HPA-D Diagnosis - Part 1

Hey, everyone, in this presentation we're going to talk about the assessment of HPA axis function. The assessment of HPA axis function is multifaceted; as you've probably gathered by now, it's a little more than just measuring saliva cortisol levels. There are three basic categories of assessment that you need to do. The first is signs, symptoms, and history; the second is laboratory tests; and the third is perceived stress questionnaires.

Before we talk about signs and symptoms, I want to make an important point. Although it's not desirable to make a diagnosis based on symptoms alone, it's important to know that not all patterns of HPA axis dysfunction will show up in lab test results. Remember, cortisol signaling issues can be tissue-specific, not just systemic, which means that you can't necessarily detect them in saliva, blood, and urine. Also, changes to target tissue responses to cortisol signaling impact tissues involved in cortisol feedback inhibition, like the hippocampus, amygdala, hypothalamus, and pituitary. Changes that increase cortisol signaling in these tissues result in more profound feedback inhibition. Increased salivary or serum or urine cortisol levels may be compensated for by glucocorticoid receptor resistance in specific tissues, and that won't show up on a lab test. On the other hand, low cortisol may be compensated for by upregulated receptor function in particular tissues, and we don't have the ability to detect this on commercial lab tests yet either. So this means that HPA-D is ultimately a clinical diagnosis, and history, signs, and symptoms play a very important role.

Risk factors for HPA axis dysfunction

Trauma *(including early life)*	Circadian disruption
Poor diet	Mental/emotional stress
Food intolerances	Environmental toxins
Chronic illness	Chronic infections
Inappropriate physical activity	Injury
Poor sleep	Lack of social support

Let's start with risk factors for HPA-D, which are listed here on the slide. They include trauma, especially early-life trauma, poor diet, food intolerances, chronic illness, inappropriate physical activity, poor sleep, circadian disruption, mental and emotional stress, environmental toxins, chronic infections, injury, and lack of social support. These can be easily identified with a thorough history during the case review process. If you use my intake process and questionnaires, there are specific sections designed to identify HPA-D. It'll also show up in people's responses in the health history questionnaire, and I'm going to discuss assessment tools for perceived stress specifically shortly.

"Red flag" symptoms of HPA axis dysfunction

- Difficulty falling or staying asleep
- Waking up feeling tired even after 7-8 hours of sleep
- Afternoon energy crashes
- "Second wind" late at night
- Waking up with heart pounding in middle of the night
- Inability to handle stress
- Impaired exercise tolerance or recovery
- Weakened immune system
- "Brain fog" and memory issues
- Extreme hunger, irritation, or agitation before meals
- Postural hypotension

The symptoms of HPA-D are diverse and nonspecific. Since nearly every cell in the body has receptors for cortisol, it can affect almost every tissue, organ, and body system. That said, there are some symptoms that, especially when seen collectively, are strong indicators of HPA-D, and I've listed them here on the slide. They include difficulty falling or staying asleep, waking up feeling tired even after seven to eight hours of sleep, afternoon energy crashes, getting a second wind late at night, waking up with heart pounding in the middle of the night, inability to handle stress, impaired exercise tolerance or recovery, weakened immune function, brain fog and memory and cognitive issues, extreme hunger, irritation, or agitation before meals, and postural hypotension, getting dizzy when standing up quickly.

Other signs & symptoms of HPA-D

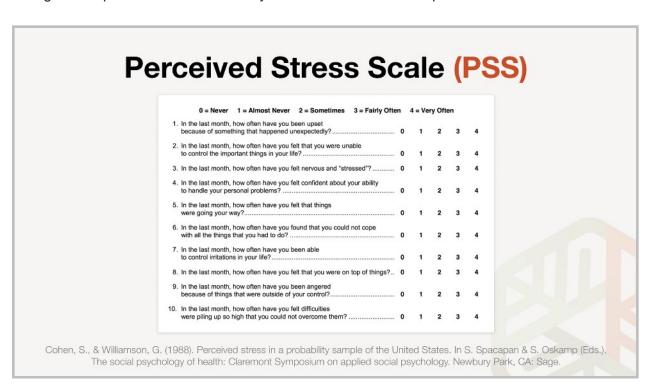|	
Muscle fatigue/weakness/pain	Increased or decreased appetite
Headaches	Difficulty with word recall
Teeth grinding	Dizziness
Cold/clammy hands and feet	Dry skin
Dry mouth/problems swallowing	Loss of muscle tone
Digestive distress	Dark circles under the eyes
Shortness of breath	Weight gain
Depression and/or anxiety	Frequent urination

