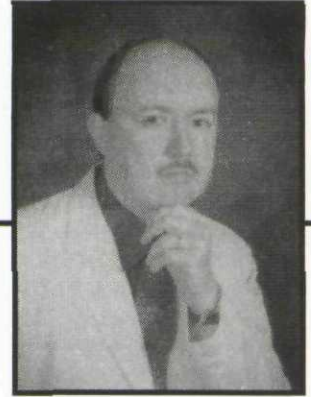




## Naturopathic Perspectives

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### The Naturopathic Approach to Adrenal Dysfunction

Throughout 'alternative' medical circles many practitioners address the condition known as "adrenal fatigue." Like many other functional medical approaches, the concept of adrenal fatigue is gaining more and more attention, with good reason as our society continues to push harder and harder at this game of life. Standard medical thinking regarding the adrenal glands is like that of other organ systems in the body; that is, they are either considered to be in satisfactory working order, or they are in failure. Rarely is the diagnosis made of hypofunction in any organ system, without the presence of notable pathologic tissue changes and function. This is especially true of the adrenal glands. True adrenal failure is also known as Addison's disease; in this condition the cortical tissue fails to produce both the mineralocorticoid and the glucocorticoid hormones. The most common cause of Addison's disease is autoimmune destruction of the adrenal cortex and tuberculosis is the second most common cause.<sup>1</sup> Currently, it is not known whether long-term adrenal fatigue contributes to autoimmune destruction of the adrenal glands. Despite this understanding, conventional medicine does not always address adrenal dysfunction in the absence of these diagnoses.

In this scheme of normal functioning versus a complete absence of function, no middle ground (and thus room for the concept of adrenal fatigue) is made possible, resulting in complete under treatment of adrenal fatigue. In mainstream conventional medicine, typically the only patient who receives treatment (using adrenal steroid hormones) for adrenal dysfunction are those with complete adrenal failure. If a patient is not in complete adrenal failure, their condition is considered 'normal' and treatment may be difficult for the patient to obtain. Only recently has conventional medicine begun to demonstrate research that shows the existence of subclinical adrenocortical disease not associated with complete adrenal failure.<sup>2</sup> The precise etiology of adrenal fatigue has not been fully uncovered at present; however progressive medical practitioners have long proclaimed that chronic severe stress can lead to clinical adrenal fatigue.<sup>3,4</sup>

It is not the direction of this article to prove the existence of adrenal fatigue. As many practitioners of complementary and alternative medicine are aware, adrenal fatigue is a condition that can be diagnosed using clinical signs and symptoms and laboratory testing, and when properly addressed, leads to a path of renewed health and vigor for our patients.

Stress is everywhere, and is increasingly categorized in any number of ways. Chronic and acute, stressors are both physical and psychogenic. Either way, the body is equipped with a highly complex system of hormones and

neurotransmitters specifically designed for dealing with stress. Regardless of its form, stress can cause the body to react in certain, predictable patterns. Hans Selye first mentioned this response, known as the generalized adaptation syndrome, in the 1930s. In the 70-plus years since its conceptual genesis, scientists and physicians continue to learn ways to effectively modulate this response in humans. Conventional and naturopathically-oriented health care practitioners both subscribe to the same biomedical model of stress and its effects on physiology. However, this is where the similarities between the two approaches stop, as major differences in diagnostic and treatment methodologies are employed to discern subclinical adrenal dysfunction.

#### Adrenal Response to Stress

Why do we respond to stress? Stress is the physical result of *perceived* threats. Stress is in one sense, our body's reaction to a threat. An excellent example of the mind-body link, numerous changes in physiology occur due to our perceptions of the general safety or danger of our environment, all of which occurs before any true harm is inflicted upon the body. Although stressors have evolved over time, our physical response to them has not. Many discussions regarding this concept have taken place; early humans enjoyed relative proportions of feast or famine, so to speak. It is arguable that today's humans, with all the luxuries of our modern age, enjoy fewer of our ancestors' acute stressors but definitely endure many more stressors and these may be experienced over a longer period of time.

