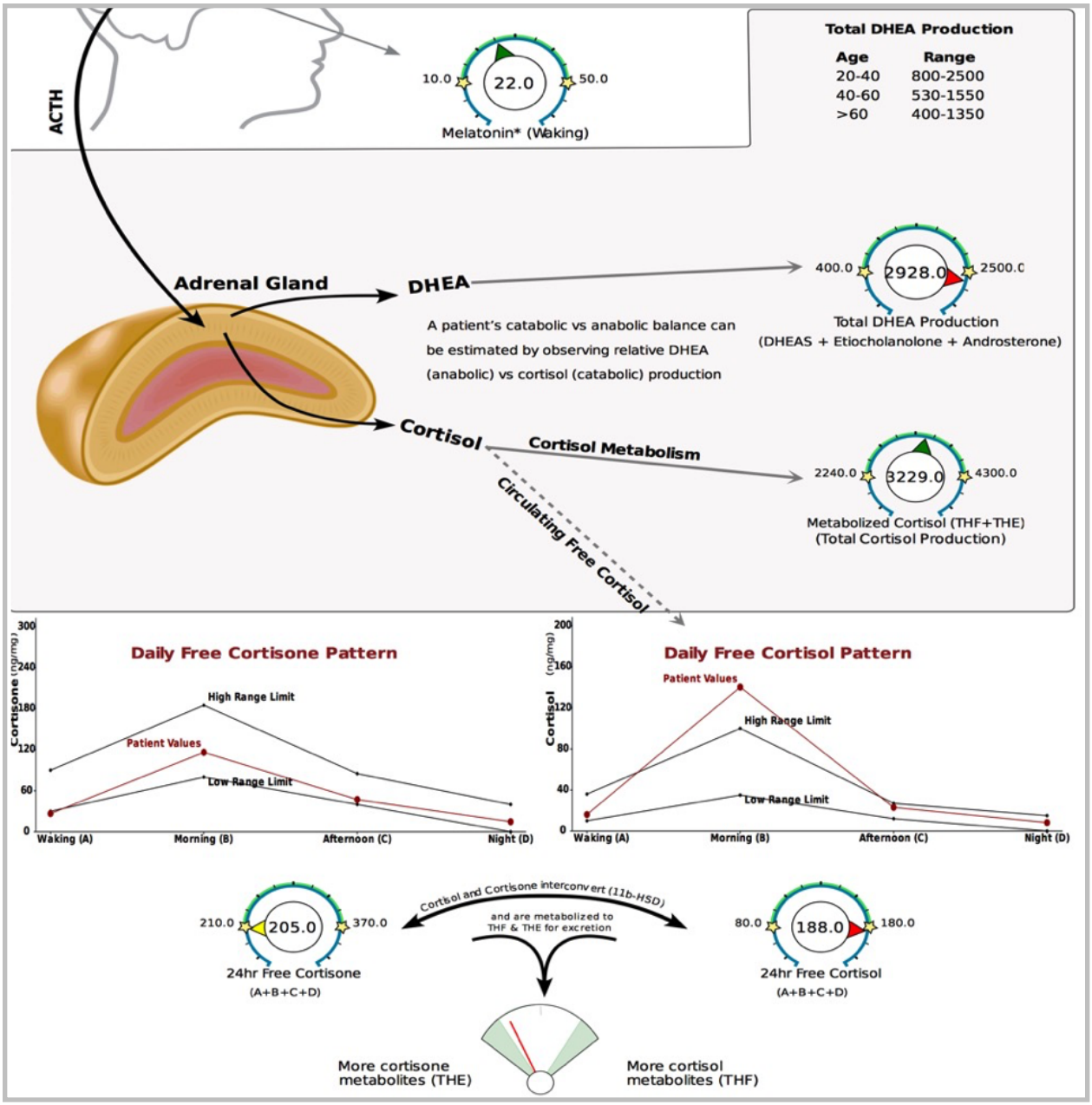
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

