Dr. Miles Nichols will be teaching a class at The Wellspring School about a functional medicine approach to working with adrenal hormone issues on June 4th. The course will cover some of the most recent research on adrenal hormones, debunk common myths about adrenals that are still prevalent in the integrative medicine community, and we will review lab testing and treatments for adrenal hormone dysregulation.

About the author and teacher of Stress, Fatigue & Adrenal Hormones: A Functional Medicine & Mindful Approach:

Dr. Miles Nichols is a doctor of acupuncture and oriental medicine, and expert in functional medicine and mindfulness as it applies to medicine. He specializes in addressing both the body and mind root causes of chronic illness and establishing preventive practices to help people achieve robust health, happiness regardless of circumstances, and an inspired sense of purpose. Dr. Miles is an author, national speaker, and he trains clinicians about how to integrate a functional medicine and mindfulness-based approach into clinical practice.

Growing up, Dr. Miles’ father was a medical doctor and state senator who worked tirelessly to serve underprivileged populations. When Miles was 15, his father passed on suddenly and unexpectedly from a heart attack. This propelled Miles to passionately dive into learning anything and everything about how to reverse and prevent chronic illness through advanced diagnostic lab testing followed by recommendations around nutrition, lifestyle, supplements, herbs, and mindfulness practices.

The Big Picture of the Adrenal Glands and the HPA Axis

The adrenal glands have gotten a lot of popularity in the functional medicine and holistic health arenas over the past many years. In fact, many lay people are familiar with the term
adrenal fatigue (which is a term that we are no longer using and will discuss later), despite it not being a classical medical diagnosis. We can only speculate about why this is, but perhaps it is related to the amount of chronic stress and fatigue that people struggle with today, especially in America.

*The American Psychological Association released a paper in 2015 analyzing stress. Through surveying they found the following:*

- 72% of Americans feel stressed about money at least some of the time
- 22% of Americans rate their financial stress as a 8+ on a 10 point scale
- 20% of Americans skip or consider skipping doctor visits due to money
- 29% say they have a sense of loneliness & isolation due to stress
- 41% say they have no emotional support and this is contributing to stress
- 20% say they never engage in activities to help manage stress
- 42% report lying awake at night at least once a month due to stress
- 33% report overeating due to stress
- 41% report yelling at their loved ones due to stress
- Women seem to report more insomnia, more isolation, more overeating, but also more motivation to make lifestyle changes than men
- Social isolation & loneliness show increases in all cause-mortality
- Psychological stress seen with increase in all-cause mortality
- Most of the studies on stress and symptoms analyze PERCEIVED STRESS

This last bullet point is significant. Notice that studies are mainly looking at perceived stress, not actual stress hormone levels. It is not to say that stress hormone levels do not have an impact, but that our perception of stress plays a VERY big role in the affect that stress actually has on our health and well-being. We will look at this concept through research-based studies as well as what we have seen clinically in the June 4th Adrenals Class at the Wellspring School.

Research strongly supports that our beliefs, thoughts and emotions regarding stress have an important role in health. Because of this, it is essential that we take both a mind and a body approach to working with stress and the adrenal glands / HPA axis. Even if we can balance hormone levels, if a person still perceives that they are under an unpleasant sort of stress,
they can still have many real symptoms and health problems. This is not to say that we should ignore stress hormone levels, as they too have many physiological detrimental effects that must not be ignored. Basically, it is essential that we work with the mind and the perception of stress in addition to balancing hormone levels if we are truly going to help someone live a healthy life that is not influenced by the negative effects of stress and one’s relationship to it.

**Re-Evaluating the Concept of “Pregnenolone Steal” as an Explanation for Adrenal Hormone Dysregulation**

One of the myths that we will debunk in the class on June 4th is the notion of “Pregnenolone Steal” as an explanation for how adrenal hormones become out of balance. This does not hold up to a deeper understanding of physiology. This is important because a new understanding changes treatment ideas (pregnenolone supplementation is commonly used and justified by this theory).

One prominent explanation for HPA axis dysregulation is commonly attributed to a process called *pregnenolone steal*. The theory proposes that during periods of prolonged stress, the body shunts pregnenolone away from DHEA and towards the cortisol pathway. This is said to result in a decrease in sex hormones. This mechanism offers a very simple and nice explanation for how our body prioritizes survival over reproduction.

Indeed, we very commonly see in clinic on lab work that cortisol levels can be elevated or normal and DHEA levels functionally low. *Pregnenolone steal* theorizes that with high levels of cortisol and low levels of the other reproductive hormones, that the body has been able to keep up with the chronic stress demands by shunting the use of pregnenolone towards cortisol and away from DHEA. The idea is that in the face of chronic stressors, the body’s supplies of pregnenolone are no longer great enough to make enough of both cortisol and DHEA. Because cortisol is necessary for survival, the body is thought to divert pregnenolone towards the DHEA pathway. *Sounds reasonable, doesn’t it?*

However, a deeper investigation into research and functional physiology has revealed several problems with the *pregnenolone steal* theory. The theory proposes that there must be some
A central “pool” of pregnenolone that can be drawn on and then converted into different hormones. Although it is true that both cortisol and DHEA are made from pregnenolone, there turns out to be a sequence of events that predetermine what pregnenolone will convert into (rather than it having an option to go in different directions).

Basically, pregnenolone is synthesized from cholesterol in the mitochondria of a cell. There are distinct regions (as we discussed earlier in the anatomy section) of the adrenal cortex referred to as “zones”. In the zona reticularis, for example, cells are specialized to make DHEA. So, if cholesterol enters a cell in that zone, it will be converted into pregnenolone in the mitochondria of the cell. Then, it will move to the endoplasmic reticulum of that cell to be converted into DHEA. Because that cell is specialized for DHEA production, the pregnenolone made in that cell is already predestined to become DHEA. The differences in hormone production in the individual zones is due to the location of the enzymes. The enzymes that are in the zona reticularis will not make cortisol for example. There is no common and shared extracellular source of pregnenolone that is used by the different cells in different zones to make different hormones, as is implied by the pregnenolone steal theory.
The mechanism is illustrated in the steroid pathway depicted above. Above cholesterol is pantothenic acid (not displayed). It could be considered the top of the steroid pathway chain. Pantothenic acid will convert into Acetyl CoA and further into cholesterol. Cholesterol then converts to pregnenolone, which becomes aldosterone, DHEA or cortisol depending on which cell it is in.

Cortisol is a derivative of progesterone (see chart above). Due to the need for cortisol during prolonged stress, and because progesterone and cortisol are both made in the same zone of the adrenal cortex, it is plausible that there may be a shunting of progesterone into cortisol, resulting in decreased progesterone.

Clinically, when chronic stress is present, we many times do see progesterone levels decrease at a greater rate than estrogen levels. This can lead to a progesterone-to-estrogen ratio that favors estrogen, known as estrogen dominance. This is also one plausible explanation behind why we can see symptoms of premenstrual syndrome and menopause associated with HPA axis dysregulation. There is a connection of the HPA axis to female hormone imbalances, but the mechanism of action is not through pregnenolone steal. It is likely through progesterone converting to cortisol at higher rates in the zona glomerulosa and therefore, hormones declining. This of course would need to be considered together with the production of progesterone in the ovaries themselves. This production tends to decrease as a woman moves towards menopause. It is during this transition that we would expect to start to see more significantly the impacts of the adrenal cell production of progesterone, since the production in the ovaries will begin decreasing at this time.

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