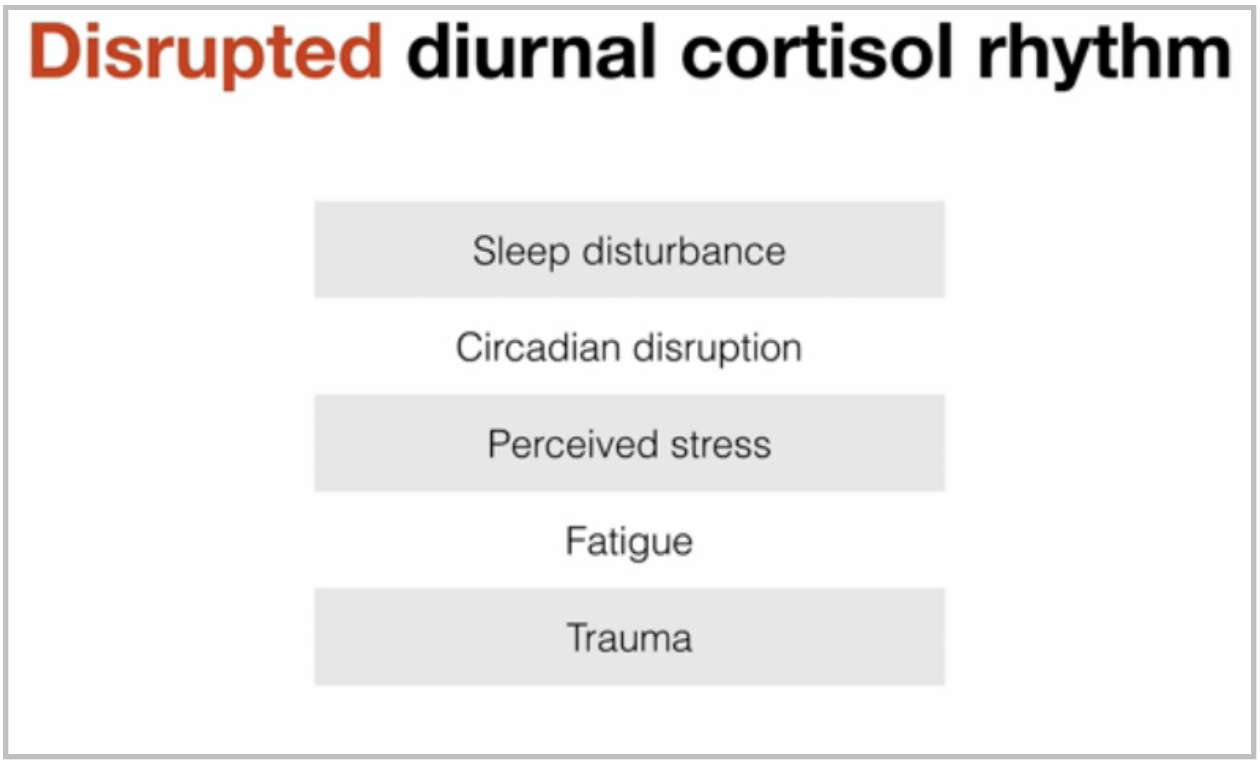
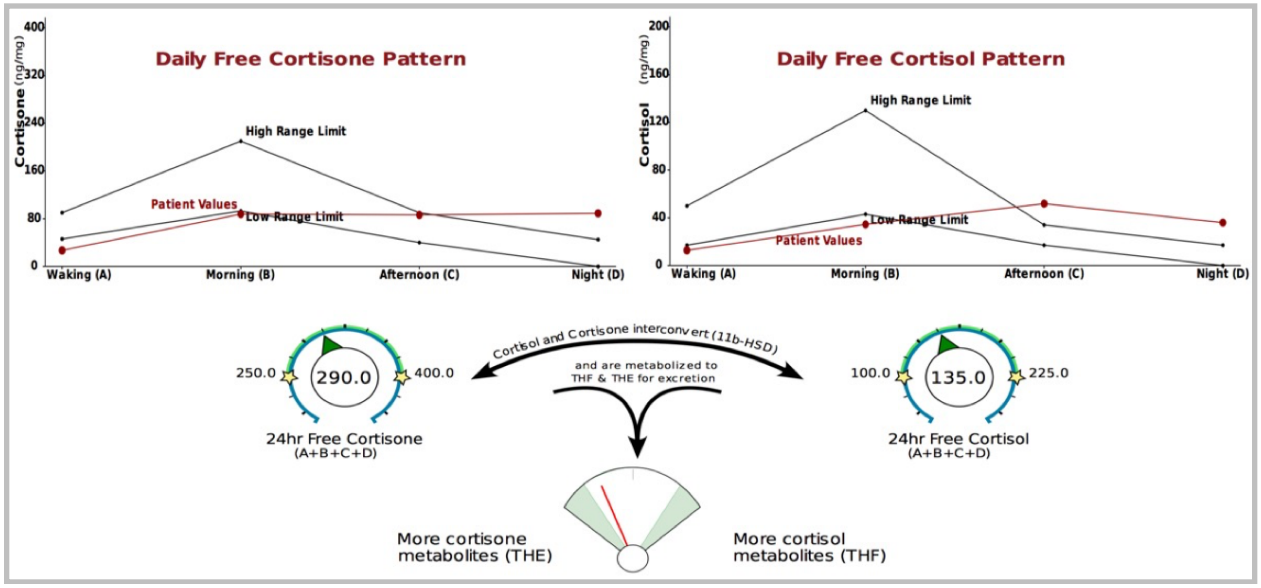
# HPA-D: DUTCH Test I - Part 3

