Herbal and Nutritional Strategies for Harmonizing The Hypothalamus-Pituitary-Adrenal Axis (HPAA) and its Affects on the Endocrine System

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I consider the HPAA to be the 'Orchestrator' of the 'Life-Force' from which all energy is disseminated throughout the body. The harmony and balance of the HPAA is central to all aspects of the endocrine system conducting in accord with one another. By enhancing the vital force and addressing the root cause of dysfunction through the conscientious application of herbal and nutritional therapies, acute and chronic illness(s), and many of the syndromes presented in wholistic health care can be prevented or alleviated and optimal wellness can be restored. We will review the effects of stress on anabolic versus catabolic activity and allostasis. You will learn how specific adaptogenic plants and nutritional agents work to reduce the negative effects of stress, regulate hormone metabolism, improve energy transfer, slow down the aging process and inhibit an array of common diseases including: Insulin Resistance, Hypothyroidism, Obesity, Cardiovascular Disease, Alzheimer's, and Cancer.

"All human beings need to be free to manifest our creators love through our own uniqueness. If we have not experienced ourselves as unconditional love, we have not lived, because that is who we really are. Our hearts need to sing the melody of the music deep within. We will always find ourselves truly happy if our "doing" in life reflects our "being", and that being is a result of the freedom to pursue union with the divine. Therefore, if we are able to enhance our physical well being, I believe we can position ourselves to live this pursuit to the fullest capacity." – Donald R. Yance

The HPAA

The neuroendocrine system is one of our major auto-regulatory systems. The complex interplay of various components of the human body is in a constant state of flux, whereby the hypothalamus–pituitary–adrenal axis (HPAA) senses all within and around us. It is then able to prioritize and decipher how energy should be directed.

The HPAA is central to our entire endocrine system. The endocrine system itself is a classic cybernetic system, with feedback mechanisms throughout at various levels (NOTE: This is one important reason why adaptogenic herbs, which normalize and strengthen this system, are so complementary, whereas drugs are completely functional). Rather than consider the seven small glands that make up the endocrine system as separate entities, as allopathic medicine does, we should view them as one. Very often when one endocrine gland manifests a problem other glands are also suffering. For example, with hypothyroidism we can often see reproductive hormones out of balance and/or insulin signaling being affected. What is even more important and often relative is that underneath all of this is an imbalance, or lack of adaptability, centered in the HPAA. It is theorized that the central regulator – the hypothalamus – is responsible for the shifting of homeostasis (allostatis). Today, articles about receptor up-regulation and receptor down-regulation are not hard to find. The disruption of the HPAA is often central to most health problems, syndromes, diseases, and even aging itself. For instance, if the HPAA is strong and vital, than a woman can often make an easy transition through menopause, but if the system is overworked and tired, than menopause can be very difficult and even other endocrine glands can suffer. I can truthfully say that almost all the people I see in my practice present symptoms that involve the HPAA.

This comprehension of the human body is important for health care providers who are seeking to maximize the quality of life and longevity of their patients. This understanding is also valuable for those interested in general prevention of illness, the best possible vitality or improving mental and physical performance. There are many common threads among the systems of the human body that control our ability to heal from injury, ward off and recover from infection and/or illness (acute and chronic), improve performance, and spare lean muscle mass, maintaining a positive nitrogen balance (anabolic state) and of course dealing with

stress (the 'stress response'). The health of the HPAA neuroendocrine system is the root of our entire body; it is truly the key to the strength of our "Life-Force".

What are the common threads to developing age-related disease(s) and often acute diseases as well?
When we are young and full of life we have the attitude that we are invincible. We never think in terms of what impact the choices we make today will have on us years down the road. What we don't realize is that all of this is changing our allostatic barometer and stressing our adaptive energy capacity. This will ultimately affect us negatively, leading to health problems and eventually a shortened life-span. Various set points shift to accommodate us for the presumed life we are living in order to survive, not just now but into the future as well. As we age we have less and less energy to enable us to manage everything well. Our body knows this and alters hormones that do help us in the short run but also cause us to suffer later. It is now a well-known fact that how you eat as a youth effects your health when you are older. There is, especially, a growing amount of evidence of this with regards to cancer. The body adapts itself to our lifestyle at an early age by enabling more stress hormones to be released and this reestablishes a hormonal state that leads to increased secretion of glucocorticoids, which itself over time, becomes a major risk factor for a variety of illnesses, and premature aging.

While many disease processes are clinically seen within a single 'cause-and-effect' model, for example; elevated cholesterol as the cause of heart disease, another view is that the disease process is actually the loss of the systems ability to respond to the multi-factorial environmental conditions in a way that keeps the system within range of normalcy. While the current model of medicine is aware of our dependency upon the environment, they fail to recognize that we are inseparably intertwined and therefore, we need to improve our relationship to the environment within and around us.

The fact is that the majority of Americans older than 40 or 50 years of age already have a major health problem. Another disconcerting fact is that the majority of illnesses are subclinical, meaning they smolder under the surface for many years before they are recognized. Whatever the condition, whether it be sickness or apparent health, by accurately assessing your current health and/or "biological age", you will gain key insights that will enable you to begin your journey to vibrant health.

While there is no established definition of "biological age", the term is frequently used to describe the functional status of the human body as opposed to chronological age. To measure this, investigators have used a variety of biomarkers including skin thickness, strength, stamina, body composition, reaction time, vision, hearing, blood and neurological tests. All of these tests however, have one common feature: they measure aspects of anabolic and catabolic activity. Biological age should include one's metabolic status as it relates to the level of anabolic activity (repair, rebuild and rejuvenate). It is the understanding that aging is fundamentally a shift from youthful anabolic metabolism to increasing levels of catabolic activity. Other models of aging, such as wear and tear, free radicals, enzyme depletion and even accumulated genetic error, can all be placed under the umbrella of this metabolic shift. For example, the observation that free radical pathology increases with age leads one to question whether this is a true cause of aging or merely an effect. And while most would agree that it is both, the fact remains that young and old bodies are exposed to roughly the same environmental levels of oxidants. Moreover, in the body of a young person, cell division is occurring at vastly increased levels compared to an old body. This increases DNA exposure far beyond that experienced by an old person. Yet, free radical pathology is uncommon in youth and is universal in the elderly. The "Metabolic Model" resolves this issue by pointing out that cell defenses, including the production of DNA repair enzymes (eg; DNA polymerase) and endogenously produced antioxidant enzymes (eg; glutathione, SOD) are influenced by anabolic hormone levels.

Over time, the effects of prolonged stress cause hormone balance to be shifted towards a catabolic process of releasing more stress hormones in order to attempt to handle the stress better. This shift actually causes more oxidative damage and diminishes levels of anabolic hormones, thus negatively effecting the whole endocrine system (thyroid, pancreas, reproductive, thymus etc.) Whether or not an aging clock truly exists, the fact remains that anabolic metabolism determines a great deal more than one's muscle mass. It influences immunity, protein synthesis, cell proliferation, bioenergetics, cell communication, endocrine function, and even mind, mood and behavior.

Perhaps the single most important assessment of the aging process is the loss of skeletal muscle mass, which is now referred to as sarcopenia. Sarcopenia is an important marker for age as well as recovery from illness, injury, and surgery. Sarcopenia differs from cachexia in that the process is much less dramatic and reflects changes in body composition rather than malnutrition. Both hyper and hypo-metabolism can alter body composition over time, tending towards higher body fat and lower body muscle. New research is confirming that small losses of muscle mass over time can reflect the influence of the stress-modulating system and may be related to increases in the expression of catabolic genes, resulting in risk for later-stage chronic diseases. Assessing the body mass index (BMI) is the standard assessment test for muscle mass.[1-5]

There are many simple tests you can use to assess health in people presumed to be healthy as well as in people with disease. I find that most people, although not yet to the point of having a disease, are far from optimal health. By recognizing signs and reviewing certain markers, you can offer a treatment protocol that promotes optimal well-being and longevity. Botanical and nutritional agents can play a pivotal role in rejuvenation and reducing age-related premature disease. The key is to focus on maintaining or enhancing both hormone balance and cellular health. By the way, in many instances it is presumed that when a certain hormone is low, for example DHEA, that it warrants hormone replacement therapy when in fact, this is not at all what is optimal for the body. This is because pure DHEA is likely to covert into the wrong hormones and can also go into androgen and estrogen pathways, causing further problems. Instead, we should first aim to support the neuroendocrine system (the hypothalamus-pituitary-adrenal-axis HPAA) by using primary and secondary adaptogens and supportive nutrients which, “lend a helping hand” towards restoring harmony and balance. Botanical compounds, such as isoflavones, flavonoides, saponins, sterols, and ecdisterones normalize endocrine health and possess an ability to bring our system back into harmony. If complete harmony cannot be achieved through this methodology then, and only then, it becomes appropriate to use more specific herbal and nutritional agents. If endocrine hormone levels cannot be normalized using herbs and nutrition hormone, intervention may be required, and then, the lowest dosage possible should be used.

