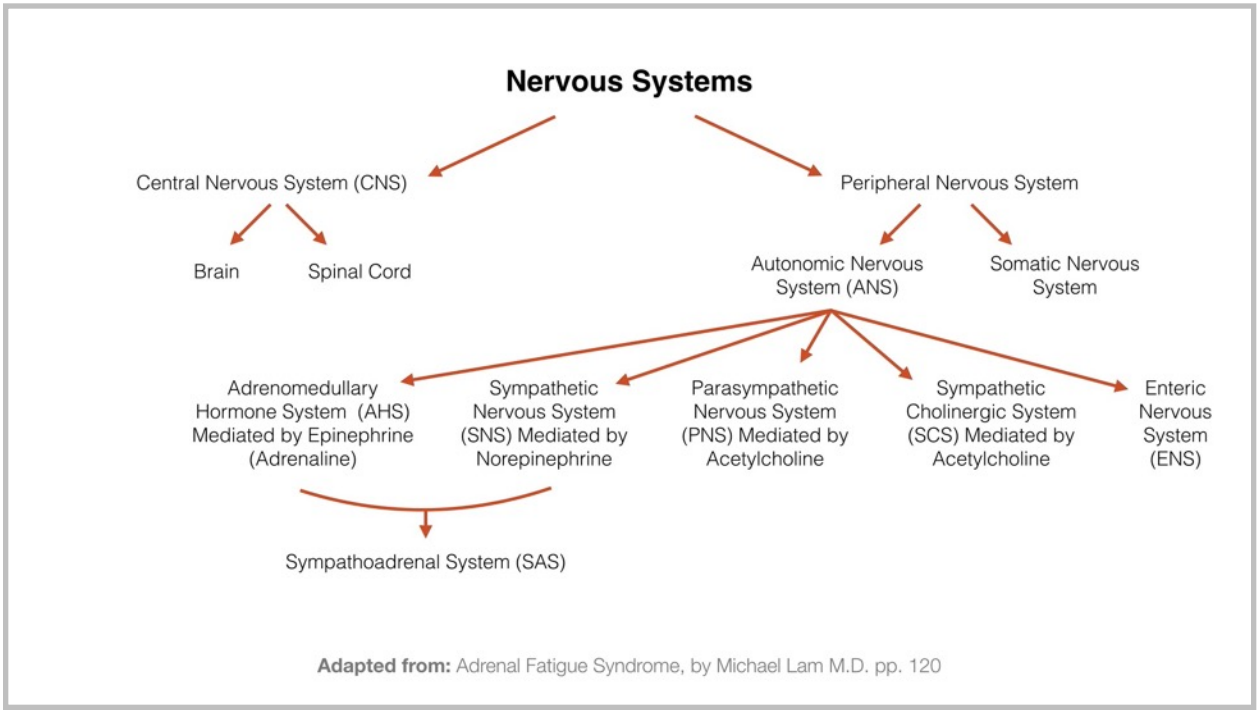
HPA-D: HPA Basic Physiology - Part 5



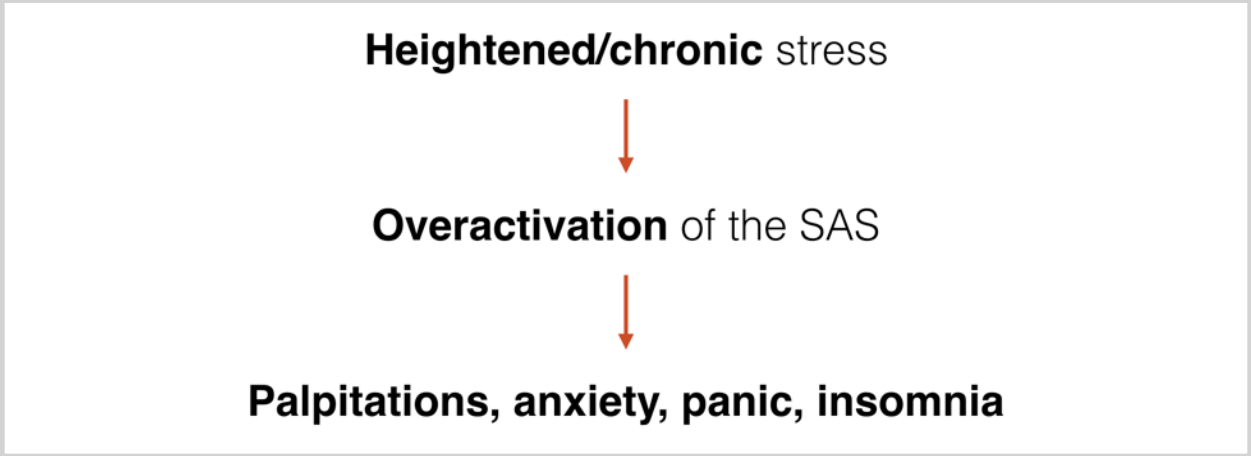
Adapted from: Adrenal Fatigue Syndrome, by Michael Lam M.D. pp. 120

Next, let's talk about the catecholamines, epinephrine and norepinephrine. Together, they comprise the sympathoadrenal medullary system, or the SAS. The SAS has two components: the adrenomedullary hormone system, which is mediated by epinephrine and adrenaline; and then the sympathetic nervous system, mediated by norepinephrine. I want to talk a little bit more about this system, which is pictured here on the slide, as it informs our understanding of how we and our patients respond to and are affected by stress.

Let's start with norepinephrine, which is also known as noradrenaline. It's synthesized and released in the central nervous system, as well as the sympathetic nervous system, which is a division of the autonomic nervous system, and a smaller amount of norepinephrine, about 7 percent, is made in the adrenal glands. Stress enters the body via our senses, it activates the locus coeruleus, the LC, which is an area of the brainstem, and then norepinephrine is released. Norepinephrine acts as a neurotransmitter and hormone, profoundly influences the way that the central