual steroids</th>
<th>Pellet/intramuscular steroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Yes</td>
<td>Yes(^1)</td>
<td>No(^2)</td>
<td>No(^2)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Saliva</td>
<td>Yes</td>
<td>Yes(^1)</td>
<td>Yes(^2)</td>
<td>Yes</td>
<td>No(^2)</td>
<td>Yes</td>
</tr>
<tr>
<td>Urine</td>
<td>Yes</td>
<td>Yes(^1)</td>
<td>No(^2)</td>
<td>No(^1)</td>
<td>No(^2)</td>
<td>Yes(^2)</td>
</tr>
<tr>
<td>Capillary blood</td>
<td>Yes</td>
<td>Yes(^2)</td>
<td>Yes(^1)</td>
<td>Yes(^3)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Notes:
1. Overestimation: metabolites interfere with immunoassays.
2. Underestimation: hormone levels not reflective of tissue uptake.
3. Overestimation: requires range adjustment.
4. Overestimation: direct contamination of oral mucosa/saliva.
5. Overestimation: direct contamination of urine.
6. Overestimation: if fingertips contaminated with topical hormones.

dosing (25-50 mg) show that high luteal progesterone levels are indeed achieved and estrogen-stimulated cell proliferation is inhibited\(^{10(10,11)}\), without a significant increase in serum progesterone levels. These findings concur with what we and others have observed that serum is not an appropriate body fluid to assess the clinical utility of topically delivered sex-hormones and that this has likely resulted in overdosing in an attempt to achieve physiological serum levels of hormones\(^{14(14)}\).
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### Fellowship Modules

#### The Fellowship in Anti-Aging & Regenerative Medicine (FAARM)

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<th>Module</th>
<th>Description</th>
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<td>A Metabolic, Anti-Aging and Functional Approach to Endocrinology</td>
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<tr>
<td>II</td>
<td>A Metabolic, Anti-Aging and Functional Approach to the Treatment of Hypertension, Diabetes, Coronary Artery Disease and Metabolic Syndrome</td>
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<tr>
<td>III</td>
<td>A Metabolic, Anti-Aging and Functional Approach to Gastroenterology, Neurotransmitters, and Neurology</td>
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<td>IV</td>
<td>A Metabolic and Anti-Aging Approach to Amino Acid and Fatty Acid Metabolism, Drug Induced Nutrient Depletion, Stem Cells and Regenerative Medicine, Spirituality and Osteoporosis</td>
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<td>V</td>
<td>Clinical Intensives (Non-CME)</td>
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#### The Fellowship in Anti-Aging, Regenerative & Functional Medicine (FAARFM)

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<th>Description</th>
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<td>VI</td>
<td>Herbology and The Functional Regenerative Matrix</td>
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<td>VII</td>
<td>Mitochondropathy, Heavy Metal Toxicities, A Metabolic, Anti-Aging and Functional Approach to Autoimmune Diseases, Cognition Enhancement and Fatigue</td>
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#### ELECTIVES

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<td>A Metabolic and Functional Approach to Children’s Health</td>
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<td>X</td>
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<td>Toxic Metals and Functional Toxicology</td>
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<td>XIII</td>
<td>A Metabolic Approach to Pain Management</td>
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<td>XIV*</td>
<td>Individualized Weight Management For The Patient</td>
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<td>XV*</td>
<td>Brain Fitness &amp; Memory Maintenance</td>
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<td>Advanced Integrative and Metabolic Cardiovascular Medicine</td>
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<td>XVII</td>
<td>Medical Acupuncture for the Integrative Physician/Practitioner</td>
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<td>XVIII</td>
<td>Integrative Neuropsychiatry</td>
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<td>XIX*</td>
<td>Sports Medicine &amp; Nutrition</td>
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<td>XX</td>
<td>Metabolic Code Triad Training</td>
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<td>XXI</td>
<td>Advanced Auto-Immune Therapies</td>
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Module B Components of Cardiovascular Disease
Module C Nutritional and Dietary Therapies for Prevention and Treatment of Cardiovascular Disease
Module D Various Conditions in Cardiovascular Disease

Sports Medicine Certification

This certification program focuses on the “science of eating,” including diet programs, recipes and nutrients that help athletes reach peak performance and success. Factors that hinder such success are also reviewed. The program discusses the body’s physiological response to exercise, treatments for sports-related conditions, biometrics, eating disorders, the aging athlete and psychology.