Appearance of Aging: Perception verses Reality

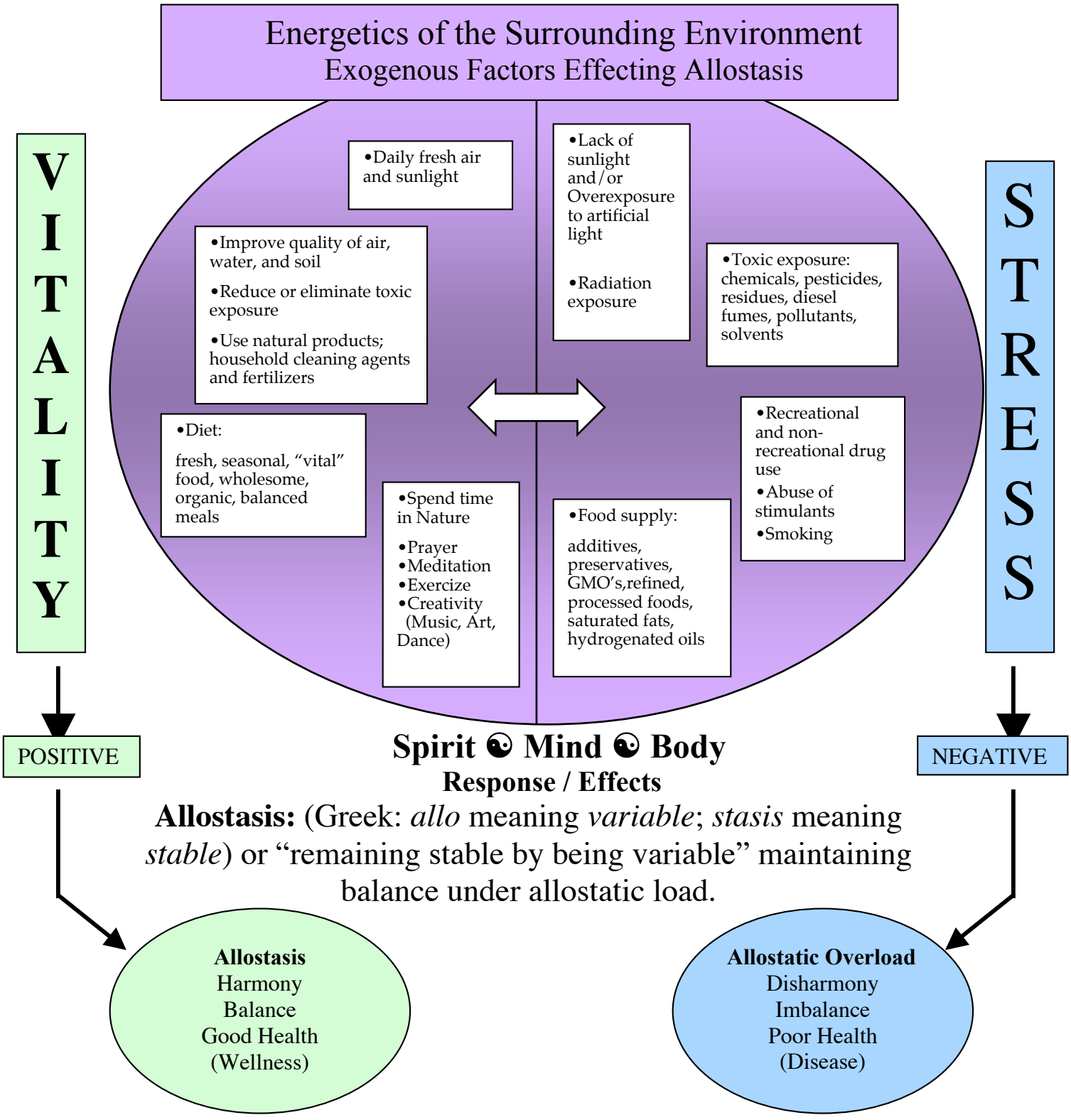
Premature aging for many relates solely to the outward appearance. The way we look does reflect some aspects of age but how we feel inwardly and the way our brain, bones and the rest of our body works is more indicative of the aging status. Our appearance is somewhat linked to our “inside” health, but it is really just an outward expression of an inward state. For example, many people wear stress on their face and the negative impact is obvious, while others hide it well. It is a simple fact that long-term stress can contribute to fat accumulation and muscle loss. Take the aging process along with stress and you have accelerated aging. Many people are mistaken when they think that much of what is happening to them is the normal aging process. It really doesn't have to be that way. As you age you don't have to become run down, overweight, get weak and tired, or be put on a half a dozen or more medications. Nobody can live forever but you can live a vibrant, healthy, energetic life. Your quality of life can be very rewarding right up to the end but you have to work at it with a healthy diet, and regular exercise, both the strengthening type and the aerobic type. You could also further help the cause by taking adaptogens and specific nutritional agents on a regular basis.

The Stress Response

For much too long and far too frequently, the term "stress" has been used in confusing and ambiguous fashions. Stress is often defined as any perceived physical or psychological change that disrupts an organism’s metabolic balance. In common usage, stress usually refers to an event or succession of events that cause a response, often in the form of "distress" but also, in some cases, a challenge that leads to a feeling of exhilaration, as in "good" stress. The term is often used to describe the event (stressor) or, sometimes, the response (stress response). Furthermore, it is frequently used in the negative sense of "distress," and sometimes it is used to describe a chronic state of imbalance in the response to stress. Here, stress will be used to describe an event that is threatening to an individual and which elicits physiological and behavioral responses as part of allostasis in addition to that imposed by the normal life cycle.

Allostasis is achieving stability through change. This is a process that supports homeostasis and means that the "set-points" and other boundaries of control must also change. There are primary mediators of allostasis such as, but not confined to, hormones of the HPAA, catecholamines, and cytokines. Allostasis also

clarifies an inherent ambiguity in the term "homeostasis" and distinguishes between the systems that are essential for life ("homeostasis") and those that maintain these systems in balance ("allostasis") as environment and life history stage change. “Allostasis is the process that keeps the organism alive and functioning . . . maintaining stability through change . . . and promoting adaptation and coping, at least in the short run.”



Allostasis: (Greek: *allo* meaning *variable*; *stasis* meaning *stable*) or “remaining stable by being variable” maintaining balance under allostatic load.

Allostasis
Harmony
Balance
Good Health
(Wellness)

Allostatic Overload
Disharmony
Imbalance
Poor Health
(Disease)

In the highly recommended book, "Why Zebra's Don't Get Ulcers" by Robert M. Sapolsky, the human response to stress is compared to that of an animal. For example, when we are threatened, i.e. a report is due in two hours and the computer just crashed, our adrenal glands respond immediately to help us avoid a destructive breakdown. Other systems in our body actually decrease their functioning during this fight or flight episode. Under severe stress, men stop producing sperm and hair and women stop producing hormones and start to store fat. In the wild, this reaction makes sense because the stress or the threat passes quickly and the animal can get back to the business of eating and procreating. However, in our world, stress overload becomes the typical pattern of our lives.

Stress is simply a fact of nature— all living creatures are in a constant interchange with their surroundings (the ecosystem), both physically and behaviorally. This interplay relates to our "adaptive energy," and is of course present in the relationships between all matter in the universe, whether they are living (animate) or not living (inanimate). Adaptive energy refers to the availability of energy to efficiently adapt. Although, there are critical differences in how living creatures relate to their environment. These differences have far reaching consequences for survival. Because of the overabundance of stress in our modern lives, stress has in fact become a negative experience in most cases.

Adaptation and Maladaptation

To cope with environmental stressors, such as heat, drought, toxins, etc., we possess cellular defense systems, which are constitutively present, but can be mobilized to minimize the effects of possible disturbances and restore homeostasis in the cell. Adaptation refers to the ability to internally adjust to various stressors in order to maintain homeostasis. The role the brain plays in adaptation (and maladaptation) to stress is being studied both experimentally and clinically. Experimental studies focus on the role of chemical signaling in the limbic system as a process determining adaptation to persistent or chronic stress, with particular emphasis on the role of peptides, steroids and mona-amines in organizing coordinated responses to defined stressors (both physical and social) and how these molecules interact. For example, we now know that different peptides evoke distinct but distributed patterns of gene expression in the brain, and that this corresponds with the pattern seen after exposure of animals to different stressors, suggesting that peptides 'code' for specific responses to defined demands.