nervous system handles stress. It influences the amygdala, which is the part of the brain that regulates mood and emotional responses like fear and anxiety, and it leads to alertness and arousal. Once the LC is activated, neurons carrying norepinephrine send signals to other parts of the brain, like the cerebral cortex and the hippocampus. In many ways, norepinephrine is like the conductor of the orchestra of the stress response. You can also think of it as a first responder. Norepinephrine activates the HPA axis and triggers the cascade that ultimately results in the production of cortisol and DHEA, and it does this in a very immediate fashion, as we talked about earlier.

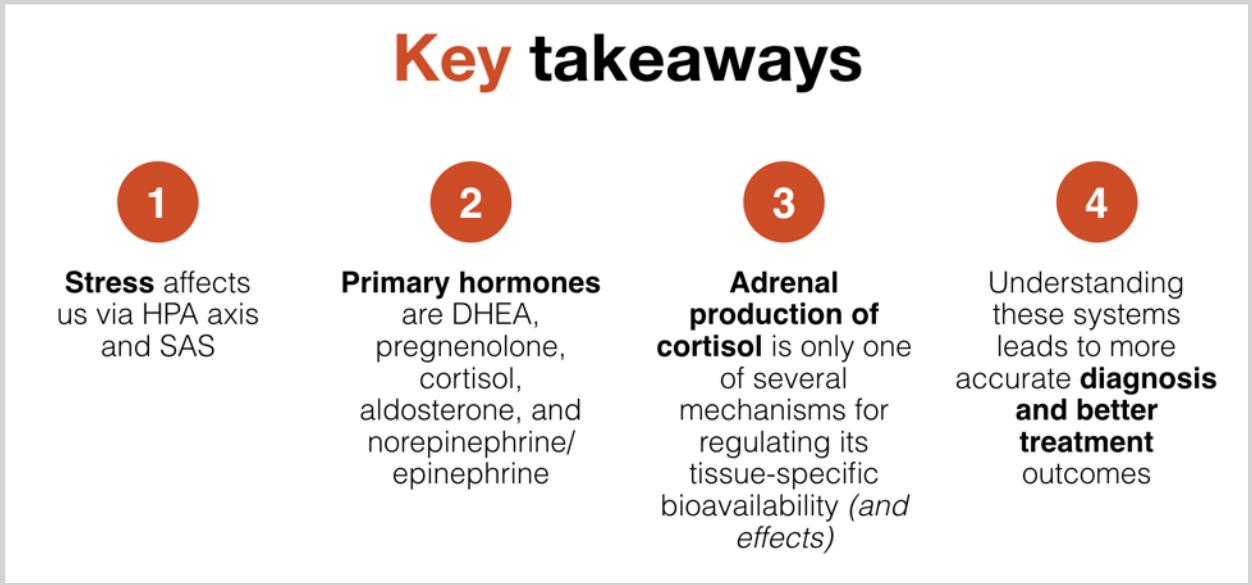
Norepinephrine stimulates arousal, so low levels of this neurotransmitter and hormone are associated with brain fog, poor memory, and depression. This is why certain antidepressants, SNRIs like duloxetine, Cymbalta, venlafaxine, or Effexor, target both serotonin and norepinephrine. On the other hand, elevations of norepinephrine lead to symptoms similar to what you'd experience on stimulants; arousal can range from pleasurable to full-on panic, including anxiety, restless sleep, increased startle reflex, palpitations, muscle tension, and teeth grinding.