Fellowship Module XIX, A – D
Module A The Body’s Physiological Response to Exercise
Module B Treatments for Sports-Related Conditions
Module C Biometrics and Eating Disorders
Module D The Aging Athlete and Psychology

Lifestyle Coaching Certification

The Certification in Lifestyle Coaching teaches the healthcare practitioner how to properly administer information that will positively impact clinical outcomes and improve the overall standard of care. The client needs to live a healthy lifestyle and this course teaches you how to teach your client the proper steps. It’s about setting up your clients to succeed.

Fellowship Module XXIII, A – D
Module A Wellness Revolution and How You Can Become a Part of the Solution
Module B Basic Nutrition
Module C Fundamentals of a Co-Active Coaching Model
Module D Counseling the Patient and Improving Energy

Certification Requirements

Completion of FAARFM Certification Modules
A4M Board Certification *(where applicable)*
Completion of corresponding USF Courses
American Academy of Anti-Aging Medicine Membership
Fellowship in Integrative Cancer Therapies

The A4M Fellowship in Integrative Cancer Therapies is the most advanced, progressive educational program on treating and preventing both early and advanced stage cancers. This program will give practitioners the tools necessary to immediately integrate cancer fighting modalities into their practice.

- **What you will learn**
  The Fellowship in Integrative Cancer Therapies consists of ten modules. 
  **Topics include:**
  - Module I - Cancer Prevention
  - Module II - The Biology of Cancer
  - Module III - Immunology of Cancer
  - Module IV - Targeted Cancer Therapies
  - Module V - Case Histories In Cancer Therapies
  - Module VI - Integrative Cancer Therapies
  - Module VII - Dietary Treatments of Cancer
  - Module VIII - Nutritional Integrative Cancer Therapies

- **Who should attend the Fellowship?**
  All healthcare practitioners can benefit from this fellowship. In addition, all healthcare practitioners, regardless of specialty, can practice ICT. Although oncologists are welcome and urged to attend this fellowship, the majority of attendees will be non-oncologists. The Fellowship is open to physicians, physician assistants, nurse clinicians, pharmacists, D.D.S. and chiropractors.

- **Completion Requirements**
  - Modules I – VIII
  - Complete the A4M Board Certification
  - A4M Membership

- **University of South Florida Master’s Degree Requirements**
  - Module I – VIII
  - Two (2) Elective Modules
  - Webcasts Required
  - A4M Board Certification
  - A4M Membership
  - Ten (10) Courses with USF
  - One (1) Ethics Course with USF

NOW ONLINE!
Because this program is in such demand we have added it to our slate of online Fellowships. You can now experience all the benefits of the live program from the comfort of your home or office.
The Aesthetic
Anti-Aging Fellowship

What is Aesthetic Medicine?
Aesthetic Medicine is a developing clinical subspecialty and field in scientific research aimed at the use of minimally invasive cosmetic treatments to enhance patients’ satisfaction with their physical appearance. This subspecialty is no longer limited to the fields of plastic surgery and dermatology, as many specialties are offering aesthetic medical procedures in order to better accommodate their patients’ aesthetic needs. A growing trend among baby boomers is that aesthetic treatments are part of a normal health routine with the goal of maintaining a natural and healthy appearance.

Why add Aesthetics to your practice?
- There were nearly 10 million surgical and nonsurgical cosmetic procedures performed in 2010. Nonsurgical procedures are represented by 83% of the total.
- Botox was the number one cosmetic procedure performed with 2.8 million procedures, up 157% from 2002.
- U.S. residents make 145 million visits for medical aesthetics procedures each year and that number is expected to triple in the next 10 years.
- The top five nonsurgical cosmetic procedures in 2010 were:
  - Botulinum Toxin A Injections
  - Hyaluronic Acid Injections
  - Laser Hair Removal
  - Laser Skin Resurfacing
  - Chemical Peels

Statistics courtesy of the American Society of Aesthetic Plastic Surgery 2010 Cosmetic Surgery National Data Bank

What is the Aesthetic Anti-Aging Fellowship?
The Aesthetic Anti-Aging Fellowship is a seven-part series consisting of a three-module didactic series and a three-module hands-on clinical training series. The Aesthetic Anti-Aging Fellowship was created in recognition of the need to establish best practice standards in Aesthetic Medicine. The Fellowship enables medical professionals to learn Aesthetic Medicine theory and receive individualized hands-on training in aesthetic procedures to provide superior patient outcomes. The clinical programs provide level 4 CME classification and are accredited by the University of South Florida Office of Professional Development. Practitioners completing the level 4 classification, required and follow-up courses can qualify as competent to perform the procedures without further supervision, in accordance with AMA Guidelines on Continuing Medical Education for new procedures and skills. There are also Advanced Fellow and Master’s Fellow designations that can be obtained.