Endocrine Hormones

Also is the role of steroids (such as cortisol and DHEA) in mediating stress-induced brain dysfunction and damage. Clinical studies focus on the process whereby social stress (e.g. chronic adversity) predisposes to major depressive disorder. The emphasis is on the role played by steroid hormones in the induction of depression; whereby both cortisol and DHEA are altered. Individual differences in morning cortisol may predispose to the risk of depression in vulnerable people. These studies are cross-disciplinary, and combine behavioral and psychiatric expertise with studies on neuroendocrine function.[6, 7]

The common denominator that contributes to a lack of longevity and good health is the accumulative effects of stress leading to overadaptation. Overadaptation refers to a syndrome that occurs over time as our adaptive capacity becomes maxed. We then have to make a certain number of adjustments and compromises in order to maintain the lifestyle that we choose. Internally, this complex process involves primary and secondary reactions and feedback mechanisms referred to as the "stress response." The stress response is a holistic process, which cannot simply be reduced to any one component. It is an integrative, moving, living process that involves several components, some of which can be scientific and rational, while other aspects may be entirely mystical. The challenge is to better understand this interwoven process.

The endocrine system is a classic cybernetic system, with feedback mechanisms throughout it at various levels. Dr. Hans Seyle theorized that the central regulator – the hypothalamus – was responsible for the shifting of homeostasis. Today, articles about receptor up-regulation and receptor down-regulation are not hard to find. The disruption of the endocrine system center, the Hypothalamic-Pituitary-Adrenal Axis (HPAA), is often central to most health problems, syndromes, diseases, and even aging itself. For instance, if the HPAA is strong and vital than woman can often breeze through menopause, but if the system is overworked and tired than menopause can be very difficult. I can truthfully say that almost all the people I see in my practice present symptoms that involve the HPAA. The HPAA is the conduit for our emotions

and psychological stress is primarily mediated through this axis. It has, like the whole neuroendocrine system, far-reaching interaction with the other hormonal systems as well as with the rest of the auto-regulation systems; therefore the state of health of the neuroendocrine system is foundational to understanding biological age assessment.

HPAA dysfunction has been shown to lead to some of the following conditions:

- dysregulation of catecholamines (fight or flight stress hormones)
- dysregulation of glucocorticoids (stress hormones)
- dysregulation of cytokines (disrupted immune system response)
- receptor desensitization (disruptions in cellular communication)
- atrophy of nerve cells in the amygdala and hippocampus of the brain
- bone mineral loss
- high lipids
- sarcopenia - loss of lean muscle mass (catabolic)
- abdominal obesity
- increased risk of cardiovascular disease
- chronic fatigue
- mild depression and anxiety
- anorexia (cachexia)
- poor sleep patterns
- altered cognitive performance
- decreased sexual behavior

Anabolic vs. catabolic activity – why is it so important?

Aging is associated with reduced anabolic hormone activity including growth hormone, thyroid hormone and sex steroid axis activity with increased abdominal fat (insulin resistance). The efforts of Selye and others to quantify catabolic metabolism laid an important foundation for the establishment of a way to assess the anabolic/catabolic index. Problems occurred in finding a reliable marker for testing. Measuring cortisol did not provide sufficient information due to its biphasic response to stress and the volatility of its fluctuation. At some point of adrenal exhaustion, cortisol levels fall below normal while the individual enters into a deeper state of stress-induced deterioration and malfunction. The ratio of serum testosterone to cortisol has been used as an anabolic/catabolic index. Cortisol normally reaches its peak early in the day then declines throughout the day. Cortisol helps regulate immune system activity that helps the body fight cancer as well as other diseases. People, whose cortisol cycle is thrown off by troubled sleep, or excess stress, may be more disease prone.[8]

Lean mass contains the body's protein content. Every protein molecule has a role in maintaining body homeostasis. Loss of any body protein is deleterious. The majority of the protein in the lean body mass is in the skeletal muscle mass. The rest comprises skin protein, immune defenses, visceral organ structure, and so on. It is the loss of body protein, not fat loss, that produces the complications of malnutrition. Protein is responsible for the metabolic activity and body structure essential for survival. Protein synthesis is also essential for any tissue repair. The chest wall and diaphragm muscles are, of course, components of the lean body mass.

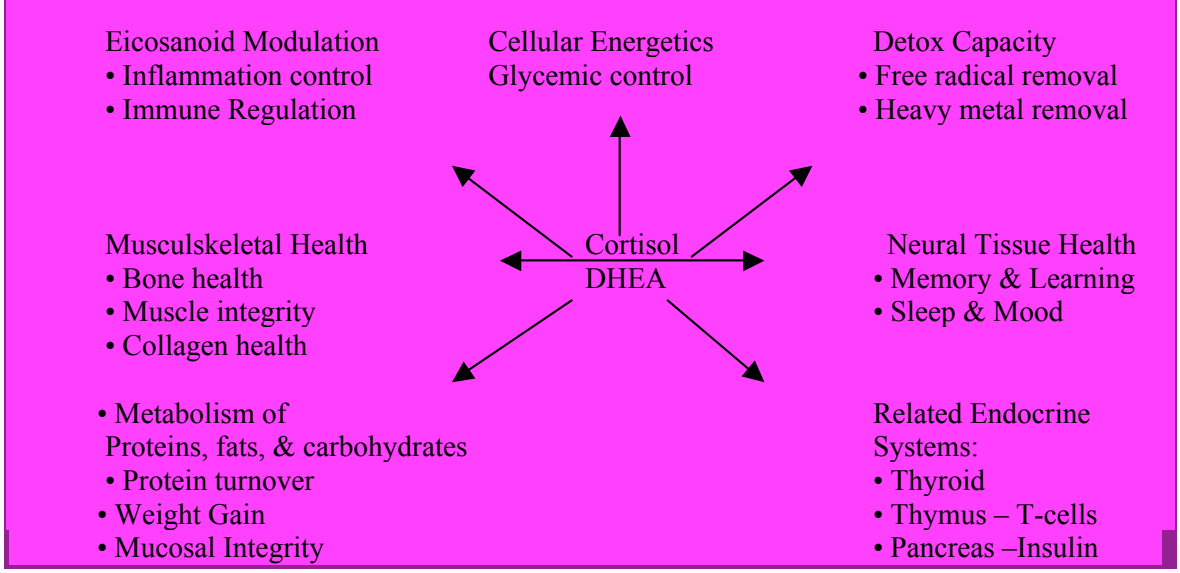
When we are exposed to stressors, our adrenal glands secrete the stress hormone, cortisol, causing a corresponding drop in our anti-aging and immune enhancing hormone dehydroepiandrosterone (DHEA). A tremendous body of research has shown that when cortisol goes up, DHEA drops and when DHEA is normal, cortisol also normalizes. Low DHEA levels are seen in those that are immune compromised, have arteriosclerosis (hardening of the arteries), diabetes, certain forms of cancer, and autoimmune diseases such as lupus. In aged animals, DHEA restores the cytokine secretion profiles and balance to those of much younger animals. In addition, DHEA increases IL-2 secretion, enhances antibody production and reduces IL-6 and TNF-□. DHEA thus appears to help reverse immune senescence.[9]

An overall restoration of anabolic metabolism can result in significant upregulation of immunity, demonstrated by greater monocyte, NK cell and T-cell numbers and activity. Since these enhancements do

in fact lead to more competent anti-bacterial, anti-cancer and anti-viral defense, one principal anti-aging goal is achieved: the restoration of immune profiles to those seen in youth.

Aging is characterized by a general decline in most physiologic functions, and in particular, by a decreased capacity to maintain homeostasis during episodes of stress. These changes are believed to reflect the accumulation of damage to cells and tissues resulting from a variety of toxic factors, either produced endogenously during normal growth and metabolism, or derived from the environment. Normal function and survival are dependent on the cell's ability to resist or adapt to such stress and to repair or replace damaged molecules. The need to enhance adaptation is critical and still often overlooked in natural medicine.