HPA-D Case Studies – Part 4

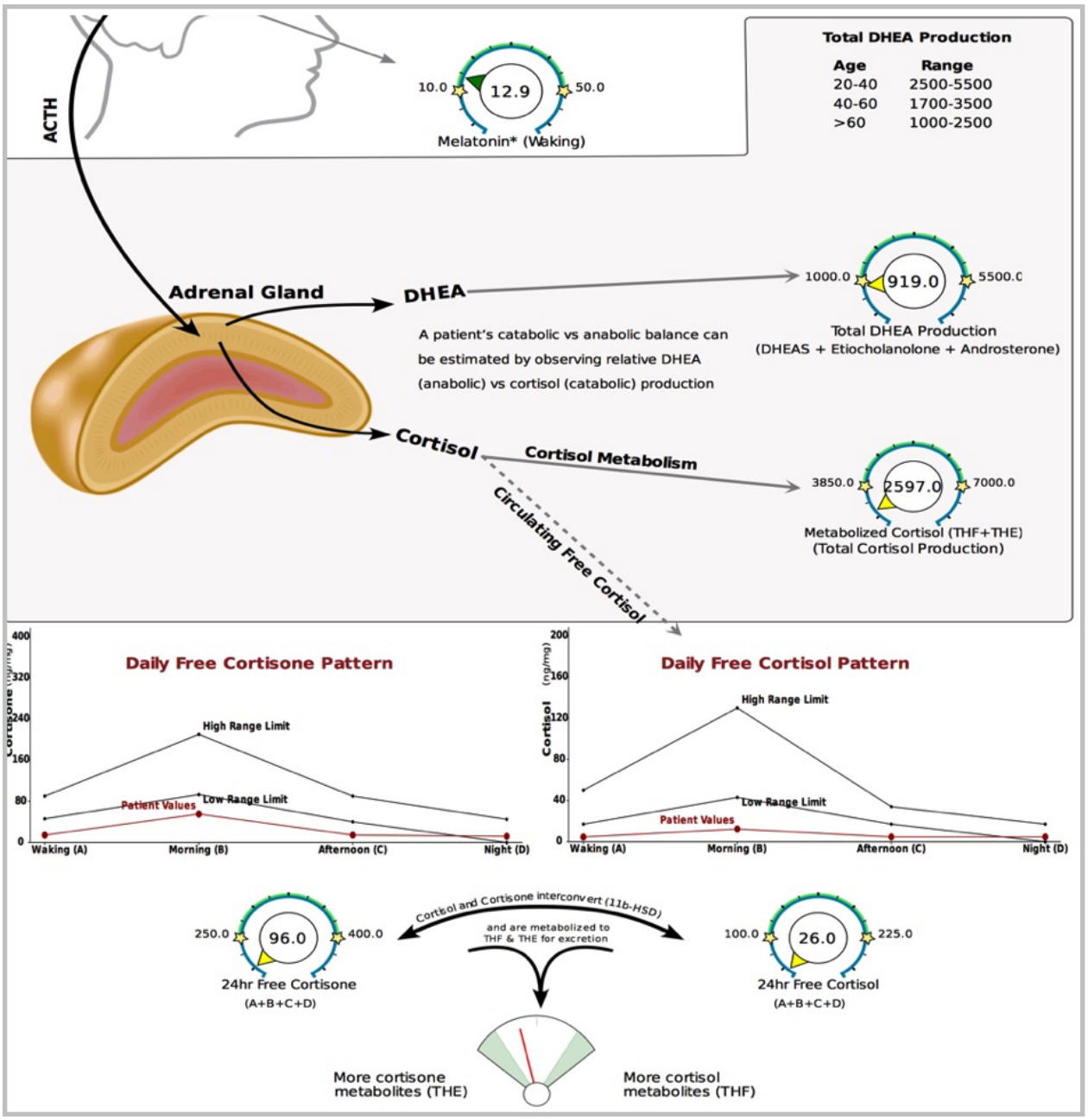
Next patient is a 35-year-old female. Chief complaints were low energy, spontaneous bleeding, dizziness, and infertility.



