

Waking up happy and full of energy every day can be a reality for you! Many people start the day wondering how they are ever going to make it through the day. Often you hear that a positive attitude is required to "Make it a great day." This can be easier said than done, especially if your body chemicals (hormones) and brain chemicals (neurotransmitters) are out of balance. If these chemicals are out of balance then you are fighting an uphill battle. On the other hand, when these chemicals are in balance, then your chances of waking up happy and full of energy become greatly enhanced.

This report will provide you with insights and tools that will help you to feel better and have more energy.

Depression, whether perceived or not, can be mental, physical, environmental or emotional in nature. In life, some periods and events can be identified as predominantly stressful moments such as the death of a loved one, car accident, or loss of employment. Even so, not every stressful moment is attached with a negative event because some can be associated with happy moments, such as employment or wedding. Apart from the major events of life, there are other elements that can make a person's moments of life stressing: allergies, infections, depression, overworking, chronic disease, sleep deprivation, guilt, blood sugar fluctuations, toxic exposures, medications and others.

Hormones, such as cortisol and Dehydroepiandrosterone (DHEA) secreted by the adrenal glands, are an essential part of the stress response physiology. While the body's complex hormonal system is skilled at handling stressful events, today's busy world that has been integrated with fluorescent lights, cell phones, traffic lights and more presents a person with frequent life stressing factors. Therefore, this constant exposure of the body to the various stressing factors increases the demand of the body for adrenal hormones; hence, resulting in emotional dysregulation.

# **Pregnenolone Steal**

The primary precursor hormone for almost all steroid hormones is Pregnenolone. The hormones derived from Pregnenolone include DHEA, cortisol, estradiol, testosterone and progesterone. They are essential in the body to maintain the needed cortisol levels during stressing times and constant or chronic stress. While this hormone can be utilized in the production of any of the mentioned hormones, an increase in demand for cortisol because of constant depression shuts down the Pregnenolone pathway hence favoring cortisol production a phenomena called "Pregnenolone stealing." Therefore, these amounts of Pregnenolone are redirected to support only acceptable cortisol levels in the body, hence leaving less of it

available to the production of the other steroid hormones. This deviation of hormones contributes to the overall depression of the body, hence making the depression worse.

## **Estrogen Dominance**

In the body, when there is a greater influence of the hormone estrogen on the tissue than progesterone, the state is called Estrogen Dominance. Many conditions and situations can lead to this imbalance including an increase in the levels of estrogen secretion in the body, decreased progesterone secretion or an exposure to exogenous estrogens.

The body has the capability of converting progesterone to cortisol; increased depression (and a higher cortisol demand by the body) often leads to a decrease in progesterone production, hence, worsening the imbalance between progesterone and the estrogens.

## No Rest for the Weary

Like most creatures on earth, the human endocrine system is designed with a flight or fight reaction, that enables us to defend ourselves or run away from danger. Fight is not necessarily about throwing punches, but dealing with an amount of smaller stressing events such as social stresses, traffic, chemical exposures, infectious agents, etc. will lead to a regularly stimulated adrenal response. Most animals relieve stress and depression by resting and allowing their bodies to calm after a stressful encounter, human being rarely do this and would rather take pills to shut the symptoms. Nonetheless, with continuous stimulation, the body's stress response becomes less sensitive to the stress stimuli hence a decrease in production of cortisol.

### Individual "Tipping Point"

To some people adrenal exhaustion can happen after a single stressful event, while, for others, is because of an accumulation of stressing elements that were never dealt with. Human beings are different from one another; hence, there is a difference in the time taken to show the symptoms of depression from one individual to another.

### What Is Adrenal Dysfunction?

Adrenal dysfunction refers to a decreased function by the adrenal glands, it is manifested as an alteration of the diurnal adrenaline hormone secretion pattern together with cortisol or as a reduced output. People who suffer decreased adrenal function mostly complain of sleep disruptions, salt or sugar cravings, fatigue, weight changes, low blood pressures, allergies, nervousness, anxiety and other symptoms.