There are some other signs and symptoms of HPA-D which may not be quite as primary but are often seen in this constellation. These include muscle fatigue, weakness and pain, headaches, teeth grinding, cold and clammy hands and feet due to autonomic nervous system dysregulation—that's not always related to thyroid function, and in fact, in my experience it's more often related to HPA-D—dry mouth, problems swallowing, digestive distress, shortness of breath, depression and/or anxiety, decreased or increased appetite, difficulty with word recall, dizziness, dry skin, loss of muscle tone, dark circles under the eyes, weight gain and frequent urination. So as you can see, these are quite diverse and quite nonspecific, and virtually all of your patients I would imagine have at least a few of these symptoms. That doesn't mean they all have HPA-D, but it's quite likely that the majority of our patients do have HPA-D as we've discussed already.

As we talked about in the etiology section, perceived stress is one of the four major HPA axis triggers. It might seem unnecessary to assess perceived stress; it's pretty obvious when we're stressed out, right? But I've found that patients have differing levels of awareness around this. Humans are remarkably adaptable. We get used to our circumstances and they quickly become the new normal, and we don't realize anything is awry. This is why I suggest using questionnaires to assess perceived stress and stress inventories. These tools help both clinicians and patients to identify the presence and source of significant stress and to take it more seriously. When patients see a very high score on these assessment tools, they're more likely to treat it as a real problem than if you just tell them that you think stress is contributing to their pathology.

Part of your job as a clinician is to communicate the seriousness of HPA-D. I have not found this to be easy. We have a prevailing cultural bias against taking stress seriously. Sayings like "I'll

sleep when I die," "the early bird gets the worm," and "tough it out" reflect our attitudes about the importance of rest and leisure. Many patients will either consciously or subconsciously deny or ignore the importance of stress in the origin and/or treatment of their condition. In part, this is because making meaningful changes with stress reduction and stress management can be really difficult. These assessment tools help, but it's also helpful to explain the four triggers of HPA-D and let them know that even if they're not feeling stressed out, HPA-D could be playing a significant role in their condition, and HPA modification strategies need to be used. Other patients, however, are more aware of the role of stress in their condition, and they're more willing to accept the role of HPA axis dysfunction in their disease presentation.

Perceived Stress Scale (PSS)

0 = Never   1 = Almost Never   2 = Sometimes   3 = Fairly Often   4 = Very Often

1. In the last month, how often have you been upset because of something that happened unexpectedly?.................................... 0   1   2   3   4

2. In the last month, how often have you felt that you were unable to control the important things in your life? 0   1   2   3   4

3. In the last month, how often have you felt nervous and "stressed"? 0   1   2   3   4

4. In the last month, how often have you felt confident about your ability to handle your personal problems? 0   1   2   3   4

5. In the last month, how often have you felt that things were going your way?... 0   1   2   3   4

6. In the last month, how often have you found that you could not cope with all the things that you had to do? 0   1   2   3   4

7. In the last month, how often have you been able to control irritations in your life?.. 0   1   2   3   4

8. In the last month, how often have you felt that you were on top of things?... 0   1   2   3   4

9. In the last month, how often have you been angered because of things that were outside of your control?.................................. 0   1   2   3   4

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them? 0   1   2   3   4

Cohen, S., & Williamson, G. (1988). Perceived stress in a probability sample of the United States. In S. Spacapan & S. Oskamp (Eds.), The social psychology of health: Claremont Symposium on applied social psychology. Newbury Park, CA: Sage.