Regulating Aspects of Cortisol to DHEA: Balance mediated through the HPAA



Adaptogens

Although, generally speaking, adaptogens are not considered "medicinal' in the normal sense of the word, they can and should be implemented into any and all holistic protocol whether treating disease, or promoting wellness. They should be used especially following illness, post surgery, and/or trauma to assist in recovery. Adaptogens combat the negative effects of stress, improve health and well being, and enhance athletic performance capacity. They increase the body's vitality and reserve, a key component to any comprehensive longevity program. They are revered because they enhance the 'Life-Force', encourage natural harmony, enhance one's adaptability, and as a result generate "radiant health." Humans, like all living things, are in a constant flux, adapting so as to harmonize within and around its environment. We are constantly adjusting to a multitude of slight or very large changes, some of which are obvious while others go unnoticed. Good health can be measured by our ability to adapt. A healthy, adaptive person will survive and/or maintain good health where an unhealthy person, less adaptive, will fall, become ill, or even perish. Darwin said that the fittest will survive. The "fittest" are those that "fit" into their environment most perfectly and can adapt to change so as to assure their state of good health. Adaptability is probably the most distinctive characteristic of life. Our over or under adjustment will lead to disharmony. An adaptogen, possesses anabolic activity, increases resistance to a wide range of stressors in a non-specific manner and normalizes hypo- and hyper- conditions.

Adaptogen remedies have been shown to normalize plasma corticosterone levels, after stressful events. *Panax ginseng* blocks morphine-induced thymic apoptosis by lowering plasma corticosterone levels, thus reducing the damage caused by excess cortisol.[10] Adaptogens, including Panax, in other situations, potentiate cortisol and ACTH, sparing the breakdown of cortisol and delaying the exhaustive state.[11] This unique stress-hormone normalizing ability is one of the primary attributes of adaptogens. Cortisol helps the body maintain homeostasis in the face of stressors, counteracts inflammatory and allergic reactions and

controls the metabolism of protein and carbohydrates. Cortisol is a very misunderstood hormone. Balance is the key. In naturally low doses it stimulates the immune system and in high doses, as prescribed in synthetic drug form, it can be immune suppressing. Remember that cortisol plays a role in counteracting inflammatory responses in the immune system and when cortisol is not available because the adrenal glands have become exhausted from too much stress, inflammation is allowed to continue unchecked and fatigue sets in. Adaptogens recognize the need to aid in providing more cortisol, or recognize cortisol is being overproduced for no apparently good reason and needs to be suppressed. The liberal usage of Rhaponticum carthamoides, along with highly specific nutrients like creatine- magnesium chelate, together offers a safe solution to this neglected issue involved in just about every age-related disease and condition. Over time, this will build anabolic activity, strengthen and preserve our adaptive energy, and reduce the negative effects of stress that may otherwise cause disruptions, illnesses and premature aging.

Specific Adaptogenic Agents with Enhanced Anabolic/Anti-catabolic Activity

***Leuzea (Rhaponticum carthamoides)*:** a natural anabolic agent that builds lean muscle, increases energy and stamina, reduces muscle breakdown during prolonged strenuous activity, and has pronounced anti-oxidative capacity and is also a neurological protectant. It is useful for re-building damaged muscle tissue, protecting against muscle and tissue wasting (cachexia and sarcopenia). It regenerates organs such as the liver, kidney, heart and brain, and activates sexual behavior. Research shows that this plant can significantly increase muscle mass, while decreasing body fat in athletes who used it while exercising. Research also shows that Rhaponticum extract is able to increase performance in athletes (i.e., work capacity, endurance, reduction of mental and physical fatigue). Rhaponticum contains an array of compounds including 8 different Ecdisterones, most notably ecdisterone, and several important phenolic compounds. Rhaponticum is most effective used as a 1:1 fluid extract, or a powdered extract standardized to 5% ecdisterone.[12-15]

***Eleutherococcus senticosus*:** anabolic effect showing to stimulate protein synthesis in the pancreas, liver and adrenal cortex. Eleuthero is the known as the 'King' adaptogen because of the extensive research that has been done with this plant medicine. Over 2500 scientific studies, spanning over the past 50 years have confirmed the disease preventive, anti-stress, immune-enhancing, and adaptogenic effects of this miraculous herb with a total lack of toxicity. Eleuthero extract has demonstrated an ability to inhibit cancer, heart disease, diabetes, radiation toxicity, and acute and chronic infections, as well as extend life span in several animal studies. Eleuthero of Russian origin contains larger amount of several bioactive compounds, especially Eleutheroside B (.6-1%), which plays a significant role in the anti-stress, insulin-trophic, immune enhancing and anabolic actions of the Eleuthero. In Russia Eleutheroside B, as well as, total eleutherosides are tested to verify potency and quality. [16, 17, 18]

***Mumie* "Russian Shilajit":** a reputed rejuvenator and immunomodulator, claimed to arrest the process of aging and prolong life. Mumie has pronounced anabolic activity, accelerates protein and mineral metabolism, increasing lean muscle mass, and has shown to build bone density (anabolic). Mumie also possesses anti-stress adaptogenic actions, anti-cancer, improves cognitive abilities and inhibits aging of the brain.[19, 20]

Rhodiola rosea: One of the greatest things Rhodiola rosea does is enhance mental and physical performance. It has been widely used by Russian athletes and cosmonauts to increase energy. Rhodiola rosea is cardio-protective, normalizing the heart rate immediately after intense exercise. It improves the nervous system and mental functions such as memory, by increasing blood-supply to the muscles and brain, and it also increases protein synthesis (anabolic effect). Both human and animal experiments demonstrate that Rhodiola rosea extract enhances immunity, increases capacity for exercise, increases the activity of superoxide dismutase, decreases serum lipids and modulates the ratio of cAMP and cGMP. Rhodiola rosea not only possesses a high nutritive value but has also shown to prolong animal life. Rhodiola rosea has extraordinary pharmacological properties: adaptogenic, antimutagen, antioxidant, liver, pancreas and kidney protective, immune-enhancing, anti-cancer, potentiates cancer therapies, anabolic, insulintrophic, and antidepressive. In this respect Rhodiola rosea appears to be more powerful than other adaptogens. Rhodiola rosea stimulates ATP, Creatine phosphate synthesis, and glycogen synthesis in the muscles and liver. It also increases muscle protein synthesis and anabolic activity.[21, 22]

Pantocrine (Cornu cervi parvum): promotes protein synthesis, building lean muscle and tissue. Pantokrin is a specific Pantocrine product manufactured by a Russian State Pharmaceutical company and is officially approved by the Ministry of Health. 'Pantokrin' is a purified aqueous-alcohol extract obtained from the young Siberian spotted deer (stage III, unossified). Stage three antlers are proven to have the highest medicinal effects. Laboratory analysis show that deer velvet contains an amazing comprehensive nutritional profile including collagen, amino acids, essential fatty acids, important phospholipids, minerals, trace minerals and other functional proteins, all vital components for human metabolic function.

It is consider an excellent tonic for the elderly providing youthful tonic-like effects. It is mainly taken when the cold *Yin* forces dominate the environment (combined with ginseng for during the fall and winter months) or when the medical doctor diagnoses a *Yang* weakness. For example, it will be used for the treatment of cold extremities or on an individual who fears cold. I consider it to be a good remedy for people with low adrenal and thyroid manifesting weakness and coldness.

Pantocrine has shown to increase work capacity, improve sleep, strength, appetite, and decrease the rate of muscle fatigue. It possesses anti-catabolic action that is invaluable to reduce wasting and debility. Pantocrine increases production of red and white blood cells and accelerates healing and recovery. [23]

Panax ginseng: Ginseng acts on the hypothalamus and has a sparing effect on the adrenal cortex, mediated through the anterior pituitary and ACTH release. Response to stress is quicker, more efficient, and feedback control is more effective so that when stress decreases, glucocorticoid levels fall more rapidly to normal. Panax also increases protein synthesis and it is these two main effects which constitutes the adaptation effect of Panax ginseng.[24,25]

***Ashwagandha (Withania somnifera)*:** Ashwagandha could be considered as the premiere herb for all negative conditions associated with aging. I consider this herb to be an excellent overall tonic that should be implemented into everyone's daily adaptogenic formula(s). It possesses anabolic effects and is known for its ability to strengthen muscles. In situations of physical stress in animals, Ashwagandha has shown similar anti-stress and anabolic activity to Panax ginseng. [26]

Specific Nutrient Agents that Enhance Anabolic Metabolism

Another important factor in improving anabolic activity, as well as enhancing the immune system, is intervention with specific nutrients that assist in adaptation and inhibit aging. This concept may be applied to any situation in which an altered supply of nutrients is used to aid in anabolic activity, and to modify inflammatory or immune responses. The most studied nutrient-adaptogens include: *creatine, arginine, carnitine, glutamine, branched chain amino acids, alpha GPC, Whey Protein Concentrate, colostrum,* and *omega-3 fatty acids*.

