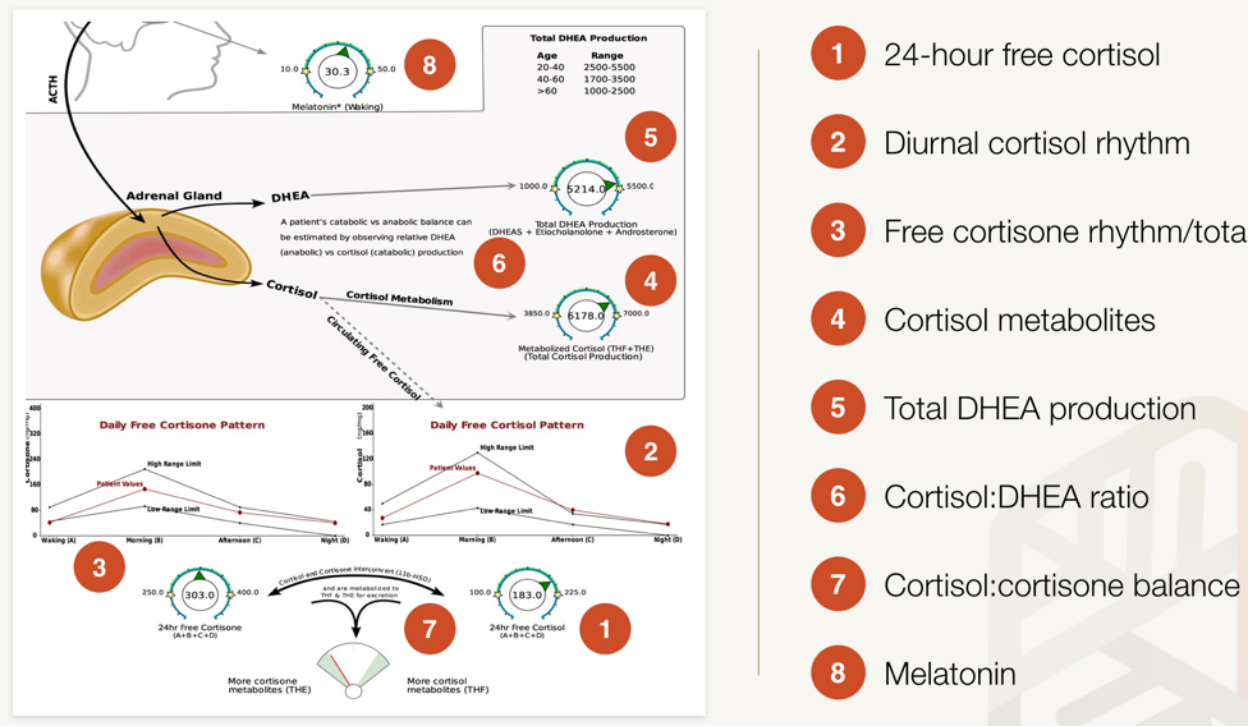
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

HPA-D Case Studies – Part 1

Hey, everyone. In this unit, we're going to cover some case studies for HPA axis dysfunction and incorporate all of the concepts we've been discussing so far in a practical way. Before we jump into specific cases, however, I want to give you an algorithm for how to look at the DUTCH test results, and this will help you to organize your thinking and make sure you're looking at everything you need to see. [Note: This algorithm is included in the Adrenal Profile Interpretation Guide handout.]



So, the first thing is to check free cortisol. Is it high? Is it low? Or is it normal? Then you check the free cortisol diurnal rhythm. Is that normal, out of range, or do they maybe have high cortisol at night? Then you check free cortisone, the total free cortisone, and then the free cortisone rhythm. You really just use this as a reality check, kind of a way of asking, "Really? Are you sure?" to compare with free cortisol.

For example, let's say you see that free cortisol is high at bedtime. You would say, "Really? Are you sure?" Then you look at free cortisone. If free cortisone is normal or low at bedtime, then maybe there was a contamination of the sample, or maybe that would just revise your thinking about how high the free cortisol was downward. If you see free cortisol that is really high in the morning, you ask, "Really? Are you sure?" Then you look at free cortisone. If you see that the cortisone is normal or even low, maybe that patient is just converting more cortisone to cortisol to start the morning. This is the nuance and the level of detail that you have to consider when you're looking at these tests.

For total free cortisone, you use it as an overall reality check to free cortisol, total free cortisol. Again, if total free cortisol is low-normal, but free cortisone is high, then I would revise that estimate for free cortisol up a little bit and vice versa.