Why is the Fellowship for you?
The Fellowship is a post-graduate training program which combines online audiovisual lectures and hands-on tutorials in a clinical setting. The Fellowship denotes peer recognition in one of the fastest growing medical specialties. Also, the Fellowship will provide medical practitioners with a maximum exposure to the scientific, clinical and industry information necessary to introduce noninvasive aesthetic procedures in their practice.

Who should attend the Fellowship?
The Aesthetic Anti-Aging Medicine Fellowship program is open to MD’s, DO’s, or MBBS individuals. The long-term objective of the Fellowship is to achieve formal sub-specialty recognition and a new status for Aesthetic Medicine.

The Fellowship program is open to those practitioners with an existing knowledge base and experience in the field of aesthetics, as well as those physicians who are new to the specialty. Ability groups will be available during the hands-on sessions to ensure participants are learning the procedures most suited to their current skills.

Completion Requirements
Completion of modules I-VII (I-III are didactic and available online; IV-VII are hands-on training)
- AAMM Membership
- 12 Case Studies:
  - 2 Botox/2 filler (4 for Module IV)
  - 4 laser/light (4 for Module V)
  - 2 chemical peel/2 sclerotherapy (4 for Module VI)
- Completion of the Aesthetics Written Exam
What is Stem Cell Therapy?
New and current Regenerative Medicines can use stem cells to create living and functional tissues to regenerate and repair tissue and organs in the body that are damaged due to age, disease and congenital defects. Stem cells have the power to go to these damaged areas and regenerate new cells and tissues by performing a repair and a renewal process, restoring functionality. Regenerative Medicine has the potential to provide a cure to failing or impaired tissues.

While some believe the therapeutic potential of stem cells has been overstated, an analysis of the potential benefits of stem cell based therapies indicates that 128 million people in the United States alone may benefit with the largest impact on patients with cardiovascular disorders (5.5 million), autoimmune disorders (35 million), and diabetes (16 million U.S. patients and more than 217 million worldwide): U.S. patients with other disorders likely to benefit include osteoporosis (10 million), severe burns (0.3 million), spinal cord injuries (0.25 million).

What is the Fellowship in Stem Cell Therapy?
The American Academy of Anti-Aging Medicine (A4M) has recognized the need for knowledge on stem cells amongst physicians and healthcare professionals, thus creating the world’s first Stem Cell Fellowship program. Stem cell therapies involve the potential replacement of cells or organs that are diseased, injured, infirmed, ailing or aged. In this modular training program, a group of experienced academia’s, involved in stem cell transplantation, present a series of topics to cover the general principles and practice of stem cell biology and evidence-based treatments for physicians to optimize the health of their patients.

Why the Fellowship is right for you
By enrolling in the Fellowship, you will learn how to treat the diseases associated with aging with stem cell therapies - the medicine of the future. After completion of this modular training program, physicians will be able to intelligently decide which stem cell protocols to recommend to their patients. Become a pioneer in stem cells and the future of Regenerative Medicine.

Who should attend the Fellowship?
The Stem Cell Fellowship program is open to physicians, PhD’s, physician assistants, nurse clinicians, pharmacists, nurse practitioners, nutritionist, chiropractors, Bachelor of Medicine, Bachelor of Surgery and more.

Completion Requirements
- Modules I-V
- Modules I-IV are didactic and available online
- Module V is hands-on training
- Complete A4M Board Certification
- A4M Membership
Sexual Health Certification Program

Why this certification is right for you
The Sexual Health Certification Program offers healthcare practitioners the opportunity to increase their knowledge and experience for evaluating, diagnosing and treating sexual health disorders in all patients of all ages, genders and sexualities. Topics such as hormone depletion affecting sexual health, sexual dysfunction, issues in gay and transgender patients are covered in this certification program.

What you will learn
- Module A: Female Sexual Health
- Module B: Male Sexual Health, Gay and Transgender Therapy
- Module C: Impact of Medical and Psychological Conditions on Sexuality
- Module D: Hormones and Sexual Dysfunction plus Sex and Pregnancy

Who should attend the certification program?
- OB/GYN’s, Urologists, Family Practitioners, Nurse Practitioners

PROGRAM NOW AVAILABLE ONLINE!

