

#### **HPA-D 3-5 – Part 12**

Now, we're going to talk about putting all of this together into a protocol.

Pattern	Free cortisol	Metabolized cortisol
High cortisol	High or normal	High or normal
Low cortisol	Low or normal	Low or normal
Disrupted diurnal rhythm	High, normal, low	High, normal, low
High free, low total	High	Low-normal or low
Low free, high total	Low	High-normal or high
High DHEA	High, normal, low	High, normal, low
Low DHEA	High, normal, low	High, normal, low
High cortisol: cortisone ratio	High, normal, low	High, normal, low
Low cortisol: cortisone ratio	High, normal, low	High, normal, low
Low melatonin	High, normal, low (usually high, or high-normal)	High, normal, low
High melatonin	High, normal, low	High, normal, low

Here are the patterns again that you'll see in clinical practice. We went over all of these in the DUTCH part one and two presentations. I've omitted a few from the list that we covered then and consolidated them down into categories that received similar treatments for the purposes of simplicity. I'm going to cover each of these in some detail on the slides that follow.

As a reminder, no matter what the pattern is, the patient does need to address diet, lifestyle, and behavioral factors to balance the HPA axis. So don't skip right to the supplement protocols and gloss over all that because you're really not going to get the same amount of positive results. Having said that, in this protocol section, I'm just going to talk about supplements, botanicals, and hormones for these particular patterns so I'm not repeating myself on every slide.



#### **High cortisol protocol**

Intervention	Dosage/Comments
HPA Balance (Vital Plan)	Contains Relora, Sensoril, L-theanine; take 1 cap BID or TID
Phosphatidylserine	PS dose: 100-200 mg TID
Acetyl-CH (Apex Energetics), 5-HTP, melatonin	As needed if circadian rhythm/sleep/mood disrupted, melatonin is low (often is in high cortisol states)
Metabolic Synergy & GlucoSupreme (Designs for Health)	Only if blood sugar high; Metabolic Synergy dose 2 caps TID; GlucoSupreme 2 caps BID
Boswellia, curcumin & fish oil	Only if significant inflammation present
CBD	Optional. Use if anxiety severe, or other conditions present

Let's start with high cortisol. This is when either free or total cortisol is high, and the other is either normal or high. So it's a concordant pattern. The primary goal here is to bring down cortisol in this particular situation. Potential causes would include perceived stress, inflammation, circadian disruption, and possibly Cushing's [disease]. And you really want to also make sure to explore the causes of inflammation, such as gut issues or infection, and to rule out Cushing's disease, which, while unlikely, does happen. In fact, just a few months ago, I had a patient who presented with really high cortisol levels, higher midnight cortisol levels than morning, and ended up having full-blown Cushing's disease.

The interventions should be HPA Balance, which contains Relora, Sensoril, and L-theanine, to bring down cortisol, phosphatidylserine to also help dampen the cortisol levels, [and] Acetyl-CH if their circadian rhythm is disrupted. So if they have high cortisol and the rhythm is out of whack, like it's lower in the morning and higher at night, [the] opposite presentation you would expect, melatonin may be necessary or helpful, or even 5-HTP for increasing melatonin levels if their sleep is disturbed. Metabolic Synergy and GlucoSupreme can be added only if their blood sugar levels are high. Boswellia, curcumin, or fish oil if they have significant inflammation present, and then [cannabidiol] (CBD) can be considered and used if their anxiety is severe or they have conditions that indicate the need for CBD.



### Low cortisol protocol

Intervention	Dosage/Comments
Vital Adapt (Natura Health Products)	Contains Eleuthero, Rhodiola, Schisandra, Ashwagandha, Cordyceps, Reishi, Ginseng, Licorice
Adrenal glandulars (Dr. Ron's)	Optional; some patients with low cortisol do well with them. 3 capsules in the morning.
Licorice	Patients with very low cortisol may benefit from additional licorice; Vital Adapt contains 10 mg of glycyrrhizin per 2mL dose; patients with low cortisol can safely take up to 100 mg/d
Acetyl-CH, 5-HTP, melatonin, L- theanine	As needed if circadian rhythm/sleep/mood disrupted, melatonin is low
Boswellia, curcumin & fish oil	Only if significant inflammation present
CBD	Optional.Use if anxiety severe, or other conditions present