Next pattern is disrupted diurnal cortisol rhythm.

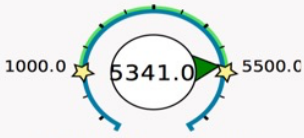



This is observed in sleep disturbance, circadian disruption, conditions characterized by high perceived stress, fatigue, and trauma.

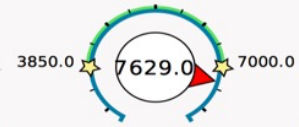



**Total DHEA Production**

| Age | Range |
|---|---|
| 20-40 | 2500-5500 |
| 40-60 | 1700-3500 |
| >60 | 1000-2500 |



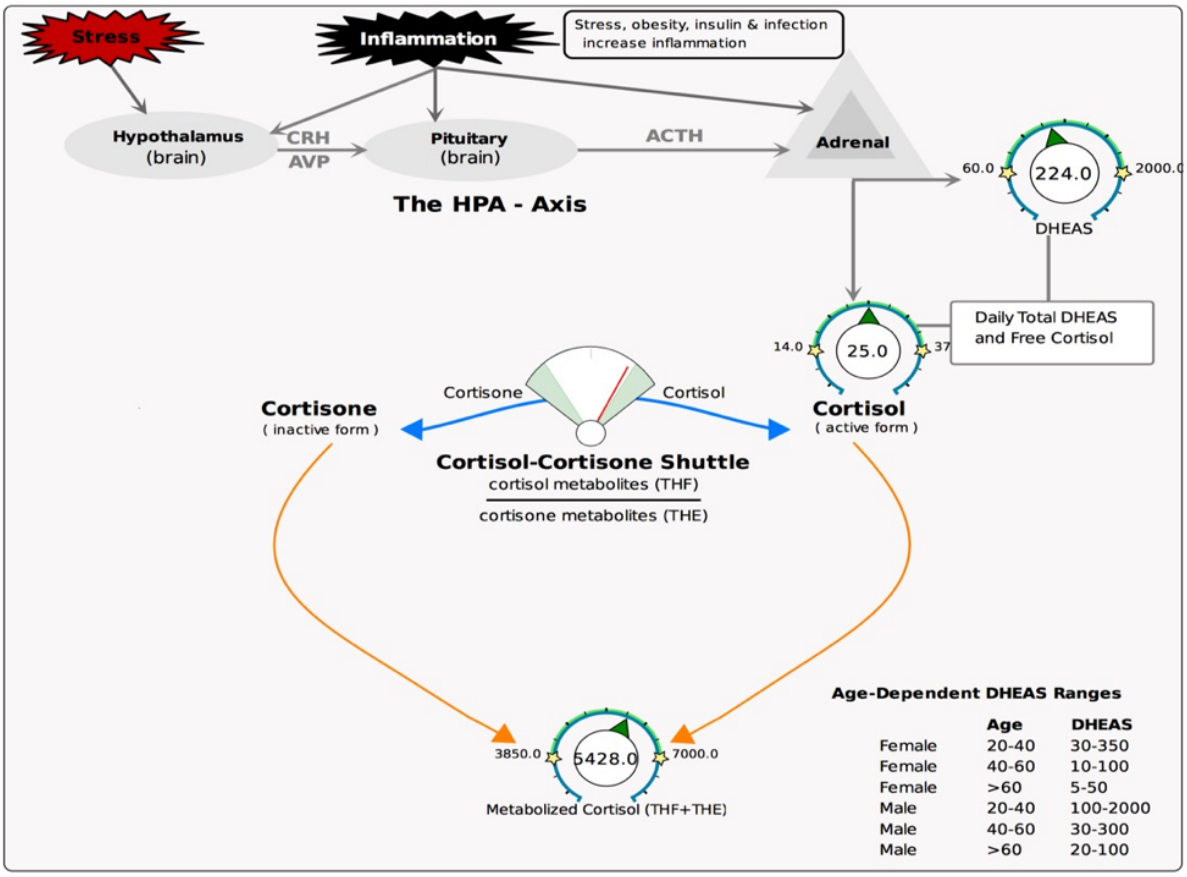

Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

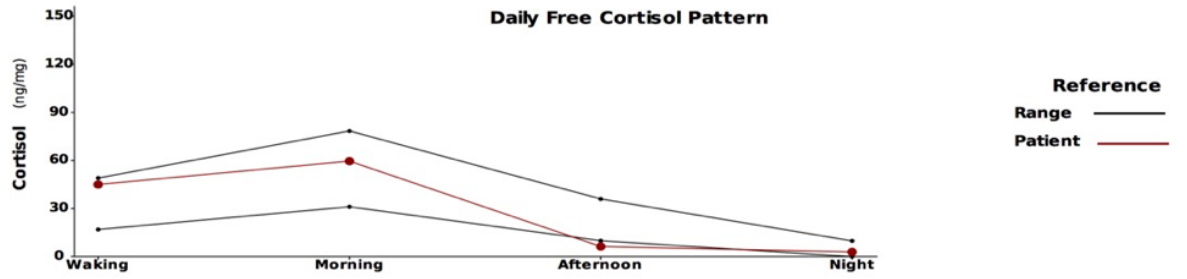



Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

So here is an example of disrupted cortisol rhythm with normal free cortisol. This is a case where the rhythm is clearly off, but when you add up and estimate the cortisol production over the full 24-hour period, it is normal. So this patient is a 19-year-old male with a history of Lyme disease, chronic fatigue syndrome, and food allergies. His metabolized cortisol was high, over 7,000 as you can see there on the right, and this is somewhat typical for chronic fatigue syndrome, but in chronic fatigue syndrome, free cortisol will often be low, which it isn't in his case.