“I practice Natural Hormone Replacement Therapy at Pill Box Pharmacy in Florida, I see many patients with low libido and sexual problems. After taking the Sexual Health Modules, I became equipped with an enormous amount of knowledge which expanded my professional skills tremendously. I learned different factors and treatments of sexual health, how to speak and ask questions about sensitive issues, and what protocols to use. By practicing what we learn in this module, your patients will come back to you with words like this: “Thank you for saving my marriage”, “Thank you for giving my wife/husband back”, “I feel great, like I’m 25 again!” and a lot more. I highly recommend this module to all medical doctors and medical practitioners who specialize in hormone replacement therapy or who practice functional medicine.” - Angela Pressman, PharmD, CPhT, Diplomat A4M, FAARM, AMMG

For the complete Sexual Health Certification Program schedule, please visit www.A4M.com or call us at 888-997-0112
BECOME A4M BOARD CERTIFIED TODAY

KNOWLEDGE IS POWER

A4M BOARD CERTIFICATION WILL GIVE YOU THE POWER TO:

• **RUN** a successful medical practice as a leading A4M Board Certified professional in your region. The credentials you earn denote recognition in the fastest growing, new high tech medical specialty.

• **TREAT** patients more effectively than traditional medical practitioners. Take an active interest in the science of longevity.

• **DEMONSTRATE** to your patients that you are committed to the prevention of diseases associated with aging. This certification process helps ensure that Metabolic physicians have grasped the essentials relating to the clinical application of Metabolic medical care.

REGISTER NOW!

• August 16-17, 2014
  Melbourne, Australia

• September 5-7, 2014
  Bangkok, Thailand

• September 10-13, 2014
  Phoenix, AZ

• October 17-19, 2014
  Bali, Indonesia

• December 10-13, 2014
  Las Vegas, NV

• February 25, 2015
  Los Angeles, CA

• May 6-9, 2015
  Hollywood, FL

• September 16-19, 2015
  New Orleans, LA

• November 2014
  Dubai, UAE

*All exam dates are subject to change.*

Register online at www.A4M.com or call 888.997.0112
Hop on over to booth #1023 and experience the magic.

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Power Greens® Premium is NuMedica’s state-of-the-art, great tasting greens and superfood drink mix, made from the highest quality of fresh fruits & vegetables available, specifically selected for their nutrient-rich properties. It supplies at least 30% of the recommended daily value of vitamins & minerals per serving. It’s loaded with energizing phyto-nutrients, certified organic wholefoods & plant extracts. Getting your fruits, vegetables, vitamins & minerals has never tasted so good!

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Patient One GastroOne™ supplies comprehensive support for gut health and function. Combining over 10 science-backed ingredients known for their beneficial effect on GI tract health and digestive comfort, GastroOne is an ideal formula for promoting healing of a compromised GI tract. A 3g dose of L-Glutamine is the foundation ingredient for its proven role in promoting normal intestinal permeability and healthy mucosal lining. N-Acetyl-D-Glucosamine, Deglycyrrhizinated Licorice, Aloe vera, Slippery Elm, Marshmallow root, Fenugreek, Mucin, MSM, Chamomile, Ginger, Quercetin, Larch tree and Zinc L-Carnosine provide added support for digestive comfort and immune health. Presented in a pleasant natural strawberry-flavored powder.

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Optimum Hormone Balance
www.optimumhormonebalance.com
972-893-6068

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The Skin Vitality Profile contains all the tests to identify how hormones affect conditions such as melasma, hirsutism, premature aging and dryness. Many physical changes occur on the skin, so understanding how hormones – or a lack of them – impact skin vitality sheds new light on effective treatments for hormone-deprived patients. Young or old, hormones play a crucial role in skin health – affecting hydration, elasticity, collagen and much more. This profile tests estradiol, Estriol, progesterone, testosterone, DHEA-S, diurnal cortisol, thyroid stimulating hormone and vitamin D. Fasting insulin is available as an add-on.

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www.webaddress.com
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Dr. Maria Blasco, Ph.D.,
Director of the Spanish National Cancer Research Center

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22\textsuperscript{nd} Annual World Congress on Anti-Aging, Regenerative & Aesthetic Medicine

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Labrix was founded by clinicians Jay H. Mead, MD, FASCP and Erin T. Lommen, ND with the goal of raising the bar on quality hormone testing. Labrix is recognized for setting a new standard for saliva testing in accuracy, reliability and turnaround times. Labrix also offers urinary neurotransmitter testing because adrenal hormones, sex hormones, and neurotransmitters are functionally interrelated. Labrix is a CLIA registered laboratory and is certified to test hormones in New York state.

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