Epinephrine, which is also known as adrenaline, is a hormone and the primary mediator of the adrenomedullary hormone system. Ninety percent of it is produced by the adrenal glands in the adrenal medulla, and the remaining 10 percent is produced in certain neurons in the body. It plays an important role in the fight-or-flight response; it initiates a number of actions that are designed to help us survive in life-threatening situations. It increases heart rate and the strength of heart contractions, it constricts blood vessels in veins, it's a bronchodilator and inhibits histamine release, it stimulates the breakdown of glycogen into glucose in the liver, which results in an increase in blood sugar, because we need sugar, glucose availability, to fight or flee. It triggers the inflammatory response to prepare for wound healing after injury. Because epinephrine is more potent than norepinephrine, its output is tightly controlled, and it's called an emergency hormone for this reason.



Chronic or acute stress increases the adrenomedullary hormone system and sympathetic nervous system, which raises both norepinephrine and epinephrine levels. The sympathetic nervous system is always active to some degree, helping us with routine stress of daily life, but the adrenomedullary hormone system, or AHS, is not typically active, and only becomes active with a significant stressor. In the initial stages of stress response, we might see signs of elevated norepinephrine as the SNS, sympathetic nervous system, is hyperactivated, so these are things like mild palpitations, some anxiety, feeling of discomfort. When stress becomes heightened or chronic, the overactivation of the SAS leads to larger than normal levels of both norepinephrine and epinephrine, and this causes more serious symptoms like severe palpitations, anxiety, panic, waking up in the middle of the night with heart pounding, so that's a big red flag for an overactive sympathoadrenal medullary system. That patient that wakes up at two in the morning with their

heart pounding, wide awake, you should definitely be thinking about stress-related pathology in those cases.



So here are the key takeaways from the basic physiology that we've covered so far. This unit is called the HPA axis, and we refer to stress-induced pathology as HPA axis dysfunction, but the reality is that stress affects us via two primary mechanisms: the HPA axis and the sympathoadrenal medullary system, or SAS, not just the HPA axis. The primary hormones involved in the stress response include the pro-hormones DHEA and pregnenolone, the glucocorticoids cortisol and aldosterone, and the catecholamines norepinephrine and epinephrine. Understanding these systems and hormones and their effect on physiology will help you to recognize the signs and symptoms of stress-induced dysfunction and more effectively explain to your patients how stress is contributing to their problems. For example, if a patient is waking up like a shot in the middle of the night with a pounding heart like we just talked about, you can explain that their stress is so significant that their emergency response system is being recruited, and that can help them to take it more seriously.