Here's the low cortisol protocol. So low cortisol free and metabolized. This is often associated with metabolic syndrome, fibromyalgia, chronic fatigue syndrome, chronic pain, cardiometabolic disease, mood disorders, autoimmune disease and cancer, Addison's [disease], and also corticosteroid or opioid use has been seen in this pattern. So we have Vital Adapt, which is a blend of adaptogens such as eleuthero, rhodiola, schisandra, ashwagandha, cordyceps, reishi, ginseng, and licorice. The dose of licorice in Vital Adapt is fairly small and unlikely to provoke hypertension except in very sensitive patients. So just keep that in mind when providing Vital Adapt recommendations. It can typically be used pretty safely. Adrenal glandulars are also optional. Some patients with low cortisol do well with them, so the dose would be three capsules in the morning. Patients with low cortisol may also benefit from additional licorice above and beyond what's in Vital Adapt. Vital Adapt contains 10 milligrams of glycerin per 2 ml dose. So patients with low cortisol could safely take up to 100 milligrams of the glycyrrhizin, Acetyl-CH, [5-hydroxytryptophan] (5-HTP), melatonin, or L-theanine as needed if circadian rhythms, sleep, or mood is disrupted or melatonin is low. Then the boswellia, curcumin, and fish oil if inflammation is present, and CBD is optional.



# **Disrupted diurnal rhythm** (only)

Intervention	Dosage/Comments
Gaia Adrenal Support	Contains Rhodiola, Holy Basil, Ashwagandha, Oats Milky Seed, Schisandra
Acetyl-CH, 5-HTP, melatonin, L- theanine	As needed if circadian rhythm/sleep/mood disrupted, melatonin is low
Relora and/or PS	If cortisol is high at night
Metabolic Synergy & GlucoSupreme	Only if blood sugar high; Metabolic Synergy dose 2 caps TID; GlucoSupreme 2 caps BID
Boswellia, curcumin & fish oil	Only if significant inflammation present
CBD	Optional. Use if anxiety severe, or other conditions present

Here's a protocol for disrupted diurnal rhythm only. If their total cortisol is normal, but their rhythm has flipped, such as they have high cortisol at night and low in the morning or it's just haywire, what you can use here is the Gaia Adrenal [Health Daily] Support. It's a formula that contains rhodiola, holy basil, and ashwagandha. It tends to not be as stimulating as Vital Adapt, maybe, so [it's] rather useful in this particular situation. Again, Acetyl-CH to reset their circadian rhythm, [5-]HTP, melatonin, and L-theanine if sleep and mood are disrupted, and you can see the rest of the consistency of these recommendations that go in sync if you start to have multiple imbalances going on at the same time.



## High free, low total cortisol

Intervention	Dosage/Comments
Acetyl-CH, 5-HTP, melatonin, L-theanine	As needed if circadian rhythm/sleep/mood disrupted, melatonin is low
Relora	Take at night before bed if cortisol is high at night and/or sleep is disrupted
Boswellia, curcumin & fish oil	Only if significant inflammation present

Here's the first discordant pattern we're going to talk about with high free cortisol and low total cortisol. In these patterns, it's really even more important to focus on the underlying cause because that's really the main issue that tends to be driving this discordant cortisol presentation. So obviously, it's kind of like you have one foot on the accelerator and one foot on the brake here. So if you go in guns a-blazing, trying to increase cortisol, it might actually drive up your free cortisol even higher, when in reality, you're trying to raise the total cortisol but are actually causing the inverse to happen. With the opposite pattern, you have these challenges. With this high free cortisol and low total cortisol discordant pattern, this often occurs or we see it in hypothyroidism, inflammation, people who are supplementing with licorice, or it can often just be normal or non-pathological. So that's why it's important to match symptoms with the presentation and the pattern that you're seeing on your tests. When you see this, you want to ask the patient [if] they are taking licorice or have been taking it. If not, then you want to further investigate thyroid function. You'll remember that some researchers are using cortisol metabolites and free cortisol to diagnose subclinical hypothyroidism, or hyperthyroidism. So it might show up in the urine here before it even shows up in the bloodwork. But you definitely want to check thyroid carefully if you see this pattern.

Remember, this can be non-pathological if someone has relatively high cortisol in the early morning and lower the rest of the day because the metabolites do lag with free cortisol production. I'm somewhat reluctant to use adaptogens in this pattern. Anecdotally, we've seen in clinical practice that adaptogens tend to raise free cortisol without affecting the metabolites very much or may even decrease metabolites in some cases. I wouldn't use adaptogens in this pattern.



I might focus on things like Acetyl-CH to reset the rhythm, 5-HTP, melatonin, or L-theanine if needed for sleep or mood disruption, relora maybe at night if free cortisol is high at night and sleep is disturbed. [However,] I wouldn't take too much of that for fear of lowering cortisol further and then boswellia and curcumin and fish oil for inflammation.