Okay, so the next thing you do is you check metabolized cortisol. That's step four. Again, is it low? Is it high? Is it normal? Is it concordant with free cortisol and free cortisone, or is it discordant with free cortisol and cortisone? In other words, is this one of these patterns where you see high free cortisol and low metabolized cortisol, or is it a pattern where you see low free cortisol and high metabolized cortisol?

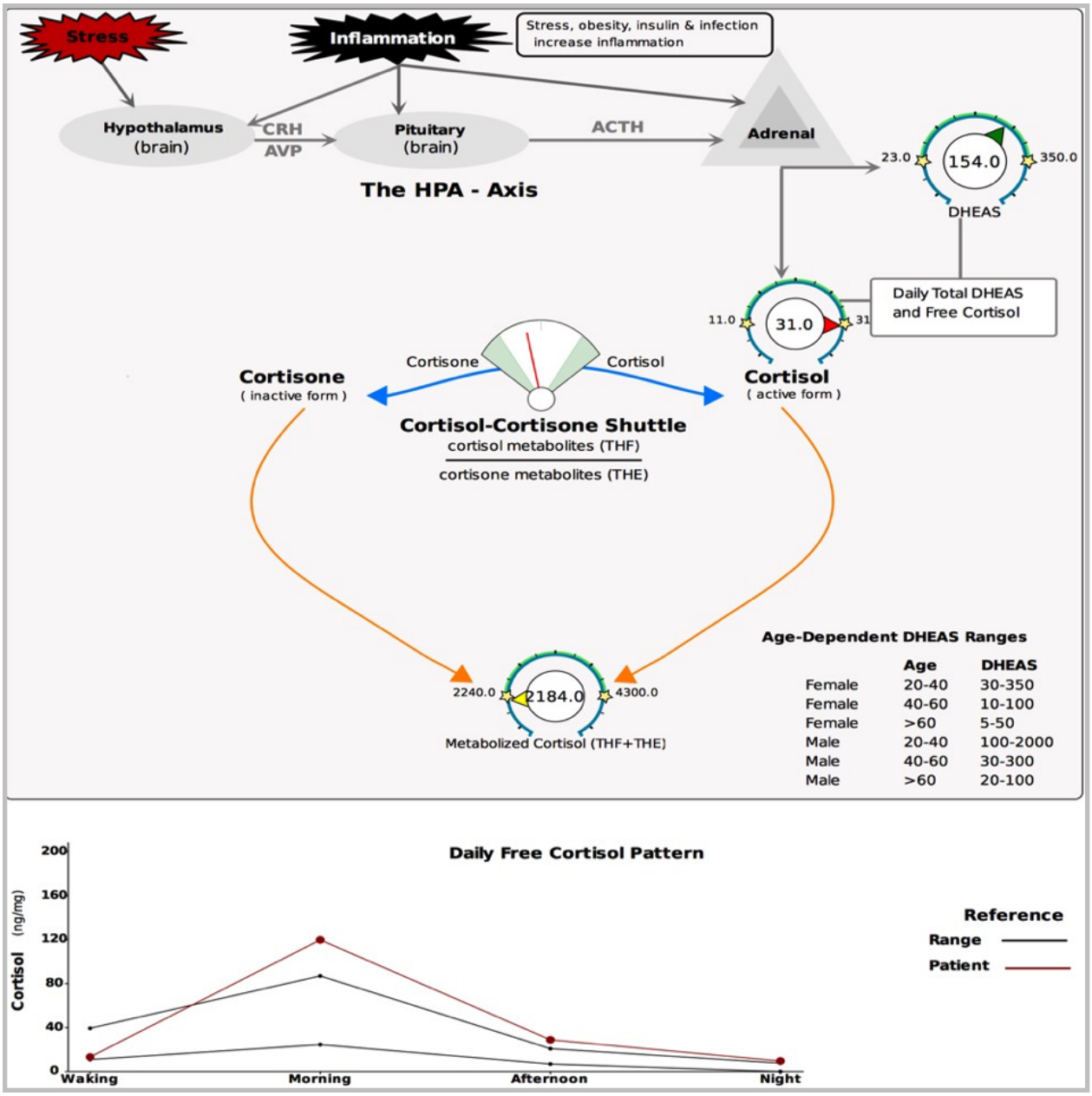
Step five is to check total DHEA. Total DHEA would include DHEA sulfate, androsterone, and etiocholanolone, if you're using the comprehensive panel, which is a better marker for DHEA production, as you know now. If you're using the adrenal panel, you'll only have DHEA sulfate, and that's one of the downsides of that panel. The reason that it is important to have all three of those markers is it can bias the overall treatment approach and also provide you some useful information. For example, if you see low DHEA-S but androsterone and etiocholanolone are high, that could suggest inflammation because inflammation inhibits sulfation in general and sulfation of DHEA in particular.