Traditionally adrenal dysfunction is defined as an alteration of adrenal hormones, which start with a rise in cortisol levels, it results in overall reduced output or cortisol diurnal production pattern is altered. A better approach in addressing adrenal dysfunction includes assessing neurotransmitter levels and HPA axis. Steroid and cortical hormones are produced in the adrenal cortex, catecholamines that include norepinephrine, small amounts of dopamine and epinephrine are produced in the adrenal medulla.

Adrenal output is also affected by production of serotonin, and levels of serotonin are influenced by the adrenal function, it is therefore recommended that the neuroendocrine system is entirely evaluated in order to get an assessment, which is optimal.

### **Causes of Adrenal Dysfunction**

This condition comes about from sudden or continuous stress. It may start suddenly or as repeated periods or repeated or prolonged stress. Sources of stress can be negative or positive. They include and are not limited to;

- Recurrent disease and illness
- Physical stress injury, diet, surgery, tobacco/ alcohol addiction, etc.

• Emotional stress – marriage, divorce, death of a loved one, strenuous work relationships, a new baby, financial insecurity, etc.

• Environmental stress – chemical pollution of air, water, food, etc.

### Who Experiences Adrenal Dysfunction?

Saliva testing exposes adrenal fatigue, which is prevalent in the US. Functional medicine clinics have established that more than 85% of patients experience some form of adrenal fatigue or dysfunction.

Adrenal fatigue hardly discriminates. It can be experienced by both women and men. It can also occur at all ages. Currently, a large number of people in their twenties are experiencing adrenal fatigue.

### The Neurotransmitter Connection

The HPA gets stimulated to produce DHEA and cortisol inside the adrenal cortex when the stress response is triggered. The adrenomedullary hormone system is the one that initiates epinephrine and norepinephrine production inside the adrenal medulla. At the outset, there is a tendency of neurotransmitter levels to increase. This is most times causes a concomitant increase in the inhibitory neurotransmitters such as GABA. Moreover, cortisol is needed during the conversion of norepinephrine to epinephrine. Consequently, a compromise in the cortisol levels brings about an imbalance of the ration between the two neurotransmitters.

Having a dynamic relationship between serotonin and cortisol and a healthy adrenal function depends on having a balanced serotonin, this is dependent on an adrenal function, which is also balanced. Serotonin facilitates the pituitary to release ACTH, which is necessary for cortisol, and DHEA to be released. Insufficient serotonin supply results in an insufficient cortisol release. Demands of cortisol by the body causes a subsequent serotonin demand in order for production of ACTH, which could cause a reduction of the levels of serotonin. Stress is considered a rate limiting factor in serotonin production as it prevents conversion of tryptophan to 5-HTP.

Patients who suffer decreased adrenal function mostly complain of weight gain, sugar or salt cravings, nervousness, anxiety, sleep disruptions, low blood pressures, fatigue and many other symptoms. Imbalances occurring in the neurotransmitter together with changes in production of cortisol may aggravate or cause such symptoms. Addressing neurotransmitter imbalances stands out as a very crucial component of successful treatment of adrenal dysfunction. Noninvasive urinary testing identifies specific neurotransmitter imbalances. It can be correlated to DHEA levels and diurnal cortisol on one report. Targeted amino acids together with other nutrient co-factors can rapidly modify neurotransmitter levels thereby promoting a long lasting and fast recovery.

# **Stages of Adrenal Dysfunction**

Phase 0

Healthy adrenal response (Cortisol levels within range with desired rhythm)

Phase 1

Acute fight or flight (Increased HPA tone)

HPA axis dysfunction (ZIG ZAG patterns )

Early adrenal fatigue (Elevated range AM)

Phase 2

Evolving adrenal fatigue (Suboptimal or low AM cortisol)

Phase 3

Established adrenal fatigue/Hypoadrenia (Hypofunctioning HPA axis)

# **Treatment Considerations for Adrenal Dysfunction**

<u>Phase 0</u>

- Multivitamin/Multimineral
- Omega 3 EFAs
- Consider vitamin D, iodine and probiotics

#### Phase 1

- Phosphorylated serine 100 mg TID or at times when elevated
- Vitamins B5 (500 mg), C (1000 mg) TID, B6 (100 mg) BID, E (800 i.u.) QD
- Melatonin (3 mg) qhs if cortisol levels elevated at night
- Lifestyle modification: deep breathing, stress management, exercise, optimal diet, etc.