So let's talk about how to assess perceived stress. The perceived stress scale, or PSS, was created by psychologist Sheldon Cohen. It's the most widely used psychological instrument for measuring the perception of stress. There are four-, 10- and 14-question versions, but the 10-question version is the most commonly used in clinical settings. This measures the degree to which situations in one's life are appraised as stressful, and it's designed to assess how unpredictable, uncontrollable, and overloaded respondents find their lives to be. It also includes a number of direct queries about current levels of experienced stress. Questions are of a general nature and relatively free of content specific to any subpopulation group, and questions in the PSS generally ask about feelings and thoughts during the last month. So as you can see here on the slide, I've put the PSS. There are questions like, "In the last month, how often have you been upset because of something that happened unexpectedly?" or, "In the last month, how often did you feel that you were unable to control the important things in your life?" And then they rate their answers on a scale of zero being "never" to four being "very often." Higher PSS

scores are associated with things like failure to quit smoking, failure among diabetics to control blood sugar levels, greater vulnerability to stress-induced depressive symptoms, and more colds and flus.

Norm Table for the PSS 10 item inventory

Category	N	Mean	S.D.
Gender			
Male	926	12.1	5.9
Female	1406	13.7	6.6
Age			
18-29	645	14.2	6.2
30-44	750	13.0	6.2
45-54	285	12.6	6.1
55-64	282	11.9	6.9
65 & older	296	12.0	6.3
Race			
white	1924	12.8	6.2
Hispanic	98	14.0	6.9
black	176	14.7	7.2
other minority	50	14.1	5.0

PSS scores are obtained by reversing the numeric responses—so for example, an answer of zero would equal four points, and an answer of one would equal three points, two equals two points, an answer of three equals one point, and then an answer of four equals zero points—for the positively stated questions, which are questions number four, five, seven, and eight, and then summing across all of the scale items. The perceived stress scale is not a diagnostic instrument, there are no score cutoffs, only comparisons within groups. But according to a poll of 2,387 respondents in the US, here are the PSS norms segmented by gender, age, and race. You can see this on the slide here, the average score for males is 12.1, the average score for females is 13.7, and then we have it segregated by age group, so the average score, 18 to 29, interestingly enough is 14.2, which is higher, and as respondents get older, their levels typically decline, so 65 and older is 12.0, and then the answers are also segregated by race. The PSS is freely available online as a PDF file, and I'll provide a link for that. We've also created it as a handout in the PDF generator that you can have your patients fill out by hand. I recommend creating it as an MD HQ questionnaire so it can be automatically scored. We did this, and I believe Ben at MD HQ can make it available to you in your MD HQ build. And finally, if you're not using MD HQ, we've created a simple online form that you can direct patients to that will automatically score the test, and that will be available in the resources section for this week's content.

Life Event	Life change units
Death of a spouse	100
Divorce	73
Marital separation	65
Imprisonment	63
Death of a close family member	63
Personal injury or illness	53
Marriage	50
Dismissal from work	47
Marital reconciliation	45
Retirement	45
Change in health of family member	44
Pregnancy	40
Sexual difficulties	39
Gain a new family member	39
Business readjustment	39
Change in financial state	38
Death of a close friend	37
Change to different line of work	36
Change in frequency of arguments	35
Major mortgage	32

Holmes & Rahe Stress Inventory

Another useful assessment tool for perceived stress is the Holmes and Rahe Stress Inventory. The PSS tells you the relative amount of stress a person is under; the Holmes and Rahe inventory does this too, but in the process of filling it out, the patient gains insight into what the major stressors in their life are. In 1967, psychiatrists Thomas Holmes and Richard Rahe examined the medical records of over 5,000 patients as a way to determine whether stressful events might cause illness. Patients were asked to tally a list of 43 life events based on a relative score. A positive correlation was found between their life events and their illnesses, and this scale has been validated across different populations in the US and abroad. There are 43 events, too many to list on this slide, but I've put the top 20 on here, and they include things like death of a spouse, divorce, marital separation, imprisonment, death of a close family member, personal injury or illness, marriage, losing your job, etc. We've also created this as a form in MD HQ, and as with the PSS, a simple page on the Kresser Institute website that you can send your patients to, which will automatically score this if you're not using MD HQ.