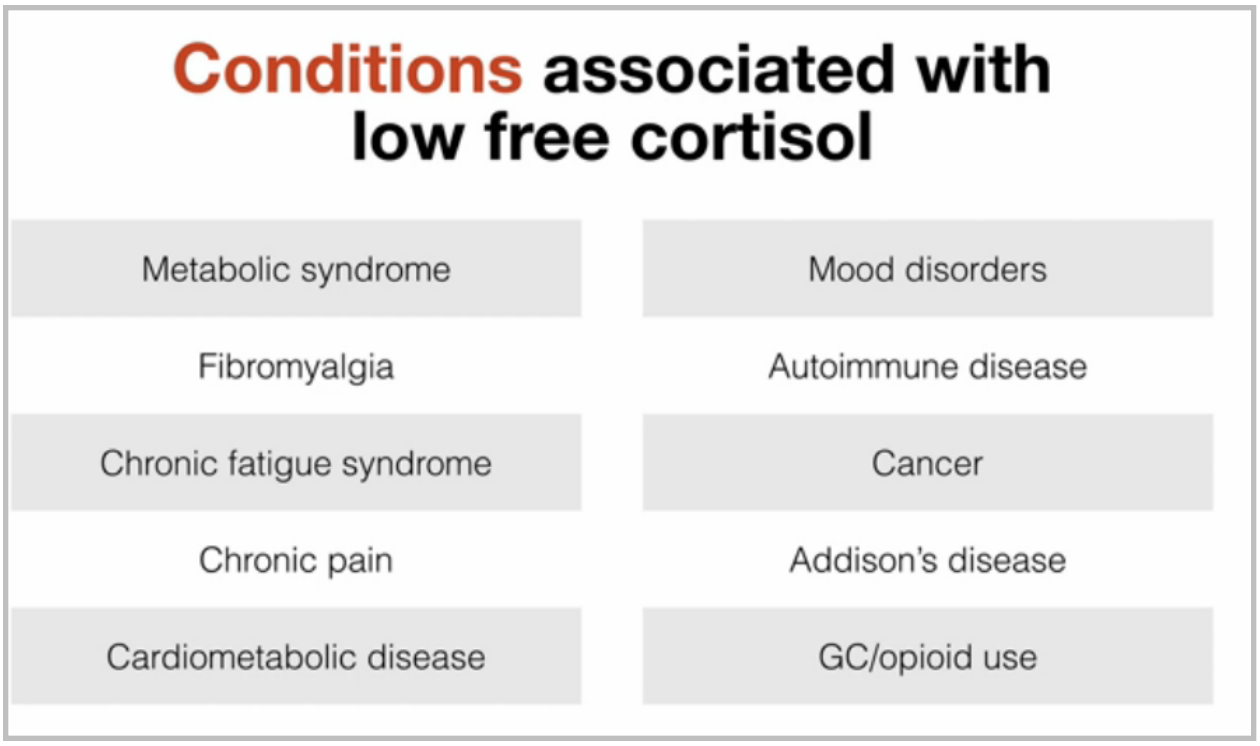
As you can see, his cortisol is low in the morning when it should be high, and that is the most important time point, as we've discussed. Then it is high or high-normal in the afternoon, depending on whether you are looking at cortisol or cortisone, and then it is high in the evening at night when it should be low, so this person has a flipped diurnal rhythm, and it is very common in patients who are dealing with chronic fatigue and other conditions characterized by fatigue. Their cortisol is low when it should be high in the morning and high when it should be low at night. They will often feel really tired in the morning. They might have that second wind at night, but they're going to have really nonrestorative sleep and significant fatigue.