#### Phase 2

- Vitamins B5 (500 mg), C (1000 mg) TID, B6 (100 mg) BID, E (800 i.u.) QD
- Adrenal glandular and herbal adaptogens in morning and at noon
- Lifestyle modification: deep breathing, stress management, exercise, optimal diet, etc.

#### Phase 3

- Vitamins B5 (500 mg), C (1000 mg) TID, B6 (100 mg) BID, E (800 i.u.) QD
- Adrenal glandular and/or herbal adaptogens in morning and at noon
- Lifestyle modification: deep breathing, stress management, exercise, optimal diet

#### Adrenal support

Successful treatment and support protocols for all individuals suffering from reduced adrenal function include;

• Lifestyle modification to include exercise, healthy sleep patterns with ideal sleeping hours of 10pm – 9am, balanced diet high in vegetables and including healthy fats and proteins, frequent laughter and deep breathing exercises.

• Avoidance of food allergies/sensitivities, caffeine, alcohol, and refined sugars

Individual treatment plans include the following and depend upon testing results (phase I, phase II, or phase III) by the saliva;

• Supplementation of dietary cofactors necessary for adrenal function including Vitamins C, B5, B6 and E

- Adaptogen therapy including licorice, rhodiola, etc.
- Adrenal glandular supplementation
- Physiologic cortisol supplementation
- Phosphorylated serine (elevated cortisol levels only)

Of great importance to note is the fact that different stages of this type of dysfunction can be present with similar symptoms. Treatment protocols may be substantially different and this depends on a diurinal pattern as well as volume of the cortisol production of every individual patient. Testing adrenal function is a crucial step in devising correct treatment plan.

Gentle to modest depression affects close to 10% of the population in the US

Depression acts as the 3<sup>rd</sup> most repeated chronic health condition throughout the US. a good number of internists, family practice providers and specialists normally see some degree of mood disorders during their practices. Virtually every clinic report on mood disorders usually identifies neurotransmitter contributors to either the symptoms or root cause of anxiety and depression.

A neurotransmitter is a chemical messenger that transmits chemicals from one neuron to another through synapses encourages exchange of information from neurons in the brain with the body's glands, organs, and muscles. There might be levels of imbalance in neurotransmitters due to many factors that may be influenced by genetics, stress, diet, medications, toxins, heavy metals, supplements and more. Symptoms of cognitive and mood concerns, stress, diminished drive, fatigue, sleep difficulties, cravings and pain issues is caused by occurrence of disability in the neurotransmitters. Conditions extending from depression and fibromyalgia to hyperactivity and autism are associated with the lack of balance of neurotransmitters. It is necessary that serotonin is used to ensure that there is a balance in the neurons, with this to be successful; there is a need to address the imbalances in catecholamine.

Neurotransmitter imbalances are extremely important and need to be sensitized in terms of the targeted treatment, cost, and compliance.

Below are the groups that are categorized for the clinical symptoms of mood disorders:

A. Emotional: Depression, motivation, loneliness, anxiety

B. Cognitive: Lack of concentration, short-term memory

## C. Physical: Insomnia, headache, fatigue, and pain

Neurotransmitters imbalances maybe associated with one of the three symptoms but others end up with all the three symptoms all together. Serotonin and Norepinephrine are used to identify the causes of the symptoms. Neurochemical shifts caused by imbalances of either or both of these neurotransmitters can lead to problems.

Imbalances in Serotonin are associated with poor impulse control, low sex drive, decreased appetite and irritability while imbalances in Norepinephrine are associated with lack of attention and a decrease in memory concentration, not socializing, and altered states of arousal.

