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### Clinical perspective on stress, cortisol and adrenal fatigue

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#### ABSTRACT

After 30+ years of clinical practice, it is this author's experience that adrenal fatigue is a common stressrelated disorder in which the symptoms are strongly influenced by circulating cortisol levels. Although adrenal fatigue has appeared in the medical literature by various names for over 100 years, its prevalence is just now coming to the forefront. Healthcare professionals can make a dramatic difference by monitoring patients' health to check for signs and symptoms of adrenal fatigue. Despite the frequency with which this health condition occurs, even many skilled clinicians have not had the opportunity to learn about it or its importance to their practice. The intent of this article is to provide the practitioner with clinically relevant information about the diagnosis and successful treatment for adrenal fatigue. © 2014 Elsevier Ltd. All rights reserved.

#### What is already known about this topic?

• Adrenal fatigue has appeared in the medical literature by various names for over 100 years.

#### What this paper adds?

• A new clinical perspective that offers a protocol for diagnosing and successfully treating adrenal fatigue.

#### 1. Introduction

Cortisol plays a crucial role in maintaining health. But in order to do so, circulating levels must be maintained in a fairly narrow range. If levels drop much below optimal, signs and symptoms of adrenal fatigue occur [1]; if they drop precipitously low, as in Addison's disease, it can be life-threatening [2]. If levels climb and remain above optimal for a period of time, signs and symptoms of metabolic syndrome appear [3]; pathologically high, and Cushing syndrome manifests [4].

Regulated by the hypothalamic-pituitary-adrenal (HPA) axis and cortisol carriers in the blood possessing different affinities for cortisol binding, the level of circulating cortisol in a healthy body

http://dx.doi.org/10.1016/j.aimed.2014.05.002 2212-9626/© 2014 Elsevier Ltd. All rights reserved. remains between 15 and 24 mcg/dL, with the adrenals producing 20–25 mg of cortisol over a 24 h period [5]. These optimal circulating levels vary in a diurnal pattern, with low being at approximately 4:30 am and high being 30–45 min after rising. There is also a midafternoon low sometime between 2:00 and 5:00 pm [6], with a duration of 15 min to 2 h.

The feedback loop that controls circulating cortisol must walk a tightrope walk, balancing at varying levels during the 24-h diurnal cycle in order to adequately supply cells, tissues and organs and keep the body functioning optimally. In addition, cortisol - sometimes called the "stress hormone" [7] – must respond appropriately to all stresses impinging upon the host. These stresses can be physical, biochemical, hormonal, physiological, mental, emotional, real or imagined. The combined stresses are sensed by the hypothalamus, which compares the amount of circulating cortisol to anticipated need throughout the entire body and, under normal circumstances, causes adequate, but only adequate, amounts of cortisol to be released from the adrenal cortex. This balancing act is carried out via a negative feedback loop of messenger hormones: corticotropin releasing hormone (CRH) from the hypothalamus  $\rightarrow$  adrenocorticotropic hormone (ATCH - aka corticotropin) from the anterior pituitary  $\rightarrow$  stimulates receptors in the adrenal cortex to prompt cortisol's manufacture and immediate release into circulation  $\rightarrow$  sensed by cortisol receptors in the hypothalamus, thus completing the loop [8]. This occurs every 3-6 s to maintain the proper amount of cortisol in circulation for preserving homeostasis according to the body's total stress and physiological needs.

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This system works with wonderful efficiency as long as the stresses are not too lasting, numerous or severe. But in current modern industrial society, this is often not the case. Stresses are often prolonged, abundant, multiple and intense. In addition, the nutrients used in greatly increased quantities during such high stress states are not replenished by the normal modern diet. Even in 'healthy' foods, nutrient quality has been diminished by the use of chemical fertilizers, which deplete the ground of the minerals and trace minerals necessary for plants to make and store the vitamin and phytonutrient rich food existed previously [9]. Thus, people today experiencing constant and multiple stressors have fewer nutrients to replenish challenged adrenals.

Chronically stressed people are caught in an untenable position. If the adrenals are strong enough to withstand this day after day and cortisol levels remain adequately elevated to handle the multiple stresses, over time the signs and symptoms of metabolic syndrome begin to appear – often taking decades to fully manifest but which can lead to adult onset diabetes [10], heart disease [11] and cancer [12]. If the adrenals are not able to keep up with the demands, adrenal fatigue appears - usually developing more quickly than metabolic syndrome, and which can become so severe as to disable them. As a physician, I have seen many people so depleted by adrenal fatigue they were unable to work or do anything beyond menial house chores, including several whose adrenal fatigue was so severe that they were unable to even dress themselves. In the face of light or moderate intermittent stress, the HPA axis walks the cortisol tightrope walk to maintain balance (homeostasis) while helping the body adapt to the stresses being experienced. With chronic and/or severe stress, this balance can be upset, resulting in either adrenal fatigue or metabolic syndrome.