Number six, you check the cortisol-to-DHEA ratio. You look at the rough cortisol-to-DHEA ratio. You don't need to actually calculate it. You just need to qualitatively look at it and see if they are producing a lot more cortisol relative to DHEA. That means they're in a catabolic state, which means there is a lot of wear and tear on the body, and it strengthens the need to treat the cortisol issue. It makes it a higher priority in the differential process of figuring out what to focus on.

Then step seven, you check the cortisol-to-cortisone metabolite balance, and this also biases overall cortisol findings, so if you see a relative excess of cortisol compared with cortisone, that's observed in hypothyroidism, inflammation, visceral obesity, high insulin, excess sodium, and licorice supplements. If you see more cortisone, that's observed in hyperthyroidism, human growth hormone, estradiol, good sleep, ketoconazole, magnolia, scutellaria, ziziphus, and testosterone.

Then step eight, finally, is to look at melatonin. This is often discordant with cortisol and can also bias the treatment and provide info on its own. If melatonin is very low, you might use more supplements and interventions for circadian disruption. If it's high without supplementation, you would be looking at the possibility of neuroinflammation.

Okay, so we'll provide you a handout with this algorithm so you can refer to it as you're learning. It's a really helpful way of systematizing how you interpret DUTCH test results rather than just trying to remember every time what you're supposed to be doing.