Her free cortisol was high. Her diurnal cortisol rhythm was normal waking, high in the morning, normal in the afternoon and night. Her free cortisone rhythm was low waking, normal at other time points, and her total free cortisone was low, so again, we see a significant discrepancy between

free cortisol and free cortisone. Number four, her cortisol metabolites were normal. Number five, her total DHEA was high. Etiocholanolone and androsterone were normal, but her DHEA sulfate was quite high. Number six, cortisol-to-DHEA ratio was normal. Then seven, cortisol-to-cortisone balance was normal, and eight, melatonin was normal.

This is an interesting case. Her free cortisol is high, but it's mostly because of that morning reading. When we see that free cortisone is low, that strengthens the idea that this could be a non-pathological finding. Her thyroid numbers are okay at first glance, but alkaline phosphatase is low, and MCV is high, both of which can indicate thyroid hypofunction. Her TSH is 4, which I would consider to be borderline based on recent studies of TSH values in euthyroid subjects. Her DHEA sulfate is high with normal etiocholanolone and androsterone. Before, we talked about situations where DHEA sulfate was low with normal or even high etiocholanolone and androsterone, and that was a sign of inflammation inhibiting sulfation, but when DHEA is high, that can point to an upregulation of sulfation. She was on methylation supplements that could potentially upregulate that sulfation pathway. So, in this case, I would address the thyroid function first and then retest and see what changes with the DUTCH test, like we did with that first case study we discussed. That's exactly what we did, but before we could run the retest, the patient became pregnant. So, clearly, addressing her thyroid helped, and we then supported her through her pregnancy, and she gave birth to a healthy baby girl.



All right, the next patient is a 47-year-old male. We briefly reviewed this case in the section on the DUTCH test. Chief complaint was generally healthy but persistent knee pain in both knees, diagnosed as tendinosis of the patella tendon for almost two years. Despite extensive modification of his athletic activities and commitment to doing that, the knees were not getting better. He believed that his internal health issues were preventing his tissue from healing.

So, number one, free cortisol is low. Number two, diurnal cortisol rhythm was low at all three time points during the day and just barely normal at night. Free cortisone rhythm was very similar, and his total free cortisone was low. Note that both the free cortisone and free cortisol are way below

the bottom end of the range. Free cortisol was 26. The range's lower end is 100. Free cortisone was 96. The lower end of the range is 250. These are still not at the levels that you'd expect to see in Addison's disease. In those cases, you'd expect to see below 10 for free cortisol. Number four, cortisol metabolites were low, so this is a case of concordance between free cortisol and cortisol metabolites. Total DHEA was low. Cortisol-to-DHEA ratio was low-normal, but that's because maybe DHEA was slightly less depressed relative to cortisol. Step seven, cortisol-to-cortisone balance was normal. Step eight, melatonin was normal.

Again, this is a patient most people are thinking of when they think of adrenal fatigue. Everything is definitely low, but as we've talked about, it's unlikely that it is because the adrenals are actually fatigued. In order to find that out, we'd have to do an ACTH stimulation test. I mean, that does happen, particularly with Addison's, but these levels are not low enough to make me think of Addison's, and it's more likely a brain, central nervous system, or tissue-specific mechanism.