#### 2. Adrenal fatigue

In adrenal fatigue cortisol levels are no longer able to rise adequately to meet the demand and people begin noticing signs and symptoms that give them a clue something is not right. In a nutshell, adrenal fatigue is the persistent suboptimal functioning of the adrenal glands, especially under stress. A more formal and elegant definition was put forth by Charles Sajous, an eminent physician early in the last century who, in 1930, wrote:

"Functional hypoadrenia [the term used for adrenal fatigue at that time] is the symptom-complex of deficient activity of the adrenals due to inadequate development, exhaustion by fatigue, senile degeneration or any other factor which, without provoking organic lesions in the organs or their nerve-paths is capable of reducing their secretory activity." [13]

Adrenal fatigue is not Addison's disease, which is the virtual failure of the adrenals primarily caused by either an infectious or autoimmune process that damages and often destroys the glands [referred to above by Sajous as "organic lesions"]. Stress rather than pathological damage is the primary cause of adrenal fatigue [14,13]. When the amount of stress continually exceeds the capacity of the adrenals to secrete sufficient hormones to make the physiological, and biochemical compensations necessary for that level of stress, adrenal fatigue occurs. In adrenal fatigue, the adrenals function but not optimally.

#### 3. Frequency of adrenal fatigue

In a 1974 publication, John Tintera, MD, a specialist in low adrenal function, said that conservatively about 16% of the population has some moderate to severe degree of hypocortisolism [a term used at that time for adrenal fatigue] but in actuality, the figure should be 67%, if all the related groups were included [15].

Although there has been no rigorous study of the frequency of low adrenal function, from the author's four decades of clinical experience, Dr. Tintera's higher estimate seems relatively accurate, especially in these stressful times. Most relevant for the physician is the knowledge that this health condition is common enough to be seen regularly by every practitioner. In contrast, the incidence of Addison's disease is approximately 4–11 cases per 100,000 (.00004–.0001% of the population) [16].

#### 4. Unique fatigue pattern of adrenal fatigue

There are many signs and symptoms of adrenal fatigue, yet there is no single pathognomonic indicator, except possibly its unique pattern of fatigue. Although fatigue is a common complaint heard by physicians – 85% of patients complain of fatigue as one of their major symptoms – there seems to be no other fatigue pattern like it.

- Early morning fatigue even with sufficient sleep [17] need caffeine or other stimulants to get going [18] and some do not actually feel fully awake until after noon meal.
- Midmorning low often compensated for by more caffeine plus sugar with fat, e.g. coffee and doughnuts to temporarily compensate for the hypoglycemia due to low cortisol.
- Afternoon low between 2:00 and 5:00 pm [19,20] lasts from 15 min to 2 h and ranges from simply wanting to take it easy for a few minutes to having to lie down.
- Substantially improved energy after 6:00 pm usually feel better than have all day.
- 'Second wind' of renewed energy around 11:00 pm (if still awake) lasts until 1:00–2:00 am.
- Much more refreshed in morning if able to sleep in about 2 h beyond usual rising time [1].

#### 5. Other common signs and symptoms of adrenal fatigue

The distinctive pattern of fatigue when combined with the symptoms below forms a syndrome that healthcare professionals can readily learn to recognise.

- Needs caffeine or other stimulants to get going and often to keep going during the day.
- Decreased stamina and energy feels run down and exhausted much of the day [21].
- Decreased productivity [22].
- Decreased resilience takes longer to recover from illness and rebound from stress [14].
- Craves salt or salty foods [22].
- Hypoglycemia and its symptoms, especially under stress (Cortisol plays intimate role in maintaining adequate blood sugar.) [22].
- Does not feel rested or refreshed even with 8 h sleep.
- Decreased libido.
- Increased frequency and/or severity of respiratory illnesses [23].
- Increased difficulty focusing, concentrating, remembering (fuzzy-headed) [22].
- Increased irritability and/or intolerance [14,22].
- Increased perimenopause or PMS symptoms [22].
- Feels overwhelmed [22].
- Mild depression [22].

#### 6. Causes of adrenal fatigue

There are many causes of adrenal fatigue but by far the most common is any type of stress that is chronic, prolonged or severe [24]. In modern life, there are often multiple stresses occurring in

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