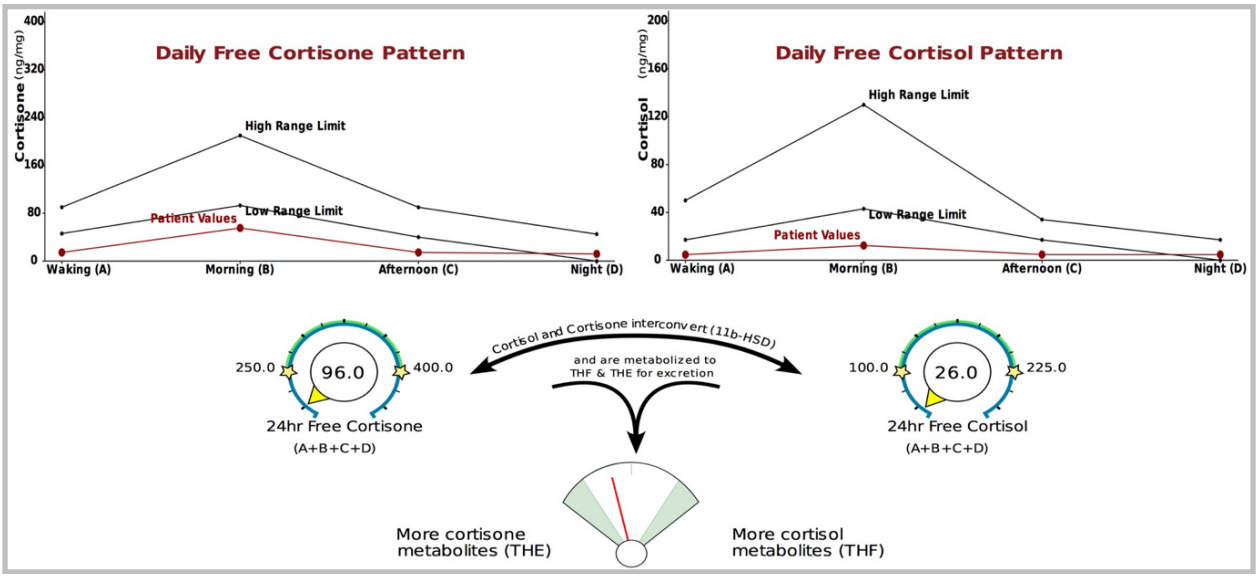




Here is a patient with slightly low free cortisol in the afternoon as the only abnormality that is showing up on his test. His total free cortisol, DHEA sulfate, and metabolized cortisol are normal.

Note that this is an older version of the test results that did not report free cortisone on the chart at that time, but if you looked at the full report, his free cortisone was normal as well. So the question is, should this be treated, and the answer is, it depends on the case. Remember, lab assessment of the HPA axis is imperfect. There are many regulatory effects on cortisol in the HPA axis that can't be tested for and won't show up in labs. This patient is a 40-year-old male with inactive Crohn's disease and severely disrupted sleep, so despite these normal test results, we still focused a lot on the HPA axis in the treatment protocol, and he benefited a lot from that focus.




The next pattern we're going to talk about is low free cortisol, so this is observed in metabolic syndrome and insulin resistance, fibromyalgia, chronic fatigue syndrome, chronic pain, cardiometabolic disease, mood disorders, autoimmune conditions, cancer, Addison's disease, and glucocorticoid or opioid use.