## **Neurotransmitter Imbalances & Mood Disorders**

Dopamine, GABA, glutamate, estrogen, progesterone, cortical and testosterone imbalances also have a part in mood disorders. It is therefore necessary to address the neurotransmitters and hormones together.

Dopamine controls the pleasure/reward pathway, memory, and control of motor functions. A reduction in demand for dopamine is caused by stimulants and contributes to depleted levels over time.

GABA maintains mood because it is important in balancing the excitatory effects of nor epinephrine, epinephrine and dopamine. Demand for GABA is caused by an overload in neuro-excitatory stimuli. A decrease in GABA levels also contributes to mood disorders and is associated with anxiety, worry, and poor impulse control.

Glutamate is a major excitatory neurotransmitter in the CNS, and is involved in most aspects of brain function including cognition, memory, and learning. Due to its excitatory role, high levels of glutamate are often associated with panic attacks, anxiety, and depression.

Sex hormones play a role in mood disorders too.

Estrogen increases serotonin receptor sensitivity, increases serotonin production, and serves as a dopamine modulator.

Progesterone is a GABA agonist and has a significant effect on the body's HPA axis to manage stress and maintain a balanced mood. Fluctuations in both estrogen and progesterone, as seen in women of all ages, correlate to fluctuations in these mood-regulating neurotransmitters.

Testing both neurotransmitters and hormones provides a comprehensive and foundational view of the body's functional neuro-endocrine status, and brings to light multiple factors that

contribute to symptoms, allowing for defined, targeted treatments and improved clinical outcome.

Neurotransmitters are chemical messengers that regulate many physical and emotional processes including movement, stress response, cognition, emotions, energy, cravings, pain and more.

Functioning primarily in the central nervous system (CNS), neurotransmitters facilitate communication between the brain and the body's glands, organs and muscles. They are released from neurons and travel across a small space, called a synapse, to reach receptors on target cells. Inadequate neurotransmitter function disrupts the signal to target tissue and has a profound influence on overall health and well-being.

In fact, imbalances in certain neurotransmitters are associated with many of the prevalent symptoms and conditions seen in doctors' offices today including Mood Disorders; depression, anxiety, Adrenal Dysfunction; fatigue, insomnia, loss of mental focus; ADD, ADHD, cognitive fog, addiction and dependency, Hormonal Imbalances: E2 dominance, E2 deficiency, low androgens and loss of appetite control: obesity and insulin resistance

These symptoms are often compounded by the use of bioactive substances including caffeine, alcohol, nicotine, and prescription medications that can contribute to neurotransmitter depletion and worsening of symptoms by suppressing or artificially stimulating neurotransmitter receptor function.

When functioning properly, the neurotransmission system has natural checks and balances in the form of excitatory and inhibitory neurotransmitters. These are classified according to their effects on the receptor site on the postsynaptic neuron. Excitatory neurotransmitters cause depolarization of the membrane, causing that neuron to "fire" and send a signal. Inhibitory neurotransmitters cause hyperpolarization, preventing the neuron from forwarding a signal. Though there are many neurotransmitters found in the body, there are six in particular that play significant roles in primary symptomatic conditions.

SEROTONIN is a key neurotransmitter that is involved in the regulation of sleep, appetite, and aggression. Serotonin imbalance is a common contributor to mood problems, and pharmacologic agents that alter serotonin levels are among the most commonly used class of drugs prescribed for anxiety and depression.

High stress, insufficient nutrients, fluctuating hormones, and the use of stimulant medications or caffeine can all contribute to the depletion of serotonin over time. When serotonin is out of range, depression, anxiety, worry, obsessive thoughts and behaviors, carbohydrate cravings, PMS, difficulty with pain control, and sleep cycle disturbances can result. GABA is the major inhibitory neurotransmitter found in the CNS and, as such, is important for balancing excitatory action of other neurotransmitters. High levels of GABA may be a result of excitatory overload, or a compensatory mechanism to balance the surplus excitatory neurotransmitter activity.