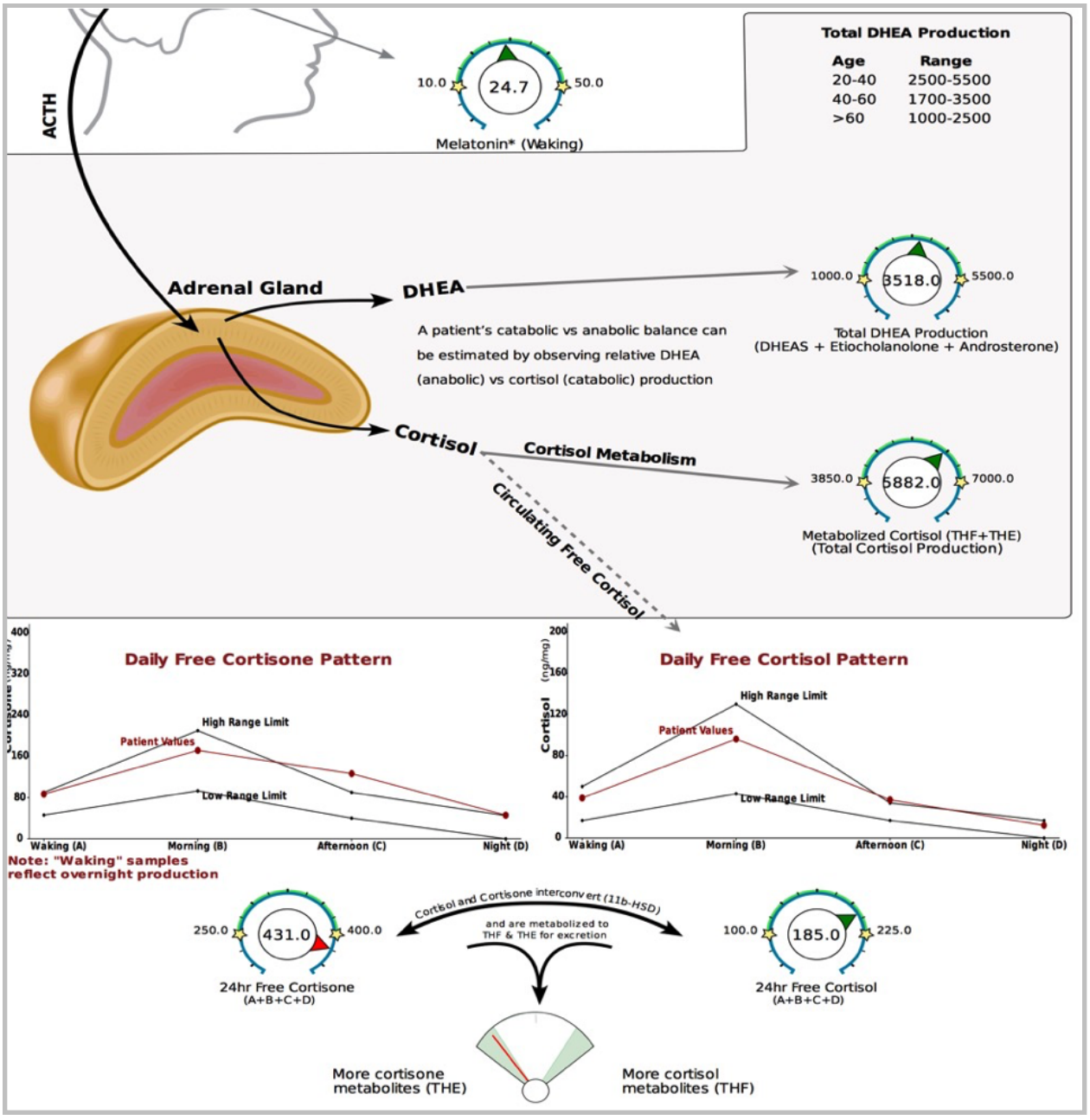
How is this presentation here connected to the patient's symptoms? Cortisol is required to resolve the inflammatory response, so if you have low cortisol, you can't turn off inflammation, and that's likely what is contributing to his ongoing knee pain. He's a semiretired, successful investor and entrepreneur, fairly low-stress lifestyle. However, he did work 70- to 80-hour weeks for about 14 or 15 years with travel, regular travel across time zones three to four times a month minimum, so he had huge stress, circadian disruption. You could almost think of this as like a PTSD kind of scenario. Then he had injuries. Remember that inflammation is one of the key drivers of HPA axis dysfunction, so an injury can be a big driver for HPA-D.

This is a great example of where HPA-D is definitely affecting the patient, but neither his previous clinicians nor he suspected that that was something that was driving his symptoms and preventing him from getting well.

Protocol for low cortisol with inflammation

Intervention	Dosage/Comments
Vital Adapt (Natura Health Products)	2 caps TID
Adrenal glandulars (Dr. Ron's)	3 capsules in the morning with breakfast
Acetyl-CH (Apex Energetics)	1 cap TID
5-HTP (Jarrow)	50 mg one hour before bed
Doc Parsley's Sleep Cocktail	One packet one hour before bed
Boswellia AKBA (Pure Encapsulations)	1 cap OD or BID
Longvida curcumin (Pro-Health)	1 cap OD or BID
Fish oil (Dr. Tobias or other)	2.4 g of EPA and 1.8 g of DHA per day

Here's the protocol for low cortisol with inflammation: Vital Adapt, adrenal glandulars, Acetyl-CH, 5-HTP, Doc Parsley's Sleep Cocktail, boswellia, curcumin, and then higher-dose fish oil to get a quick anti-inflammatory effect.