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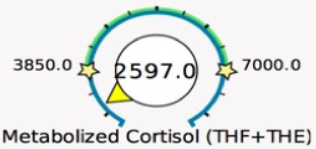
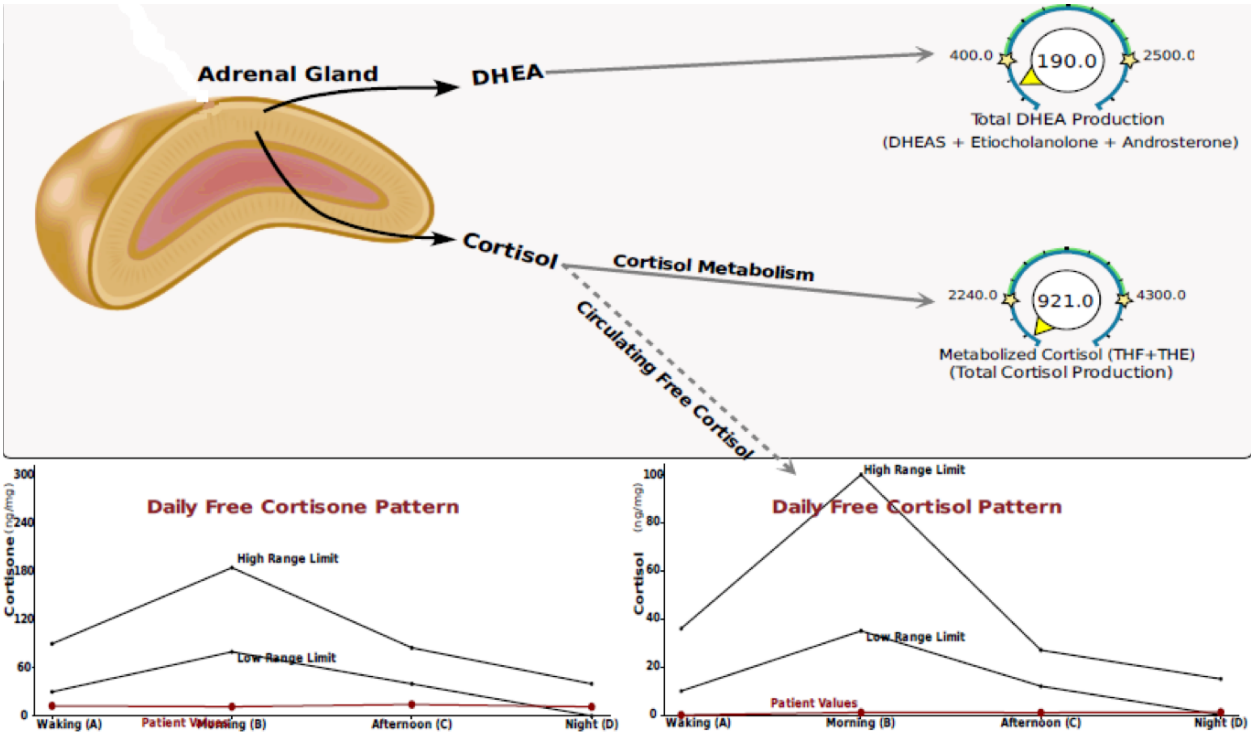
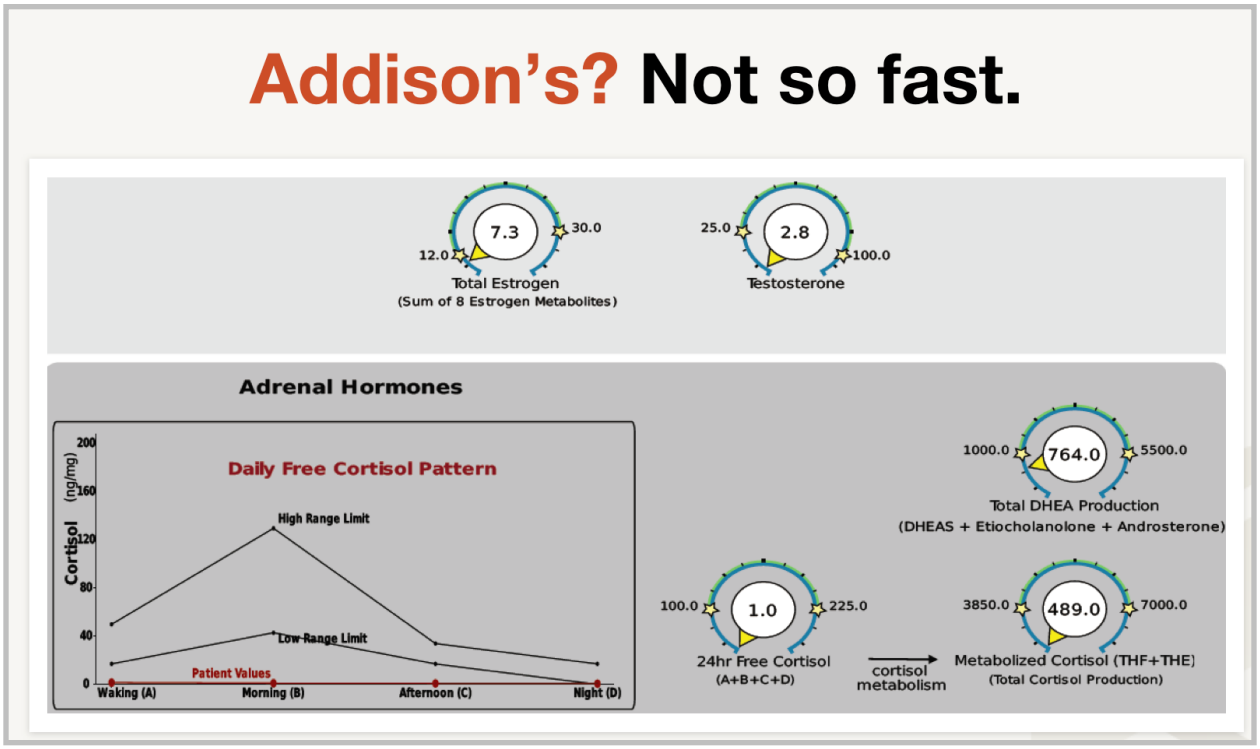