Creatine Magnesium Chelate: a nonessential dietary component that, when supplemented in the diet, has shown physiological benefits in athletes, and recently in patients with various muscle, neurological and neuromuscular disease(s), dementia, heart disease, chronic fatigue, cachexia and sarcopenia. Creatine plays a very powerful role in energy metabolism as a muscle fuel in regenerating adenosine triphosphate (ATP). ATP is a molecule that is present in all living cells and operates as the energy source for the majority of the chemical reactions, which take place in cells. Creatine supplementation given to older people restored phosphocreatine resynthesis rate (PCr) to that of youthful adults. Creatine magnesium chelate provides the body with a readily available source of magnesium while also making the creatine more active by protecting it from cyclization.[27]

Finally, creatine biosynthesis has been postulated as a major effector of **homocysteine** concentration in the plasma, which has been identified as an independent graded risk factor for atherosclerotic disease. By decreasing homocysteine production, oral creatine supplementation may, thus, also lower the risk for developing coronary heart disease or cerebrovascular disease. Homocysteine metabolism is sensitive to methylation demand imposed by physiological substrates such as creatine.[28, 29]

The HPAT (Thyroid) axis

The hypothalamus-pituitary-thyroid axis is a key part of the energy transfer. The hypothalamus produces thyrotropin releasing hormone (TRH) which stimulates the anterior pituitary to release thyroid stimulating hormone (thyrotropin, or TSH), which in turn triggers the thyroid to produce T4.It is likely that all cells in the body are targets for thyroid hormones. While not strictly necessary for life, thyroid hormones have profound effects on many "big time" physiologic processes, such as development, growth and metabolism. Many of the effects of thyroid hormone have been delineated by study of deficiency and excess states. Thyroid hormones stimulate diverse metabolic activities in most tissues, leading to an increase in basal metabolic rate. One consequence of this activity is to increase body heat production, which seems to result, at least in part, from increased oxygen consumption and rates of ATP hydrolysis. By way of analogy, the action of thyroid hormones is similar to blowing on a smoldering fire. A few examples of specific metabolic effects of thyroid hormones include:

Lipid metabolism: Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma. They also enhance oxidation of fatty acids in many tissues. Finally, plasma concentrations of cholesterol and triglycerides are inversely correlated with thyroid hormone levels - one diagnostic sign of hypothyroidism is increased blood cholesterol concentration.

Carbohydrate metabolism: Thyroid hormones stimulate almost all aspects of carbohydrate metabolism, including enhancement of insulin-dependent entry of glucose into cells and increased gluconeogenesis and glycogenolysis to generate free glucose. People with low thyroid suffer from poor glucose transportation and poor insulin response. This adds to the complexity of less than optimal energy transfer and weight accumulation often seen in people with a low thyroid.

When the hypothalamus/pituitary/adrenal/thyroid (HPAT) axis is not operating to its potential proper metabolism is impaired including carbohydrate and /or fats digestion and utilization; for example gall bladder problems are more common in people with hypothyroidism because of reduced bile flow needed for proper fat digestion.

The Importance of Thyroid Hormone for Efficient Energy Transfer

Thyroid hormone spreads throughout the vascular system to the many tissues of the body, where it activates cellular, nuclear, and mitochondrial receptors that induce protein synthesis. Protein synthesis is a fundamental anabolic process that involves a synergistic endocrine enhancement of thyroid hormone-inducing growth-hormone regulation.

Thyroid hormone is a basic regulator of growth and development and some of the proteins induced by thyroid hormone are directly related to energy production, which is a catabolic state involving oxidative phosphorylation (the production of Adenosine triphosphate (ATP) energy). The majority of mitochondrial proteins produced in the cell are induced by thyroid activation of the nuclear DNA. These proteins migrate to the mitochondrial surface, where a transport protein prepares the form and function the protein will take in the body.

Since mitochondrial energy production accounts for the vast majority of total energy production, mitochondrial function is a necessary and essential aspect of the regulation of basal metabolic rate. In other words, either decreased thyroid hormone or mitochondrial dysfunction can lower basal metabolic rate and induce the symptoms of hypothyroidism (cold hands and feet, sensitivity to cold weather, psychological depression, cognitive difficulties, dry skin, scaly scalp, brittle hair, menstrual problems, constipation, diminished stomach HCl production, etc.)

Approximately 65 percent of the U. S. population is overweight; 27 percent is clinically obese. Research is pointing to the fact that an under active thyroid might be the number one cause of weight problems, especially among women. Weight gain during periods of stress which people often experience involves a shunting of thyroid hormone. I often see this in my practice. Here you need to treat underneath the thyroid condition that is manifested, and treat the HPAT always building your protocol with adaptogens. In the short term this will not manifest in drastic improvements but over time, sometimes years, the metabolism can get back to healthy efficient state. Anabolic metabolism increases, muscle to fat ratio improves, and

the system is much more equipped to handle stress without it causing huge disruptions within the endocrine system. Stress does not always have to be emotional to affect the thyroid. I have see people who exercise excessively manifest hypothyroidism as a result of stress this imposes on the system. This is mostly true in endurance related activities such as long distance running which is extremely catabolic.

Prolonged Stress can cause Thyroid Dysfunction

What accounts for this epidemic of thyroid problems? And what should you do about it? Before answering these questions, let's remember that the thyroid can't be viewed in isolation from the rest of your endocrine system. On the contrary, it sits at the very center of the action, and it is just as vulnerable to stress and lack of support as every other part of your body. Understanding how those stresses create illness and thyroid disease will also show us how to create balance and wellness.

In certain people, particularly woman, virtually any type of situation characterized by prolonged increased secretion of stress hormones, a predictable pattern of altered thyroid hormone metabolism occurs. Generally what happens is a pattern of low TSH production and a blunted TSH response to TRH, a decline in T-3, and an increase in rT-3. Stress can cause thyroid dysfunction that causes a built-in survival mechanism that hinders proper fertility in a woman. Balanced cortisol and thyroid hormones are critical to normal fetal development.

Building the adaptive energy with adaptogens and specific nutritional agents, which can act as companion adaptogens, could help the 65% of people in the United States who are considered either overweight or obese by influencing them towards a healthier endocrine state and causing a shift to a more efficient metabolic rate for weight management. This is an entirely new way of addressing the complexity of weight management including thyroid dysfunction that could lead to a long-term positive outcome in maintaining a healthy weight during and after weight loss programs.

Prolonged Stress causes HPAA Disorders which leads to

Thyroid Hormone and Insulin Dysfunction

•Cortisol inhibits 5'diodinase (shunting T-4 to T-3 conversion)

•Cortisol will cause alpha 1 and alpha 2-receptor site over-sensitivity (hyperthyroidism) or insensitivity (hypothyroidism) Blood Sugar and HPAA disorders

•Elevated cortisol will cause insulin insensitivity/resistance and insulin insensitivity/resistance will cause elevated cortisol

•Insulin insensitivity/resistance will cause alpha 1 and 2 receptor site insensitivity/resistance (hypothyroidism) and hypothyroidism will cause insulin insensitivity/resistance

•Decreased cortisol (which can follow elevated cortisol) causes reactive hypoglycemia, and reactive hypoglycemia will cause HPAA exhaustion

Insulin Metabolism

The pancreas releases insulin produced by beta cells after you eat carbohydrates. This causes a rise in blood sugar. Insulin ensures your cells receive some blood sugar necessary for life, and increases glycogen storage. However, it also drives your body to use more carbohydrates, and less fat, as fuel. And, insulin converts almost half of your dietary carbohydrates to fat for storage, not to mention the combined effect that elevated insulin and prolonged elevation of cortisol can do together. In other words, eating excess refined carbohydrates essentially sends a hormonal message, via insulin, to the body (actually, to the adipose cells). The message: "Store fat." Not only does an increase in insulin levels tell the body to store carbohydrates as fat, it also tells it not to release any stored fat. This makes it impossible for stored body fat to be burned for energy. So, a person whose diet contains a high amount of refined starches and sugars is likely to have a weight (fat) problem, which the body perceives as a survival tactic in case of an unlikely future famine. These deposits of sticky, saturated fatty acids increase the risk of stroke, heart attack, and arteriosclerosis

When the cells of the body stop responding properly to the insulin, which happens to some degree in almost all of us as we age, this is called insulin resistance or Syndrome X. Insulin resistance causes higher levels of insulin, blood sugar, and free fatty acids, which cause major damage to our body and pose a serious threat to our health. Diabetes, hypertension, cancer, obesity, high levels of cholesterol and other lipids, heart disease, kidney disease, female infertility and neuro-degeneration can all be the result of high insulin levels. If you want to use more fats for energy, the insulin response must be moderated. Low serum insulin levels in animal studies have shown to lengthen lifespan. Insulin is a direct player in the aging process, which supports the evidence showing that reducing calories results in a longer life. Scientists have known for decades that controlled famine can extend the lifespan of mammals by as much as 50 percent and that lean mammals are less prone to diseases of old age. Recent research reveals that when the chemical messages sent by an insulin-like hormone are reduced inside the fat cells of a fruit fly, the fly's lifespan increases by an average of 50 percent. [30]

Altered body composition may occur from increased fat and/or loss of lean muscle, which results in an increase of fat-to-lean body mass. Although the most common form of altered body mass seen today is from excess fat, decreased skeletal mass by loss of bone, such as seen in osteoporosis, is also a form of altered body composition.