These high levels result in a 'calming' action that may contribute to sluggish energy, feelings of sedation, and foggy thinking. Low GABA levels are associated with deregulation of the adrenal stress response. Without the inhibiting function of GABA, impulsive behaviors are often poorly controlled, contributing to a range of anxious and/or reactive symptoms that extend from poor impulse control to seizure disorders. Alcohol as well as benzodiazepine drugs act on GABA receptors and imitate the effects of GABA. Though these substances do not cause an increase in GABA levels, understanding their mechanism can give us additional insight into the effects of GABA.

DOPAMINE is largely responsible for regulating the pleasure/reward pathway, memory, and motor control. Its function creates both inhibitory and excitatory action depending on the dopaminergic receptor it binds to. Memory issues are common with both elevations and depressions in dopamine levels. Caffeine and other stimulants, such as medications for ADD/ADHD, often improve focus by increasing dopamine release, although continual stimulation of this release can deplete dopamine over time.

Common symptoms associated with low dopamine levels include loss of motor control, cravings, compulsions, loss of satisfaction and addictive behaviors including: drug and alcohol use, smoking cigarettes, gambling, and overeating. These actions often result from an unconscious attempt to self-medicate, looking for the satisfaction that is not occurring naturally in the body.

Elevated dopamine levels may contribute to hyperactivity or anxiety and have been observed in patients with schizophrenia. High dopamine may also be related to autism, mood swings, psychosis and attention disorders. L-DOPA is a precursor to dopamine, and is used therapeutically for low dopamine conditions such as Parkinson's disease. These medications can cause elevations in dopamine.

NOREPINEPHRINE, also called noradrenalin, is an excitatory neurotransmitter produced in the CNS, as well as a stress hormone produced in the adrenal medulla.

Norepinephrine is involved in a wide variety of actions including attention, focus, regulating heart rate, affecting blood flow, and suppressing inflammation. Involved in arousal, it prepares the body for action by relaying messages in the sympathetic nervous system as part of the autonomic nervous system's fight-or-flight response. High levels of norepinephrine are often

linked to anxiety, stress, elevated blood pressure, and hyperactivity, whereas low levels are associated with lack of energy, focus, and motivation.

EPINEPHRINE, mostly known as adrenaline, is synthesized from norepinephrine in both the CNS and the adrenal medulla. This excitatory neurotransmitter helps regulate muscle contraction, heart rate, glycogen breakdown, blood pressure and more, and is heavily involved in a stress response.

Elevated levels of epinephrine are often associated with hyperactivity, ADHD, anxiety, sleep issues, and low adrenal function. Over time, chronic stress and stimulation can deplete epinephrine stores leading to difficulty concentrating, fatigue, depression, insufficient cortical production, chronic stress, poor recovery from illness, dizziness and more.

The Norepinephrine/ Epinephrine Ratio is an indicator of the conversion of norepinephrine to epinephrine. Because cortisol stimulates the enzyme responsible for this conversion, low cortisol, in addition to depletion of cofactors including magnesium can inhibit this conversion, leading to an elevated ratio.

Glutamate refers to an excitatory neurotransmitter. In the nervous system, it is the most abundant. This neurotransmitter takes part in many aspect of the normal brain functions including learning, memory and cognition. However, high glutamate levels bring with them excitotoxicity. This process brings about damage of the nerve cells due to excessive stimulation. Depression, OCD, difficulty in concentration, anxiety, and panic attacks are all associated with elevated glutamate levels. Low glutamate levels on the other hand result to low energy levels, sleeplessness, memory loss, agitation, and depression.

# **Putting It All Together**

One noninvasive urine sample can help identify neurotransmitter imbalances. Testing comes in handy in providing a tool that helps understand every patient's specific neuroendocrine imbalances. These imbalances can be corrected using targeted nutritional therapy, diet, lifestyle interventions, and BHRT. An optimal approach is the best since it measures every of the six neurotransmitter levels that are identified together with a full panel of hormone. Of great importance is the need to understand the relationships of different neurotransmitters plus their relationship with sex hormones and adrenal function.