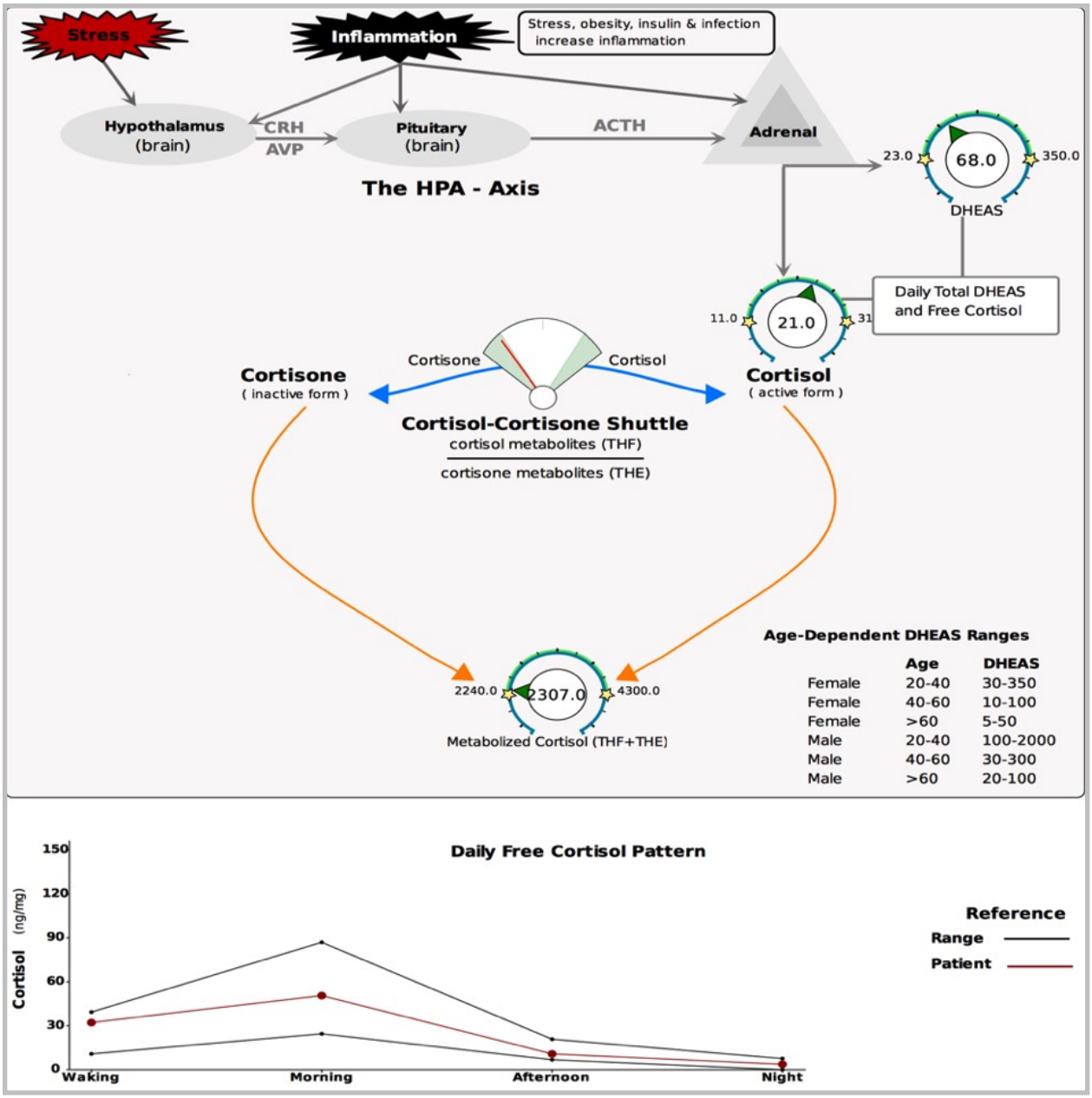


All right, let's look at the first case. This is a 34-year-old female. Chief complaints in her words were, "Chronic fatigue and depression. Also thyroid symptoms despite all my thyroid tests coming out within normal range." As we'll find out in the blood chemistry unit, "normal" is a relative term with thyroid markers. She had dry skin, hair loss, often felt cold, had cold hands and feet and bad circulation. As you can see, the test results largely confirmed her suspicion, so we'll go through our eight-step algorithm here.

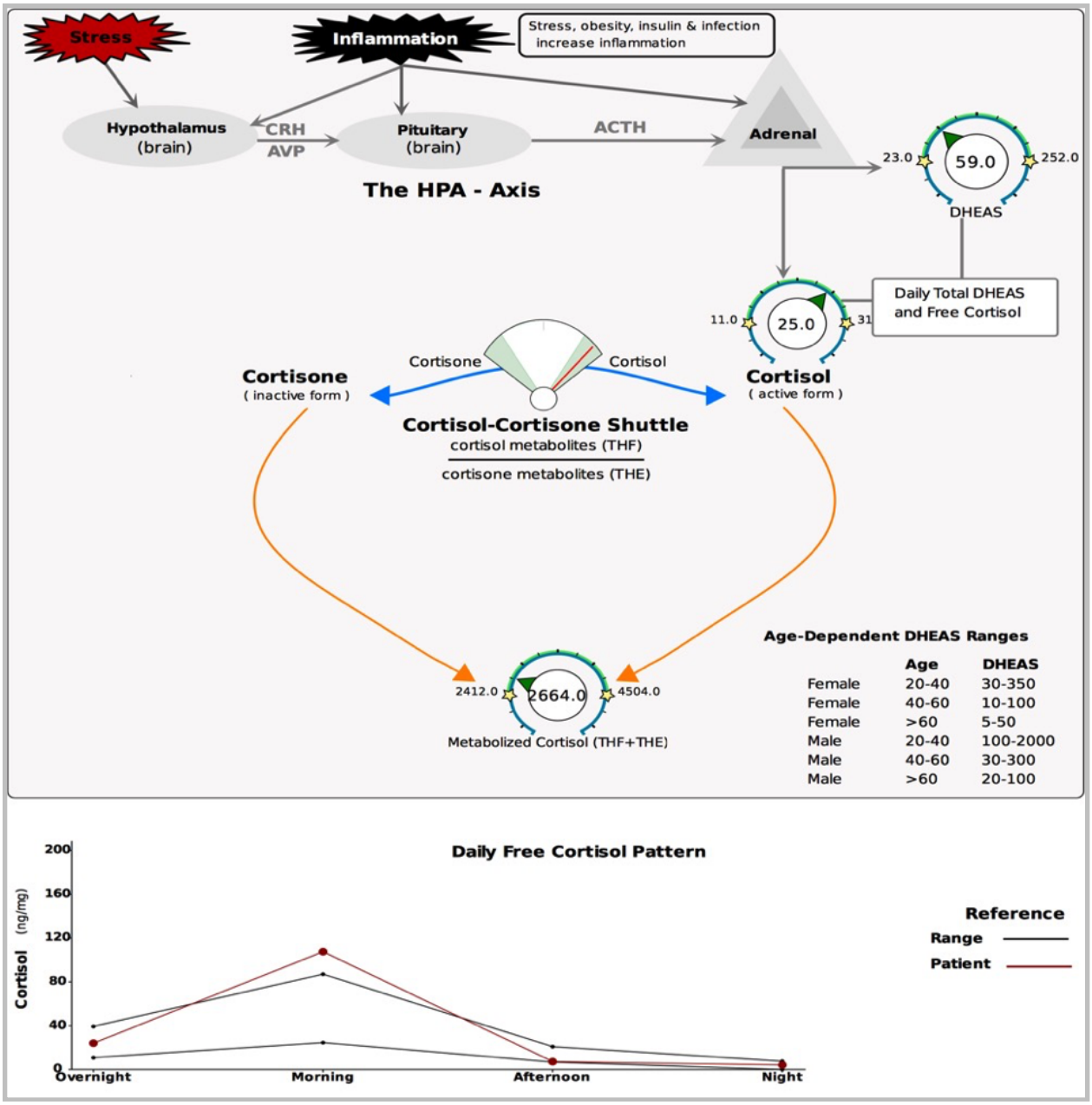
Number one, her free cortisol is high, borderline high. The range goes up to 31, and she's at 31, so the lab marked it as high. Number two, we look at her cortisol diurnal rhythm. It's high in the