Exercise reduces the circulating level of insulin; thus, physical activity could exert a protective effect against both heart disease and cancer through this metabolic pathway. Exercise in any form is important for anyone wishing to maintain or increase his or her health and well-being.

Primary Markers:

MAINTAIN OR ENHANCE CELLULAR HEALTH	
(1) Mitochondrial efficiency: **Oxygen** **Carbohydrate** **Lipid**	Energy transfer (ATP, cellular respiration)- CO Q 10, magnesium creatine, magnesium glycol glutamine, carnitine, alpha lipoic acid, PAK, and primary adaptogens. (also check endocrine status)
(2) Redox / antioxidant balance	Reduce the production of free radical damage and even more importantly improve free radical scavenging capability – glutathione enhancement etc. Adaptogens, companion adaptogens, carotenoids, lipoic acid, carnosine, vitamin C, E, tocotrinols, and A, selenium etc.
(3) Methylation	Homocysteine – Folic acid, B-12, B-6, Choline (as AGPC), Betaine etc.
(4) **Control inflammation** (inflammation is involved in all degenerative diseases including cancer, heart disease, and dementia)	C-reactive Protein (CRP) – Companion adaptogens, enzymes such as bromelian, red yeast rice etc.
(5) Maintain healthy lipid metabolism	HDL / LDL ratio, triglycerides, lipoprotein A, apolipids a & b, and E[4]
(6) Normalize blood viscosity	Fibrinogen, D-Dimer – Adaptogens, companion adaptogens, vitamin E, enzymes (lumbrokinase, nattokinase, and bromelian)
(7) Immune status	T-Helper Cell 1 (TH1) & T-Helper Cell 2 (TH2)
MAINTAIN OR ENHANCE ENDOCRINE/HORMONE BALANCE	
(1) Anabolic vs. Catabolic activity	HPAA status: DHEA – cortisol balance, creatine clearance - urine
(2) Insulin/Glucose Metabolism	Hemoglobin A1C, fasting glucose & insulin levels; *Reduce glycation, inhibit advanced glycation end products (AGE), Leptin (a related hormone of significance)
(3) Thyroid	TSH, T-4 (free & total), T-3 (free, total & reverse), Basal Metabolic Rate
(4) Testosterone	Free and total Testosterone, SHBG, DHT, Prolactin, estrogen.
(5) Human Growth Hormone	Insulin like growth factor – I (IGF-I)
(6) Body Composition	Body Mass Index (BMI)
(7) Pineal Gland	Melatonin

Insulin and Glucose Normalizing, Antidiabetic, and Insulintrophic Herbs

Adaptogens, such as *Panax quinquefolius*, root & berry, *Aralia manchurica, Oplapanax horridum* (Devils club), *Rhodiola rosea* and *Eleuthero leaf*, have a specific affinity for improving insulin utilization, as well as balancing and strengthening the HPA axis, and many other beneficial effects. Other herbs, including ***Ocimum sanctum* (Holy basil),** which I classify as secondary adaptogen, has adaptogenic, energy mobilizing and insulintrophic actions. Another secondary adaptogen, *Oplapanax*, properties are similar to ginseng. Oplapanax enhances the HPAA and central nervous system during depression and asthenia. It's recommended to take in case of impotency, physical and mental fatigue, hypotonia, sexual dysfunctions, after operations and hard diseases, and diabetes.

Specific nutritional supplements such as; lipoic acid, vanadium, chromium, magnesium and vitamin D that can also play a pivotal role in modulating insulin secretion and utilization, via improvement of adrenal, pancreas, and liver functions.

***Eleutherococcus senticosus* (root & leaf)**: in diabetes – the leaf of Eleuthero is more effective than the root at regulating blood glucose levels.[31, 32]

***Rhaponticum carthamoides**:* improves insulin sensitivity: stabilizes blood sugar, anti-diabetic, pancreas protective, anabolic.[33, 34]

***Panax quinquefolius (root & berry)*:** hypoglycemic, insulintrophic, berry promotes weight loss in insulin resistant individuals, improving insulin sensitivity.[35, 36]

***Rhodiola rosea*:** antidiabetic, insulin-tropic - enabling better insulin sensitivity and signaling.[37]

Cordyceps sinensis: hypoglycemic activity, improves glucose disposal.[38, 39]

***Ocimum sanctum*:** hypoglycemic, antidiabetic.[40, 41]

Mucuna pruriens: antidiabetic, inhibits diabetic related cataracts.[42, 43,44]

Inhibition of Glycation and AGE

Glycation is the name of a process in which glucose reacts with protein in an undesired way. This results in sugar-damaged proteins (similar to browning food in the oven) called ***advanced glycation end products*** (AGE). The formation of AGE happens in everyone and is a major factor in the aging process itself. These damaged proteins may lead to premature signs of aging (neuropathy, dementia, wrinkles and brown spots) and in the long run to damaging effects on most organ systems within the body. Glycation reactions are accelerated in the diabetic patient and contribute to the development of diabetic complications. **Turmeric, Grape seed & skin, and Green tea** have pronounced anti-oxidative protection from glycation. **Lipoic acid** has been shown to control the formation of AGE and reduce protein damage from glycation in both humans and animals.

Testosterone, an essential hormone for health

Optimal testosterone levels are of great importance in both men and woman for every aspect of health however, I am not in any way suggesting testosterone replacement therapy, as I am not recommending any hormone replacement therapy. You can achieve healthy testosterone levels in a gentle, harmonious way with herbal and nutritional supplementation.

The newest finding about testosterone and heart disease is very exciting. It turns out that testosterone actually dilates the coronary arteries, improving blood flow to the heart. This alone could explain the earlier finding that testosterone diminishes or eliminates angina. Angina happens when the heart muscle is not getting enough oxygen from the blood. Maintaining healthy testosterone levels may in fact be an important treatment for heart disease. Testosterone also helps prevent diabetes, and may help treat diabetes.[45]

According to a recent study, low androgen levels in men correlated with increased risk of atherosclerosis.[46] Normalizing free testosterone levels in men improves strength and increases protein synthesis as well as muscle mass. It also has been shown to decrease body fat, and particularly visceral body fat, and increases libido. Mood is also improved with testosterone, particularly in the older population. Higher endogenous testosterone has been correlated in many studies with a reduction in a number of cardiovascular risk factors, among them; lower - blood pressure, total cholesterol (TC), LDL-cholesterol (LDL), triglycerides (TG), visceral body fat, waist-hip ratio (WHR), serum insulin, fasting and post-prandial glucose, higher HDL-cholesterol (HDL) and greater insulin sensitivity.[47]

A consistent finding in the scientific literature is that obese men have low testosterone and very high estrogen levels. Central or visceral obesity (pot belly) is recognized as a risk factor for cardiovascular disease and type II diabetes. Boosting testosterone levels decreases the abdominal fat mass, reverses glucose intolerance, and reduces lipoprotein abnormalities in the serum. Further analysis has also disclosed a regulatory role for testosterone in counteracting visceral fat accumulation. Longitudinal epidemiological data demonstrate that relatively low testosterone levels are a risk factor for development of visceral obesity.[48, 49]

Botanicals that enhance testosterone

Tribulus terrestris is a natural aid to help impotence, low libido, and male infertility.[50] It enhances energy and vitality, and builds lean muscle growth. The increase in DHEA and testosterone levels by Tribulus will promote protein synthesis, positive nitrogen balance as well as faster recuperation and recovery from muscular stress. Tribulus, therefore has a positive effect on strength and stamina. It is safe to use and it is not a hormone. Other positive changes observed in a number of cases were a reduction in cholesterol, enhanced mood and well-being.[51] Tribulus was found to be superb for people with high cholesterol, as it stimulates the bile flow and breakdown of fats in the liver, thus contributing to more regular bowel patterns and elimination of toxins from the liver.[52] It is also a kidney detoxifier, a mild diuretic, and possesses some cancer inhibiting activity and immune enhancing activity.[53, 54] Most of the Tribulus sold commercially is of little to no value. The quality of this herb is dependant on the **Protodioscin** content.[55] It is critically important that the Protodioscin be a minimum of 15% for effectiveness. The analysis of market products showed considerable variations of 0.17 to 6.49% in the Protodioscin content.

