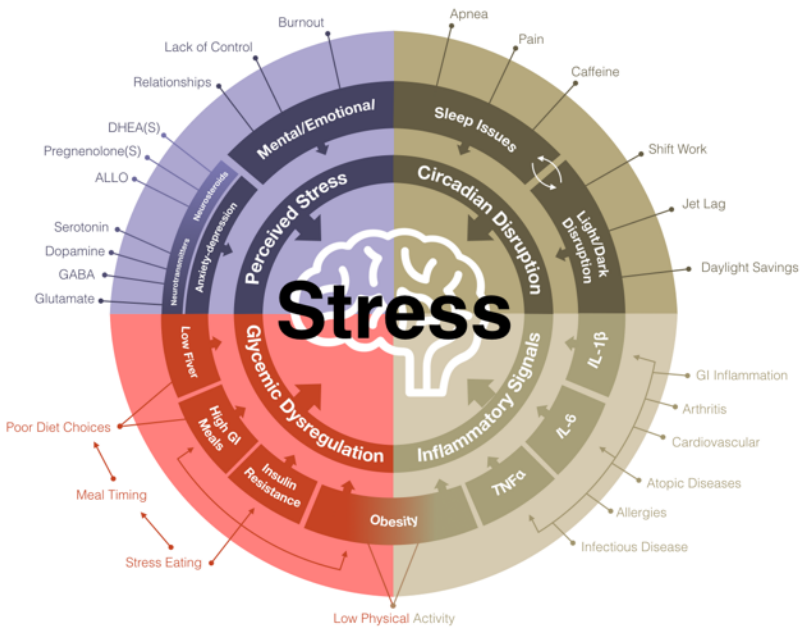
HPA-D: Etiology – Part 1

Hey, everybody, in this presentation we're going to discuss the etiology of HPA axis dysfunction and other stress-related pathology.

It's crucial to understand that HPA axis dysfunction can be caused by several aspects of the modern lifestyle. When we typically think of stress, we think of psychosocial and emotional stress, and those definitely are big contributors, but remember that stress is most broadly defined as any event in which environmental demands, internal demands, or both tax or exceed the adaptive resources of an individual. Any event that causes allostatic load is a stressor; doesn't have to be psychological or emotional. So for example, if you have a patient that's independently wealthy and they're lying on a beach in Thailand without any cares in the world, they could still be under stress if they have SIBO, iron overload, and undiagnosed gluten intolerance.



Adapted from: Guilliams, T. The Role of Stress and the HPA Axis in Chronic Disease Management. Point Institute, 2015. p. 80

In his book, Dr. Guilliams refers to four categories of stressors that lead to chronic HPA axis dysregulation. I'm not going to cover every aspect of this in detail—you can see Tom's book for that—but I'm going to review these so you can recognize them, assess them, and educate your patients about them. This will help your patients to understand the seriousness of HPA-D and the need to address all the diet and lifestyle pathology factors that contribute to stress-related pathology. So, if you see a patient and you start talking about this stuff to them, they may say something like, "Hey, I'm not stressed out, I feel pretty relaxed and calm," but when you explain what's on this slide to them, it can really help them understand that HPA axis dysfunction goes far beyond emotional and psychological stress, and I really can't overemphasize the importance of this

enough. The more I do this work, the more I believe that stress-related pathology is the elephant in the room when we're talking about chronic disease. It's really difficult to get patients to take these changes seriously, and I know this because as much as I know about it, it's something that I still struggle with. Nearly all clinicians I know struggle with it as well, and probably most of you listening to this are included in that, and I think it's imperative for us to lead by example as much as possible, because after all, if we can't recognize the significance of HPA axis dysfunction and all of these factors in our own constellation of signs and symptoms, and if we can't experience that ourselves, we're not going to be able to present a convincing case to our patients.

Now, the first category we're going to discuss of the four is perceived stress, and this is what most people think about when they think about stress. Now, within that category there are four key factors that determine the magnitude of the HPA axis response to perceived stress, and thus the relevance of a stressor. Number one is the novelty of the event, number two is the unpredictable nature of an event, number three is the perceived threat to body or ego, and number four is the sense of loss of control. Some use the mnemonic "NUTS" to remember this and to talk about it with their patients, which I think fits pretty well; novelty, unpredictability, threat and sense of no control. We're going to discuss some ways to assess perceived stress in your patients when we get to the diagnostic section.

Stressors that fall into this category include relationship difficulties, financial trouble, public speaking, work stress, chronic illness (definitely highlighted by the loss of control, and the physical effects of chronic illness would be part of another category), illness of a family member, or any event perceived as harmful and uncontrollable. Within this category, we would also consider internal stress perception caused by neurotransmitter imbalances, which can often manifest as

mood disorders like depression or anxiety, and these neurotransmitter imbalances can also affect the HPA axis by modulating the central nervous system sensitivity to stress or through cortisol feedback inhibition.

Lab experiments have shown that the extent to which an animal is given options to respond effectively to a stressor influences how much psychological breakdown will occur. Control is a key factor in protecting an animal or a human being from stress-induced disease. This is one reason that psychological stressors can actually be more harmful to us than physical stressors. We generally have more control over, or at least the ability to respond to, physical stressors. For example, if someone confronts us in a dark alley, we can run away or fight or do something else to protect ourselves. If an earthquake hits, we get under a doorway or a table, but normally we don't have the same options with psychological stressors. We can't fix the computer that just crashed, taking the 20-page report we were working on along with it, by smashing it with our fist, even though we might try. Nor are we likely to solve our conflict with the IRS by punching out the auditor they've sent to our home—wouldn't recommend that.