Central to the stress response are the adrenal glands. In addition to the mineralocorticoids (hormones that assist in maintaining electrolyte balance), the primary 'stress' hormones that the glands produce are epinephrine, norepinephrine, and cortisol. These hormones assist in helping us to adapt to and survive stressors. In addition to the aforementioned hormones (keeping in mind that cortisol, epinephrine and norepinephrine have numerous other physiologic uses), the adrenal gland also produces hydrocortisone, testosterone, estrogen, dehydroepiandrosterone (DHEA), pregnenolone, aldosterone, androstenedione and progesterone, as well as several other intermediary hormones. In the event of an acute stressor, the body's immediate reaction is typically one of alarm, during which the sympathetic nervous system prepares the body for the well-known "fight or flight" state. When in this mode, adrenal stress hormones lead to increased heart rate and blood pressure while blood is diverted from less crucial areas such as the gastrointestinal tract to the heart, brain and



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► skeletal muscles in preparation for survival mode. These physiologic events are central to the development of adrenal fatigue.

Typically, the majority of individuals have little problem adjusting to life stressors when they appear, and once these stressors dissipate, these people display 'healthy' psychophysiologic function in that the hormone levels achieved to deal with the stressor return to baseline levels. However, when one is unable to continually adapt after prolonged periods of stress, adrenal dysfunction becomes clinically apparent.<sup>5</sup> Most often, these people are unable to maintain previous levels of energy in all realms of life and progressively deteriorate as times goes on. In fact, depression and substantial decreases in performance are considered hallmark symptoms of maladaptation to stress.<sup>6</sup>

During the early course of adaptation to long-term stressors, the primary hormones released from the adrenal glands are the glucocorticoids. Glucocorticoids can drastically change biologic functions, and mainly do so in the direction of preparing the body for both short and long term survival. The glucocorticoids will mobilize stored proteins (i.e. muscle tissue) and fatty acids, while increasing the liver's ability to synthesize glucose, all in order to supply the body with ample sources of fuel. A primary end effect of these processes is to raise blood sugar.<sup>7</sup> As the exposure to the stressor continues, and the adrenal glands continue to churn out glucocorticoids and other stress-related hormones, the delicate feedback-induced balance on the hypothalamic-pituitary-adrenal (HPA) axis becomes skewed. Cortisol typically exhibits a diurnal rhythm during which it steadily rises from its lowest point in the late evening to its highest level in the early morning hours between 6 and 8 a.m. As the day progresses, cortisol levels should slowly decline to their low point again by midnight.

As the sympathetic nervous system continues to be stimulated by stressors, the pituitary gland now begins secreting adrenocorticotrophic hormone, (ACTH) which drives the adrenal gland to continue its output of cortisol and dehydroepiandrosterone (DHEA). As the body attempts to compensate for the hyperfunctioning of the adrenal glands, the pituitary gland now begins to downregulate its sensitivity to cortisol. Normally, as hormone levels rise, they act on other organs to decrease their own production – much like a thermostat regulating heat in a home. The pituitary gland does this in an attempt to turn down its production of ACTH, the hormone that drives adrenal production. However, if the stress exposure continues, the adrenals continue to manufacture cortisol. Blood glucose levels continue to be elevated, and cells become insensitive to insulin due to overproduction in response to high blood glucose. Long-term elevations in cortisol lead to two main divergent changes in the body. As mentioned previously, muscle protein continues to be broken down in order to provide fuel for the body, leading to decreased muscle mass. At the same time, the body attempts to store fuel sources (as adipose tissue), primarily around the abdomen. Adrenal hyperfunction is marked by insulin resistance, mild obesity, hypertension, and elevated triglycerides and lipids.