Low	free,	high	total	cortisol

Intervention	Dosage/Comments
HPA Balance	Contains Relora, Sensoril, L-theanine; take 1 cap BID or TID
Vital Adapt?	Contains Eleuthero, Rhodiola, Schisandra, Ashwagandha, Cordyceps, Reishi, Ginseng, Licorice
Phosphatidylserine	PS dose: 100-200 mg TID
Acetyl-CH, 5-HTP, melatonin	As needed if circadian rhythm/sleep/mood disrupted, melatonin is low (often is in high cortisol states)
Metabolic Synergy & GlucoSupreme	Only if blood sugar high; Metabolic Synergy dose 2 caps TID; GlucoSupreme 2 caps BID
Boswellia, curcumin & fish oil	Only if significant inflammation present

Here's the opposite pattern, low free cortisol and high total cortisol. This often occurs in obesity, insulin resistance, hyperthyroidism, chronic stress, glucocorticoid use, and chronic fatigue syndrome. Again, you really have to focus on the underlying cause in these situations. This is often obesity and insulin resistance related. That's where I typically see this pattern. Hyperthyroidism is pretty rare. But if the patient's not obese, and they present with this pattern, it is almost always a chronic stress response. If that's the case, then using adaptogens may be warranted and possible. As I said, just anecdotally, adaptogens seem to increase free cortisol without substantially increasing total cortisol levels. But you really want to retest perhaps more quickly than you would otherwise to make sure that you're not driving their total cortisol up. And that's why I put a question mark here for Vital Adapt. You could use either HPA Balance or Vital Adapt, phosphatidylserine and/or Acetyl-CH to reset the rhythm, and then Metabolic Synergy or GlucoSupreme for blood sugar issues, [and] boswellia, curcumin and fish oil if inflammation is present.



## **High DHEA**

Intervention	Dosage/Comments
HPA Balance	Contains Relora, Sensoril, L-theanine; take 1 cap BID or TID
Vital Adapt	Contains Eleuthero, Rhodiola, Schisandra, Ashwagandha, Cordyceps, Reishi, Ginseng, Licorice
Circadian nutrients (melatonin, L-theanine, etc.)	If sleep or circadian rhythm is disrupted
Metabolic Synergy & GlucoSupreme	Only if blood sugar high; Metabolic Synergy dose 2 caps TID; GlucoSupreme 2 caps BID
Boswellia, curcumin & fish oil	Only if significant inflammation present

Let's talk about high [dehydroepiandrosterone] (DHEA). [The] primary causes are typically [polycystic ovary syndrome] (PCOS), acute stress, obesity, benzodiazepine use, antidepressants, and [attention deficit disorder] medication. If DHEA is high in the context of any other patterns that were already discussed, just treat accordingly to that pattern. But if cortisol is entirely normal and the DHEA is high, which is pretty rare in my experience, you can consider this particular protocol here. The first thing to think about if you're using the DUTCH comprehensive or DUTCH Plus is total DHEA high or is it just DHEA sulfate? When you see elevated DHEA sulfate and other markers are normal, it's probably not even pathological and it doesn't really require treatment. If DHEA sulfate is significantly elevated and total DHEA is normal, the possible causes could be things that actually upregulate sulfation, such as a high-protein diet, liver detoxification supplements and herbs, or methylation supplements.



#### **Low DHEA**

Intervention	Dosage/Comments
HPA Balance	Contains Relora, Sensoril, L-theanine; take 1 cap BID or TID
Vital Adapt	Contains Eleuthero, Rhodiola, Schisandra, Ashwagandha, Cordyceps, Reishi, Ginseng, Licorice
Circadian nutrients (melatonin, L-theanine, etc.)	If sleep or circadian rhythm is disrupted
Metabolic Synergy & GlucoSupreme	Only if blood sugar high; Metabolic Synergy dose 2 caps TID; GlucoSupreme 2 caps BID
Boswellia, curcumin & fish oil	Only if significant inflammation present

If total DHEA, which is a combination of DHEA sulfate, etiocholanolone, and androsterone, [is] high, it could be related to obesity, stress, or PCOS. You want to address obesity and PCOS, and then you can use the adaptogens in HPA Balance for the stress component. [A] similar process [is used][ if DHEA is low. You first think about whether total DHEA is low or just DHEA sulfate. If it is low DHEA sulfate with normal total DHEA, that is often caused by inflammation or glucocorticoid use. Remember the patient [with inflammatory bowel disease] who we discussed who had normal DHEA but low DHEA sulfate, and he was taking cortex and also had a lot of inflammation? That's this particular type of case. If total DHEA is also low, stress, aging, rapid weight loss, opioids, glucocorticoids, birth control or [hormone replacement therapy], antipsychotics, or diabetes medication could be to blame. So you want to address those underlying causes first and foremost.

You can also use adaptogens and other supplements as necessary to address the stress response component. Things such as HPA Balance, Vital Adapt, and other circadian nutrients. And then, of course, there's Metabolic Synergy, boswellia, the things that we've talked about for inflammation and blood sugar. As you can see here, the protocol for low DHEA is really the same as high DHEA. So remember that adaptogens have a balancing effect and cortisol is not low or high here. We're just talking about DHEA being the only piece of the puzzle that's off. You really should look at these other patterns that we've discussed previously so that you have some good guidance of how to intervene.