Eurycoma longifolia jack: enhances testosterone and libido; also possess anti-ulcergenic, anxiolytic, fever –reducing, anti-tumor and anti-parasitic activities. Known compounds include a variety of quassinoids (1-6). At a research center in Kuala Lumpur, Malaysia, 30 married men, aged 31-52 years old, took Eurycoma extract regularly for three consecutive weeks. Interviews indicated that 48% felt healthy, active and energized, and 40% felt increased sexual desire. The subjects showed an increased free testosterone index. Increased testosterone levels help improve libido, energy and muscle mass. Their levels of DHEA, gradually increased from 26% after one week to 47% after three weeks. Most subjects demonstrated increased satisfaction in their sexual health and performance. One mechanism experts believe is responsible for the effects of Eurycoma may involve an ability to modulate negative feedback to the hypothalamus and pituitary glands, so the body continues to produce testosterone at sustained optimal levels.[56, 57]

Epimedium brevicornum and/ or grandiflorum: enhances androgenic hormone levels, as well as increases peripheral circulation, vasodilation, and improves neurological activities. The herb can stimulate the growth of the prostate and testes. Studies show that taking this herb can increase sperm production and urinary excretion of 17-ketosteroids. The herb's glycosides can regulate hypothalamic sex endocrine activity. It is effective in antagonizing the impotency induced by hydrocorticosterone administration. It is reported to also prevent cortisone-induced osteoporosis, regulates immune system response, and is used to inhibit and treat cancer.[58-61]

Growth Hormone

An entry of "human growth hormone" (HGH) into any common Internet search engine will yield thousands of hits. Most of the products on the market have little to no benefit. HGH hormone is present in high amounts during youth and fall precipitously as we age. Restoring HGH has been touted by many as the proverbial 'fountain of youth'. While HGH may or may not provide a way in which humans can significantly increase their life span, it does show promise in preventing or even reversing the harmful effects of sarcopenia in both elderly women and men.

If HGH levels fall under what is optimal, than insulin resistance increases, and the body shifts from utilizing glucose for energy to free fatty acids. Consequently, the level of blood fat and glucose both rise, resulting in hyperglycemia, hypertriglyceridemia, and a number of the other metabolic results of aging. Growth is known to play an essential role in the regulation of body fat levels, immunity, muscle mass, wound healing, bone mass and possibly thousands of other functions yet unknown. Growth hormone deficiency (GHD) is associated with the following, all of which can be significantly reversed with replacement of HGH: a decrease in lean body mass, bone density, skin thickness, sense of well-being, rate of wound healing, immune responsiveness, and aerobic capacity. In addition, GHD is associated with an increase in the following, all of which have been reduced in clinical trials of HGH: LDL, atherosclerosis, total body fat, hospitalization rate and sick days from work.[62]

While HGH supplementation might sound like the fountain of youth to some, there can potentially be significant drawbacks. Although mainstream medicine can no longer ignore the potential anti-aging

benefits of HGH supplementation, anti-aging proponents would be unwise to turn a blind eye to some reported significant side effects, including water retention, headaches, lethargy and joint swelling. Whereas these side effects may be lessened with lower doses of HGH, supplementing with this powerful hormone should be avoided and natural, safe precursors should be implemented as effective agents for HGH regulation. Also, HGH replacement therapy doesn't come cheap, with injections costing as much as thousands of dollars monthly.

The amino acid L-arginine, taken together with L-lysine (before bed) has shown to significantly raise HGH levels, as well as increase bone mineral density. Other amino acids that beneficially affect HGH include Creatine, Alpha-GPC, and Glutamine. Pantokrin, the purified extract made from the Spotted Deer velvet antler has shown to raise HGH, as well as the Ayurvedic herb, Mucuna pruriens.

An early study done in 1981 showed that 1200 mg of arginine and 1200 mg of lysine, when taken together, produced a measurable increase in HGH secretion. Interestingly, neither of these amino acids showed an effect on HGH levels when taken separately, even at the same doses.[63] A more recent study, done in 1997, again showed that relatively low doses of arginine and lysine (1500 mg), when taken together increase HGH levels.[64] While most studies have been done in people less than 30 years of age, a study done at the Louisiana State University College of Medicine has shown that even the elderly can benefit from amino acid supplements. Nine men, aged 32 to 64, were given 2000 mg of the amino acid glutamine; 90 minutes after ingestion, HGH levels increased over 400% from baseline.[65] Recent research suggests that creatine can raise growth hormone levels equal to that of intense exercise.[66] Alpha-Glyceryl Phosphoryl Choline (A-GPC), another amino acid compound naturally increases the secretion of HGH, and thus offers a unique health benefit that distinguishes it from other "GH secretagogue" agents. Another effect is that A-GPC is a potent choline donor. The choline provided serves as the precursor for the synthesis of phosphatidylcholine (PC) from other lipid-based compounds. Since PC is a major component of cell membranes, it can also lead to changes in cell membranes of anterior pituitary cells, thus enhancing the stimulatory effect of other related hormones on HGH.[67]

Mucuna pruriens is a unique herbal agent from India that has been used traditionally in Ayurvedic medicine. Mucuna is the richest source of L-dopa. L-dopa has been extensively researched and in prescription-form is the most widely used drug for Parkinson's disease, which is caused by a dopamine deficiency and mitochondrial dysfunction. The body uses L-dopa to manufacture dopamine. Dopamine is extremely important and a vital brain neurotransmitter that makes possible the transfer of information from neuron to neuron. Dopamine also regulates motor control, sex drive, immune function, **growth hormone** levels, Somatropin release, and motivational behavior. Low dopamine levels in the brain have shown to cause a decline in hypothalamic releasing factors. Due to aging, a 20-40% decline in dopamine production hinders the ability of the hypothalamic/pituitary axis to stimulate testosterone release in men and woman.[68]

Mitochondrial efficiency vs. dysfunction

A very critical aspect of cellular energy is the mitochondria. Dr. Denham Harman first proposed the importance of mitochondria to aging in 1972. Mitochondria, of course, are the key to the body's production of energy. It is in the mitochondrial membrane that ATP, the body's universal energy molecule, is produced. Mitochondria are thus important aspects of both the neuroendocrine and the free radical theories of aging. This is the point of interaction between the free radical theory and the neuroendocrine theory. We have all learned and forgotten the Krebs cycle in high school chemistry and biology. It is one of the important processes involved in mitochondrial energy production. Other important mechanisms of ATP production are the *respiratory chain*, which operates in the inner mitochondrial membrane and fatty acid oxidation. Special conditions that involve primary deficiencies of L-carnitine, coenzyme Q(10), creatine, carnosine and cofactor-nutrients, such as PAK, magnesium, NADH and vitamin-responsive enzyme defects must be systematically considered, because supplementation with these substances may be curative or produce dramatic improvements.[69]

Natural agents that enhance mitochondrial efficiency

Coenzyme Q10 (CoQ10), or ubiquinone, is found in small amounts in meats and seafood. CoQ10 plays an important role in the production of energy within each cell of the human body. It resides in the mitochondrial membrane and is a naturally-occurring cofactor in the electron transport chain, the biochemical pathway in cellular respiration, from which ATP and most of the body's energy are derived. CoQ10 is considered essential for the health of all the body's cells, tissues, and organs, in particular the heart. CoQ10 is a key cofactor to the process that produces 95% of the energy consumed at the cellular level. Lower levels of energy in cellular mitochondria are linked to many age-related diseases including, diabetes, Parkinson's, Alzheimer's, and heart disease. CoQ10 can also function as an antioxidant. Although CoQ10 is found in all human cells, its highest concentrations occur in the heart, liver, kidneys, and pancreas. It is found naturally in the organs of many mammalian species. Given that CoQ10 is naturally so widespread in the body, it is extremely safe even at high doses. Most healthy young individuals produce adequate quantities of CoQ10 to meet their bodies' needs. However, when mitochondrial bioenergetics are inhibited by a drug, like a statin, or reduced simply because of aging, or when there is a need for higher levels of CoQ10, in heart disease for example, it becomes an essential nutrient. Various studies have confirmed that as we age our body's supply of CoQ10 slowly diminishes, making CoQ 10 a vital nutrient for anyone wishing to inhibit premature aging. The exciting *clinical* research on CoQ10 is simply remarkable. I would go as far to say it is almost criminal that Physicians do not routinely give this remarkable compound to their patients. In my practice I have witnessed miraculous effects in people with a variety of disorders when using CoQ10, unlike any other nutrient.