In the final stages of the stress response, the adrenal glands begin to fatigue and cortisol output declines. The body's ability to synthesize cortisol and other glucocorticoid hormones is severely compensated, resulting in several physical changes. People experiencing adrenal fatigue are excessively fatigued, may become depressed and unable to concentrate, and experience painful headaches, low blood pressure, sensitivity to carbohydrates and inability to tolerate alcohol.<sup>8</sup> Furthermore, when cortisol production declines, the body can become overburdened with inflammatory processes as well; cortisol is an anti-inflammatory molecule and its absence allows for increases in inflammatory eicosanoids and cytokines, leading to eventual tissue damage and degeneration.<sup>9</sup>

Once a diagnosis of adrenal fatigue has been firmly established (there are several methods for achieving this, each of them with their own merits and disadvantages), treatment may be pursued. Note: similar to thyroid dysfunction, one may obtain "normal" hormone levels despite overt signs and symptoms that say otherwise. Oftentimes the diagnosis of adrenal fatigue is made based on resting cortisol levels obtained throughout the day. These levels do not necessarily discern the adrenal glands' ability to increase production to counter the effects of stress. A more accurate measure of adrenal capacity can be obtained using ACTH. When ACTH is administered in a trial dose, output of cortisol should at least double; if this does not occur then true adrenal fatigue is likely. However, adrenal fatigue can be strongly suspected if a person reports high amounts of stress with many adrenal fatigue symptoms and normal or low cortisol levels are measured. Alternatively, a person with symptoms of adrenal dysfunction may have high levels of cortisol; in this case these persons should receive adrenal supportive treatment from the standpoint that eventually they will reach a place of adrenal fatigue. Each of these clinical scenarios is reflective of different stages in adrenal dysfunction; the reader should also keep in mind that these are oversimplified for the purposes of this article.

Oftentimes practitioners are faced with several projects when treating patients with adrenal dysfunction. In addition to the symptomology of adrenal fatigue, practitioners will often find themselves treating the additional damage caused by overuse of stimulatory products; these are often recruited by the patient in response to the incredible fatigue associated with this condition. Left unrecognized and untreated, people with adrenal fatigue do what most do when faced with insurmountable fatigue: they continually increase the amount of cheap energy sources such as coffee and caffeinated beverages and simple carbohydrates due to their sugar content. Sugary and high glycemic foods only confound the blood sugar problems associated with this condition, while caffeine only serves to increase the rate at which energy is consumed, thereby leading to even greater demand on the adrenal glands.

From a naturopathic perspective, treatment of adrenal fatigue rests on using therapeutic nutrition, botanical medicines, and lifestyle adjustments. All of these treatments are designed to support adrenal gland function; depending on where a patient is along the spectrum of adrenal dysfunction, differentiation in the general treatment protocol is made. In extreme cases of adrenal fatigue, small amounts of bioidentical hormones may be used to support the adrenal glands in their initial recovery process.



## Treatment

**Lifestyle changes:** This approach is the most basic yet of course, the most difficult to achieve. The stressors that a person faces today are many and are generally of a long-term duration. Long gone are the brief, alarm phase reactions to acute stressors. Modern people, instead of fighting for survival against predators, exposure, and starvation, are faced with stressors that seem to be ever present (bills, career, the IRS, etc.). More easily stated than achieved, the underlying theme is the same: in order to reduce the toll on the adrenal glands, one must reduce or place into perspective their own individual life stressors. Although one may not have absolute control over the origin of some stressors, there are other choices that can be made. These include obtaining enough sleep, making healthy dietary choices, and engaging in stress-reducing activities such as gentle exercise. Another powerful means of reducing stress involves learning to change our perceptions of the stress, an exciting topic for another day. All of these "medicines" serve to reduce the overall stress burden thereby preserving adrenal function.

## Clinical Nutrition

Widely recommended as part of adrenal supportive therapies, use of vitamins may be key to assisting adrenal function.