Next patient is a 25-year-old male. Chief complaint is he has been suffering from depression and dysthymia since 2004, possibly longer. He generally feels emotionally numb with a vague malaise and anxiety. He described himself as not having a blunted affect, and he does have emotions, but it just feels like there is a layer of insulation around them. He has disturbed sleep. He woke frequently

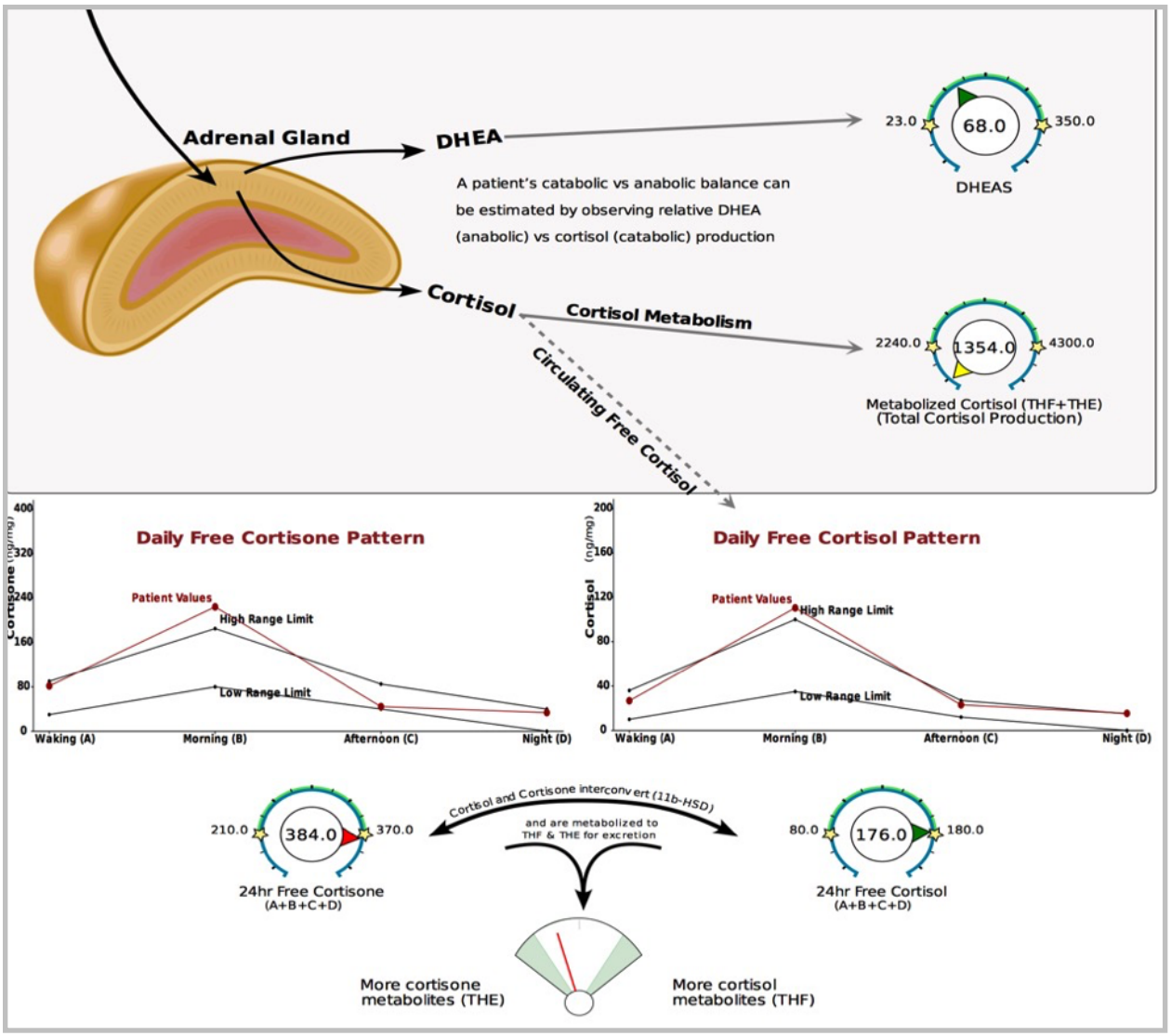
through the night, often feeling hungry and needing to eat. His free cortisol is high-normal. Diurnal cortisol rhythm is normal at all time points except slightly high in the afternoon. Free cortisone rhythm was very similar, higher in the afternoon and borderline high at night. His total free cortisone was high, so that biases the cortisol finding upward. Cortisol metabolites were normal but toward the upper end. Total DHEA was normal. Cortisol-to-DHEA ratio was normal. Cortisol-to-cortisone balance was low, favoring cortisone. Melatonin was normal.