Carnitine is essential in the transport of long chain fatty acids into the mitochondrial matrix and plays a key role in the oxidation of lipids. This means that carnitine improves fatty acid utilization and energy production. Carnitine significantly reverses age-associated mitochondrial decay. It increases cellular respiration, membrane potential and cardiolipin levels. Carnitine has been shown to improve energy production within brain cells and is considered a neuroprotective agent because of its antioxidant action and membrane stabilizing effects.

Alpha lipoic acid helps break down sugars so that energy can be produced from them through cellular respiration. In addition, recent research has discovered that alpha lipoic acid plays a truly central role in antioxidant defense. It is an extraordinarily broad-spectrum antioxidant able to quench a wide range of free radicals in both aqueous (water) and lipid (fat) domains. Moreover, it has the remarkable ability to recycle several other important antioxidants including vitamins C and E, glutathione and coenzyme Q10, as well as itself! For these reasons, alpha lipoic acid has been called the universal antioxidant.

There are several botanical agents that have also shown to enhance mitochondrial activity. Two examples would be Rhaponticum carthamoides and Rhodiola rosea. Standardized *Rhaponticum carthamoides extract* (RCE), to 5% ecdisterone, normalized phospholipids, which play the structural role in the mitochondrial membranes. The administration of ecdisterone increased protein uptake in skeletal muscles. RCE promotes an increase in the amount of ATP, creatine phosphate, and carnosine, and normalizes Ca2+ content in skeletal muscle. This effect leads to greater energy efficiency and muscle mass development. During intense muscular work, RCE hinders disorders of energy metabolism (maintains a stable level of glycogen and macroergic phosphates in the skeletal muscles) and increases the blood supply to the muscles and brain.[70-73]

Rhodiola rosea root extract (1:1), a well noted adaptogen, possesses a broad-spectrum of health benefits that include mitochondrial protective activity and antioxidant activities. It increases intracellular oxygen diffusion and efficiency of oxygen utilization and reduces oxidative damage.[74, 75]

Amino Acids and their key functions

Nutrient	Comments	Key functions or effects
Arginine	•Endogenous synthesis is decreased in trauma and sepsis	•Precursor of polyamines and nucleic acids •Precursor of amino acids involved in connective tissue synthesis •Improves wound healing •Precursor of nitric oxide •Secretagogue for Growth Hormone (HGH), & insulin •Immune modulating: Increases T cells & enhances T cell response
Glutamine	•Most prevalent free amino acid in the human body •Synthesized mainly in skeletal muscle •Catabolic conditions are associated with marked decline in skeletal muscle and plasma concentrations	•Precursor of purines, pyrimidines acid nucleotides, and amino sugars •Precursor of glutathione •Increases HGH •Major metabolic fuel for enterocytres, colonocytes, and immune cells •Adjunctive to chemotherapy & radiation •Most important substrate for renal ammonia excretion •Protects structural and functional integrity of intestinal mucosa •Maintains or augments cellular immune functions, especially those associated with cell mediated immunity
Branched chain amino acids	•Sparing effect on muscle glycogen degradation	•As nitrogen donors in the formation of the amino acids glutamine, alanine and aspartate during exercise •Lowers lactate production •Increases protein synthesis and/or minimizing protein degradation
Creatine Magnesium	•Plays a powerful role in energy metabolism as a muscle fuel in its role in regenerating ATP. •Mitochondrial nutrient	•Anabolic: increase lean muscle growth •Increases cellular energy and aerobic exercise •Improves heart function •Neuroprotective •Raises Human Growth Hormone (HGH) •Reduces homocysteine
Alpha GPC (Glyceryl Phosphoryl Choline)	•Acts as a precursor of acetylcholine (ACh) •Choline donor	•Increases phosphatidylcholine (PC) •Increases HGH •Improves lipotrophic functions (methyl group transferases) in the liver •Improves mental focus and stimulation of cognitive function
Carnitine	•Reverses age-associated mitochondrial decay •Enhances energy by transporting fatty acids for energy, via *beta oxidation*	•Improves exercise ability and heart function •Improves blood and oxygen flow •Alleviates depression in the elderly •Neuroprotective, improves memory •Lowers lipoprotein(a) levels, raises HDL •Liver regenerative, improves neuropathy

Closing insights

Twelve tips to implement in your daily life to reduce stress and for complete wellness:

1. Reduce or eliminate your access to the news. Consider watching the news on TV or reading a newspaper every other day, or even 1 or 2 x a week rather than 2 or 3 times per day.
2. Reduce noise pollution by avoiding large crowds of people, reducing listening to the TV and radio, and eliminating artificial sounds. Try listening to soft relaxing music, or birds early in the morning, or even just the evening breeze.
3. Avoid refined sugar, refined carbohydrates and refined fats. Avoid sweet baked foods in the morning and between meals. Eat 7 to 10 half-cup servings of organic vegetables and 4 to 5 fruits every day. Don't skip meals and make sure all your meals are balanced (protein, fats, carbohydrates).
4. Break or reduce bad habits such as smoking, drinking alcohol, staying up to late at night, etc.
5. Do a variety of moderate regular exercises. Too little or too much exercise can add stress, but regular moderate exercise can reduce stress.
6. Breathe. Breathing is a powerful distressing tool. Spend time outdoors each day, or whenever possible. Sunlight and fresh air can do amazing things for improving stress defense.

7. Laughter – having a good sense of humor is always helpful.

8. Take your time and slow down. Often we are in too much of a hurry when we don't need to be.

9. Take a candlelight essential oil and Epsom salt bath before bed 2 or 3 nights a week.

10. Get seven to eight hours of sleep every night. I believe general speaking people should sleep a bit longer in the winter than the summer.

11. Be positive and believe in yourself. Negative self-talk and continually doubting your abilities hampers your body's ability to heal. Notice the beauty around you. Smell the flowers, watch the sunset and listen to the wind. Love your family and friends and be forgiving. **Forgiveness reduces chronic stress and increases one's sense of control.** When you learn how to forgive, you develop the emotional confidence to "get over" any difficulty.

12. Prayer: Upon waking and before falling asleep read something spiritually uplifting, perhaps the bible or and an inspirational book. Sit and contemplate allowing the spirit that dwells within you to be filled with God's Grace. Truly this will reduce stress and manifest wellness. Think these thoughts throughout the day:

    Gratitude: As you wake up in the morning, give thanks for your breath and the gift of your life.

    Laughter: Try and laugh each and every day. Laughter is extremely important for a healthy long life. It is not only good to laugh at something funny but also be able to laugh at something that doesn't quick go right – a spilled drink on your new shirt,

    Beauty: Find a favorite spot in nature. In times of stress, remember what that spot looks and feels like.

    Calmness: Learn to maintain your sense of peace in any situation, no matter how upsetting. A 45-second technique called Positive Emotion Refocusing Technique can calm you whenever you feel angry, hurt, depressed or bitter about an unresolved grievance or a relationship problem…

    Love: Look for people who are in love, and smile at their happiness. Love needs to be given as well as received. Call up a few close friends, and tell them you care about them. The pursuit of love is our true dive calling.

We do not stop playing because we are old; we grow old because we stop playing. There are two important additions to staying young, being happy, and pursuing your dreams. You have to laugh and find humor every day. You've got to have a dream. When you lose your dreams, you die. There are so many people walking around who are dead and don't even know it! Anybody can grow older. That doesn't take any talent or ability. The idea is to grow up by always finding the opportunity in change.

Remember, growing old is mandatory; growing up is optional. We make a living by what we get, while we make a life by what we give. The purpose of life is but one thing – it is to examine all aspects of our life and bring them into alignment with our relationship with the Divine. This includes our attitudes and thoughts, our eating, our cooking, our sleeping, our exercising, our working, our playing, our meditating, our worship, our life and our death, body and soul, mind and spirit.

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