### *Vitamin B-5 (Pantothenic acid)*

Vitamin B-5 is nearly ubiquitous in nature, found in many foods and every cell in the body. This vitamin carries out its many vital functions in the body as part of the enzyme complex coenzyme A (CoA). CoA is involved in adrenal cortex function as it serves in increasing production of glucocorticoids and other adrenal hormones.<sup>10</sup> Because of this association with production of adrenal hormones, B-5 is commonly referred to as an antistress vitamin and is mentioned as a treatment in nearly all conditions in which proper adrenal gland function has a demonstrated role (stress, allergies, asthma, arthritis, psoriasis, and infectious processes). In addition, research utilizing B-5 in laboratory animals has been shown to enhance adrenal cortical function.<sup>11</sup> In human subjects, B-5 was shown to attenuate the elevation in urinary cortisol metabolites that were expected to be produced as a by-product of adrenal stimulation using ACTH;<sup>12</sup> this experiment suggests that B-5 may also lower secretion of cortisol during times of stress. Thus, the utility of B-5 in adrenal fatigue is due to its supportive nature in producing adrenal corticosteroids. Additionally, as part of the enzyme CoA, B-5 is necessary for proper metabolism of carbohydrates and fats (leading to energy production) and the synthesis of the neurotransmitter acetylcholine. B-5 is found in many non-processed foods such as brewer's yeast, egg yolks, cheese, peanuts, fish, chicken and numerous vegetables, to name a few. B-5 is even made in the intestines by the bacterial flora. Despite the widespread availability of this vitamin, supplementation with B-5 is recommended for adrenal support.

### *Vitamin C (Ascorbic Acid)*

Vitamin C is a vitamin with multiple functions and uses in the body. In fact, reading about the benefits of vitamin C in the research leads one to believe that this vitamin is useful in nearly all aspects of health! Indeed, vitamin C benefits adrenal function as well. Because of the vitamin's water-

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soluble status, it doesn't stay in the body long before being used or lost through elimination. However, there are areas of the body where vitamin C concentrates; these are typically areas that are very metabolically active. The adrenal glands are one area, typically storing close to 30 milligrams on average. Vitamin C is quickly utilized in the body and replacement is necessary – especially when one is exposed to high amounts of activity or oxidative processes. Long-term stress is also thought to compromise the amount of stored vitamin C in the adrenal glands.

In one study, researchers looked at the ability of vitamin C to improve adrenal function in a surgical setting. In this study, patients with lung cancer were able to better adapt to the stress of surgery when supplemented by vitamin C as manifested by normalized levels of cortisol and ACTH.<sup>13</sup> In another study, when vitamin C was given at a modest dose of 1 gram three times a day, researchers noted a blunting of the effect of exogenously administered ACTH in raising cortisol levels.<sup>14</sup> Additionally, vitamin C is needed for the synthesis of two important "stress" hormones, norepinephrine and epinephrine, both of which are produced in states of high stress. Because of its supportive function in the production of adrenal hormones and the fact that large amounts are stored and utilized by the adrenal glands, supplementation with vitamin C in the treatment of adrenal dysfunction is recommended.

### *Phosphatidylserine (PS)*

Phosphatidylserine is phospholipid with fat-soluble properties. PS is found throughout the human brain and is vital to neuron membrane function.<sup>15</sup> PS is also found in the mitochondrial membrane, where it is thought to serve as a storage supply for other phospholipids.<sup>16</sup> PS is synthesized in the body, however at a high metabolic cost. PS can also be obtained from dietary sources, and is found in most foods, albeit in small amounts. PS can increase levels of the neurotransmitters acetylcholine, norepinephrine, serotonin, and dopamine as well.<sup>17</sup> PS is considered to enhance neuron function and acts as a compensatory adaptive mechanism to cell deterioration. PS may be helpful in optimizing the stress response and at the same time providing substrate for tissue repair as a result of the catabolic actions of stress hormones.

PS is also thought to blunt the activation of the HPA axis in response to stress; PS may be able to prevent the production of high amounts of ACTH and cortisol in response to physical stress.<sup>18</sup> In one study, PS was given to a small group of healthy men prior to the start of exercise; these men displayed a leveling of ACTH and cortisol in comparison exercising without being pretreated with PS.<sup>19</sup> Another experiment involved treating subjects who were exposed to 2 weeks of an intense weight training program with PS. Treatment led to decreased levels of cortisol after the exercise session, and interestingly, subjects reported a lower incidence of muscle soreness and depression, both hallmarks of overtraining.<sup>20</sup> The effectiveness of PS in attenuating stress-related hormone elevations appears to be dose dependent, however.<sup>21</sup>