morning sample. It's high in the afternoon sample, it's high at night, and it's low on the waking sample, so she does have a disrupted rhythm. Number three, her free cortisone is normal in the morning and afternoon and high at night, so this biases the free cortisol diurnal disruption down a little bit. Number four, her cortisone metabolites are low, and we see a discordant pattern here because she has the high free cortisol and low metabolized cortisol, and we know that hypothyroidism is one of the conditions that can cause that. Number five, her total DHEA, which isn't pictured here, is normal. Number six, her cortisol-to-DHEA ratio was slightly elevated. Number seven, her cortisol-to-cortisone balance was normal. Number eight, her melatonin was low-normal.

In terms of other lab findings, her thyroid-stimulating hormone, or TSH, was normal, but her free T4 and free T3 were borderline low. Now, remember that some researchers have actually suggested using urinary cortisol metabolites to diagnose subclinical hypothyroidism and hyperthyroidism. This suggests that an imbalance in the free and metabolized cortisol level may show up prior to the serum markers going out of range, and in this case, we decided to do a therapeutic trial of desiccated thyroid, even though her serum markers were normal, rather than addressing the HPA axis directly, and these markers improved significantly. We did give her some support for her HPA axis, but I think my point here is that sometimes these test results can be indicators of other underlying causes that you need to address rather than just exclusively focusing on the HPA axis.



So, here's what happened after that retest. We only did thyroid treatment. We did give her some lifestyle and behavior suggestions for HPA axis modification but no HPA axis supplements. We can see that her free cortisol is now normal. It dropped from 31 to 21. Her diurnal rhythm is normal. It's interesting that supporting her thyroid seemed to affect that as well. Her free cortisone was normal at all time points, and overall, her cortisol metabolites were normal, though still definitely on the low end, so we might then focus on her HPA axis specifically to bring that up. Her total DHEA was normal. Her cortisol-to-DHEA ratio became normal. Her cortisol-to-cortisone ratio was slightly favoring cortisone, and then her melatonin was still a little bit low-normal. This is now a representation of what her HPA axis function looks like with normal thyroid function, and we decided to wait another month and then retest before doing additional treatment.



Here's what that second retest looked like. Free cortisol is normal still. Diurnal rhythm was a little bit high on the morning sample and low-normal in the afternoon and at night. Free cortisone was normal. Cortisol metabolites still a bit low but definitely higher than before. They've progressively been coming up. Total DHEA was normal. Cortisol-to-DHEA ratio was normal. Cortisol-to-cortisone ratio was now favoring cortisol, and her melatonin was still low-normal.

You may notice here that, and as I mentioned, the morning cortisol reading is slightly high. That's probably nonpathological. We discussed this when we talked about patterns. Cortisol maxes out in the early morning sample because overnight and early morning are when cortisol production is the highest, but the metabolites lag behind by about 90 minutes, so it can show kind of a falsely

elevated level in the morning. If someone is relatively high in the early morning and then normal throughout the rest of the day, we miss that disproportionate amount of the metabolites that come from the morning sample. Given that many of her complaints had resolved by this third test, and most of the markers were within the normal range, we decided not to do any specific HPA axis supplementation.

This is hopefully a really good example of how important it is to address the underlying cause and how sometimes when you see results, even when the results are pointing to a certain thing, such as HPA axis dysfunction that can itself be an underlying cause, sometimes there is a deeper cause that you can address without even specifically focusing on the other pathology. That comes up when we talk about SIBO and other things as well, so it's really this core principle in functional medicine that I continue to talk about and I spent so much time on in the introduction of this course is that we always want to drop down as deep as we can go to find that underlying cause. I always find new examples of that in my own work, and I've been doing this for a long time. It's so important for me to keep that in mind, and it's so important for you as well.