Changes in adrenal hormones and sex hormones can result in neurotransmitters being imbalanced. Neurotransmitter imbalances affect hormone function and production. Testing both hormones and neurotransmitters offers a comprehensive view of the functional neuroendocrine status of the body. It also brings to light extra factors, which may be contributing to these symptoms. Below are general guidelines on different diets for the main purpose of bringing down inflammation in the body. If you have any question about certain foods, feel free to check and see if it appears on this list. Avoid making substitutions except for those outlined in the instructions or those recommended by your medical or nutritional practitioner. Of course, you ought to avoid any foods that your body is allergic or intolerant even if the foods are listed here.

Whenever you can, always settle for fresh foods. Opt for organically grown vegetables and fruits to get rid of chemical residue and pesticide consumption. Always thoroughly rinse your vegetables and fruits. Look for organically raised chicken, lamb or turkey if you choose to go for animal sources of protein. Trimming visible fat is the way to go. Prepare them by stir-frying, grilling, stewing, baking or broiling. Another excellent source of omega-3 essential fatty acids and protein is cold-water fish for example halibut, mackerel and salmon. For those who do not tolerate fish, you should talk to your doctor about possible substitutions. The practitioner may suggest alternative supplemental fish oil. Avoid shellfish because it can cause some allergic reactions.

One of the most important considerations of your diet is that ALL food should be organic. Toxins and additives can also be a major factor in contributing to neurotransmitter and hormone imbalance.

# Anti-Inflammatory Diet

Fruits; Water packed or frozen cannes fruits, unsweetened fruits and fruit juices (with an exception of those that are specifically prohibited)

Starch; Buckwheat, tapioca, amaranth, quinoa, millet, brown rice and non gluten grains

Cereal/Bread; Any made from buckwheat, rice, quinoa, amaranth, arrowroot, tapioca, soy, millet, millet and buckwheat

(Side note: The optimal diet should limit all grains and reduce fruits since these breakdown to sugar.)

Meat; All fresh fish such as lamb, turkey, chicken, wild game, trout, sole, cod, salmon and halibut, eggs

Legumes; Lentils, peas and dried beans

Seeds and nuts; Nut butter, pumpkin, sunflower, tahini, sesame, walnuts, cashewnuts, almonds all made from these seeds

Vegetables; Sautéed, steamed, raw, baked and juiced vegetables (except those, which specifically prohibited)

Fats; Sesame, sunflower, safflower, expeller/cold canola, flax seed oil, olive oil, dressings, almond, pumpkin made from all these oils, butter

Spices; Turmeric, thyme, tarragon, rosemary, parsley, oregano, ginger, garlic, garlic, dill, cumin, cinnamon

Sweeteners; Stevia, molasses, brown rice syrup

### **Foods To Exclude**

Fruits; All citrus fruits, dried fruit, fruit drinks, grapes, lime, lemon, grapefruit, oranges

Starch; Rye, kaput, spelt, barley, oats, corn, wheat and every glutten containing products

Cereal/Bread; All wheat, barley, rye, kamut, spelt, oat and every gluten containing products

Meats; Canned meats, sausage, frankfurters, cold cuts, pork

Seeds and Nuts; Pistachios, pea nut butter, peanuts

Dairy Products; Non dairy creamers, frozen yogurt, ice cream, butter, yogurt, cream, cottage cheese, cheese, milk

Vegetables; Creamed in or canned casseroles, nightshade family vegetables including tomatoes, yellow or green bell peppers, red, eggplant and all potatoes (except sweet potatoes and yams)

Fats; Spreads, mayonnaise, salad dressings, hydrogenated oils, processed oils, shortening, margarine, etc.

Beverages; Tea, coffee, alcoholic beverages, soda pop all caffeinated

Spices; Paprika, cayenne pepper

Sweeteners; Brown, white or refined sugar, maple syrup, honey, corn syrup and high fructose corn syrup

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