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## Botanical Medicines

Mentioned earlier, often the first (and incorrect) approach to treating fatigue that results from adrenal dysfunction is to use ergogenic aids such as coffee or other stimulants. While the herbs *Coffea arabica* and *ephedra* do have useful purposes as stimulants, these substances should not be employed in cases of adrenal dysfunction. A more appropriate class of herbs (and the most misunderstood, perhaps) are the adaptogens. In general, adaptogens are medical herbs that allow an organism to attain a state of nonspecific, increased resistance in order for the organism to combat stressors and adapt to challenges, whether they are chemical, physical or biological. This grouping of herbs play an important role in the practice of holistically minded physicians in that they are useful for enhancing an individual's resistive powers to the chronic effects of high amounts of stress. Much of the original research into plant adaptogens involved looking at their effects in athletes; beneficial results were found and with the recent resurgence of natural medicines, adaptogenic herbs are becoming popular among many patient populations that have a large stress component as a common circumstance. While much research is underway that is designed to elucidate the exact mechanism of these herbs, some evidence points to modulation of hormone and neurotransmitter production and degradation as a major effect. It is important to note that adaptogens are not stimulatory in nature; this is a relatively common misperception and is key to their use in adrenal dysfunction. Adaptogens can be used in all patients along the spectrum of adrenal dysfunction to support their adaptive capabilities. It is important to note however, that in extremely fatigued and debilitated patients, some adaptogenic botanicals may be physically perceived as stimulatory in their effect. For this reason, moderate caution and low doses should be used in the completely fatigued patient. The adaptogenic approach to adrenal fatigue is perhaps one of the most remarkable concepts in naturopathic medicine; to approach the patient from this perspective (bolstering their adaptive capabilities through modulation of hormone and neurotransmitter physiology) is a true approach to assisting the body in healing itself, rather than approaching symptoms directly. In fact, treatment of symptoms only in adrenal dysfunction is highly unlikely to produce any lasting benefit for the patient.

Many botanicals are considered to have adaptogenic effects; some more than others. Some of the most researched adaptogenic herbs are licorice (*Glycyrrhiza glabra* and Korean Ginseng (*Panax ginseng*). One of the main mechanisms of action of both herbs is the ability to decrease the amount of endogenously produced hydrocortisone that is degraded by the liver. In this way, hydrocortisone and cortisol are preserved, thereby reducing the demand on the adrenals to produce more. The constituents in licorice have the ability to inhibit the enzyme 11-beta-hydroxysteroid dehydrogenase, which converts active cortisol to inactive cortisone.<sup>22</sup> *Panax ginseng* complements this effect by increasing serum cortisol concentrations<sup>23</sup> and by stimulating adrenal function.<sup>24</sup> As mentioned previously, there are many botanicals with adaptogenic capabilities; a brief listing includes:<sup>25</sup>

American ginseng (*Panax quinquefolium*)  
Ashwaganda (*Withania somnifera*)  
Astragalus (*Astragalus membranaceus*) root  
Borage (*Borago officinalis*)  
Bupleurum (*Bupleurum chinense*)  
Cola nut (*Cola nitida*)  
Devil's club (*Oplopanax horridum*)  
Echinacea (*Echinacea spp.*)  
Ginseng (*Panax spp.*)  
Licorice (*Glycyrrhiza glabra*)  
Oats (*Avena sativa*)  
Prickly ash (*Xanthoxylum clava-herculis*) bark  
Rhodiola (*Rhodiola rosea*)  
Siberian ginseng (*Eleutherococcus senticosus*)  
Scullycap (*Scutellaria lateriflora*)  
Suma (*Pfafia paniculata*)  
Turmeric (*Curcuma longa*)

## Conclusion

The concept of adrenal fatigue is gaining more and more attention as naturopathically minded clinicians and laboratories have discerned useful diagnostic and treatment methods for this condition. Much work remains to be done regarding this approach, however the treatment of adrenal fatigue leads to considerable health improvements in those affected. This approach is further proof that physical structure cannot be separated from physical function; both are interrelated and must be approached in this manner for true clinical improvement to take place. The treatment of adrenal fatigue is of course not limited to the treatments described herein; many other approaches are available and should be explored.

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