This is another good example of where you have to look at the whole picture. He had depression, malaise, anxiety, and disturbed sleep. He woke frequently, often feeling hungry at night, and these are classic signs and symptoms of HPA axis dysfunction. At first glance, his labs are relatively normal, but the total free cortisone is high, and that biases the cortisol finding upward. The free cortisone rhythm suggests that the production in the afternoon and evening is high, and it fits with his symptoms. Cortisone metabolites were also high, and that suggests he is producing a lot of cortisol, but the body is trying to protect itself by inactivating cortisol to cortisone. I would treat this patient for HPA axis dysfunction based on the overall clinical presentation.

Protocol for high-normal cortisol with disrupted diurnal rhythm

Intervention	Dosage/Comments
HPA Balance (Vital Plan)	1 cap TID
Kavinace (Neuroscience)	1-2 caps before bed
Acetyl-CH (Apex Energetics)	1 cap TID
5-HTP (Jarrow)	50-100 mg 1 hour before bed
Metabolic Synergy (DFH)	2 caps TID

Here's the protocol for high-normal cortisol with disrupted diurnal cortisol rhythm. We have HPA Balance; Kavinace; Acetyl-CH for the rhythm; 5-HTP, which can help with sleep and improve mood; then Metabolic Synergy for its balancing effect on blood sugar to prevent those frequent hunger episodes, which are suggestive possibly of hypoglycemia. So, addressing the circadian disruption is really the most important thing in this patient.



The next patient is a 29-year-old female. Constant fatigue, lack of energy, feeling bloated, full all of the time, constant headaches, and irregular bowel movements. Free cortisol was high-normal, almost out of range. Diurnal cortisol rhythm was normal waking, high morning, high-normal afternoon, and high at night. Free cortisone rhythm was similar. Total free cortisone is high, so that supports the free cortisol finding. Cortisol metabolites were very low. The lower end of the range is 2,240, and she was 1,354, so this is a discordant pattern. Total DHEA is normal. Cortisol-to-DHEA ratio is low. Cortisone-to-cortisol balance was normal. Melatonin was not tested, so actually when I said total DHEA was normal, I meant DHEA sulfate. This was the advanced adrenal panel.

Pop quiz here. What should you be thinking about right away given the symptoms and the labs? Yep, hypothyroidism. This patient had a TSH of 3.6, which is high. It's not out of the lab range, but it's well above what a normal TSH is. Her total T4 and T3 were normal, but her free T3 was low at 1.9. She had antibodies to both thyroglobulin and thyroperoxidase, so this is probably early-stage Hashimoto's. It's a case where it makes the most sense to first address thyroid pathology and then

retest and assess HPA axis function at that point. From there, you may be able to treat in a more appropriate way.

Now, if the patient is having significant symptoms of HPA axis dysregulation, like this constant fatigue and lack of energy, it is certainly not inappropriate to give her some support, HPA axis support, while you're addressing her thyroid function too, but it's a little more complicated when you have the high free cortisol because if you give adaptogens, that could increase the free cortisol further without bringing the metabolized cortisol up. Sometimes it's easier to address the thyroid first and then see what the panel looks like after that.