There's another important difference in the effect that psychological and physical stressors have on us. In most cases, psychological and emotional stressors tend to last much longer than physical stressors, and therefore they are more likely to cause illness and disease. Our bodies have evolved over millions of years to respond to physical stressors we might expect to face in nature, such as a predator. In the natural world, the fight-or-flight response serves us very well; our metabolic rate increases, our pulse speeds up, our blood pressure and oxygen consumption rise, our muscles tense, and our heart output increases by up to four- to fivefold, and all of this is in an attempt to deliver more blood to the skeletal muscles that will enable us to fight or flee. We're primed and ready to take action, and that's a survival response that has served us very well. Then in the process of fighting or fleeing, we expend all of that energy that was mobilized by our body; this is key. And after that, it's time to rest, assuming we've survived the threat. Our blood pressure and heart rate return to normal, our respiration slows, and our energy is again available for longer-term functions like digestion, reproduction, and tissue repair and growth.

In the face of psychological stressors that are more common in our modern life, however, we don't often discharge the buildup of stress hormones and neurotransmitters that are flowing through our body to get us ready for fight or flight. Our blood pressure and heart rate rise, and our muscles tense the same way that they do in response to a physical stressor, but we don't respond. We don't fight and we don't flee. The chemicals that produce the stress response continue to flow through our body and we end up in a chronic state of hyperarousal. This overstimulation of our sympathetic nervous system is a major causative factor of stress-related disease, including high blood pressure, arrhythmias, digestive problems, chronic headaches, backaches, sleep disorders, and chronic anxiety. As an interesting related note, some approaches to healing trauma, like Peter Levine's work, are based on his observations of animals in nature, and, for example, when animals get into some kind of fight or altercation, after that's over they typically walk away and then they might do something to discharge the buildup of stress hormones. For example, you might see ducks, after they've gotten into a scuffle, they'll walk away and they'll shake their wings pretty intensively for a period of time, and many animals exhibit this kind of behavior. Humans are perhaps somewhat

unique in that we don't do this, although you could argue that certain behaviors like overconsumption of alcohol or use of recreational drugs or overeating are our attempt, sort of misguided evolutionary attempt to deal with that buildup of stress hormones.

The non-specificity of the stress response has significant implications for those of us living in the industrialized world. Losing a job, worrying about a mortgage payment, and going through a difficult lawsuit will produce the same basic stress response in the body that being confronted by a lion did for our ancestors. The difference is that while our ancestors' bodies were specifically adapted to handle the physical stressors they were likely to encounter, our bodies are poorly adapted for dealing with the chronic psychological and emotional stressors that have become a normal part of modern life. A large body of evidence suggests that stress-related disease emerges predominantly out of the fact that we so often activate a physiological system that has evolved for responding to acute physical emergencies, not chronic psychological stress.

Another important concept to understand is the non-subjectivity of the stress response. People typically use the word "stress" to describe the nervous tension they feel under the pressures of life. It's important to note that these sensations don't accurately define stress, nor are they necessarily perceived when people experience stress. Stress is not simply nervous tension, as Hans Selye pointed out. He said stress reactions do occur in lower animals and even in plants that have no nervous systems. Indeed, stress can be produced under deep anesthesia in patients who are unconscious and even in cell cultures grown outside the body. One can feel nervous tension without activating the physiological mechanisms of stress, and it's possible to experience stress without feeling tension.

This has important implications for those of us living in the modern world. Popular and even medical literature often views stress as dramatic but isolated events such as a death in the family, sudden loss of employment, a divorce, or change in residence, and these are certainly profound stressful events for most people, but the insidious and chronic daily stress that often goes completely unrecognized probably has more serious and far-reaching biological consequences. We've become so habituated to this internally generated stress that it doesn't register as anything out of the ordinary for most people, even as it wreaks havoc on our bodies.

Dr. Gabor Mate, author of *When the Body Says No: Understanding the Stress–Disease Connection*, has written extensively about the connection between stress and chronic disease. In particular, he writes about how we've become habitually numb to the stress response and warning system. He says,

> The fight or flight alarm reaction exists today for the same purpose evolution originally assigned to it, to enable us to survive. What has happened is that we've lost touch with the gut feelings designed to be our warning system. The body mounts a stress response, but the mind is unaware of the threat. We keep ourselves in physiologically stressful situations with only a dim awareness of distress, or no awareness at all. Just like laboratory animals unable to escape, people find themselves trapped in lifestyles and emotional patterns inimical to our health. We no longer sense what is happening in

> our bodies and cannot therefore act in self-preserving ways. From this perspective, there's nothing wrong with the stress response, it's functioning exactly as it was intended, to protect us from harm. Instead, the problem lies with our reaction, or more accurately, our lack of reaction to stress. Our bodies are sending us signals, but we've lost the capacity to recognize them and respond appropriately.

And I think this is a really important concept to recognize in our work with patients. When we ask them if they're under stress, many will say yes but others will say no, and you really cannot trust patients' reports on their subjective interpretation of their experience of stress.