This is a 47-year-old male with chief complaint, in his words, was “persistent knee pain in both knees, diagnosed as tendinosis of the patella tendon for almost two years. Despite extensive modification of my athletic activities and commitment to physical therapy, my knees are not getting better. I believe that internal health issues are preventing my tissue from healing.” As you can see, his intuition was correct. His free cortisol is very low, not in the range where you would

expect Addison's, which would be below 10 for free cortisol, but still quite low as indicated by the gauges there. His metabolized cortisol was also quite low, and this patient had high blood sugar and a toxic level of vitamin D, a very high level of vitamin D, and that can cause hypercalcemia and increased bone resorption, which could be contributing to his condition. Cortisol, as you know, is an anti-inflammatory hormone, so when cortisol levels are really low like this, the patient won't be able to resolve the inflammatory response, and they'll get stuck in a chronic inflammatory catabolic state, and this is exactly what was happening with his tendinosis and difficulty recovering from exercise. He also had Blastocystis hominis but no significant gut symptoms, so it is possible that was contributing to low-grade inflammation, though it is very difficult to know that, as you will recall from the gut unit.




Here is a lab result from a patient who did have Addison's disease, so you can see very low DHEA, very low metabolized cortisol. The level was 921, the lower end of the range was 2,240, and then extremely low free cortisol. If you look at the graphs there, you just see a flat line all the way across for cortisone and the flat line for free cortisol that is almost off the chart. It is just at the very bottom of the chart. We referred this patient out. His total free cortisol, which isn't pictured on this slide, by the way, it was 3. So, as I mentioned before, if you see a total free cortisol below 10, that is a red flag for Addison's. I referred him to an endocrinologist, and he did, in fact, have Addison's.




However, Addison's is quite rare. That lab I showed you on the last slide was the single case that I'd seen in my entire career so far. Most cases of very low or flat-line cortisol that you will see are caused not by Addison's disease but by medication use, so both glucocorticoids and opioids can suppress cortisol production.

The results on this slide are from a young male patient who was on opioids, and his total free cortisol was 1, as you can see there, so that obviously would be a huge red flag. You might be thinking of Addison's when you see that. His metabolized cortisol was 49, in the range of 3,850 and up, and his total DHEA was quite low. His testosterone and estrogen were really low as well. His testosterone was 2.8, in the range of 25 to 100, but in this case, it is not Addison's. It was opioid-based suppression of cortisol.

When we talked about corticosteroid suppression of cortisol on a previous section of the HPA axis unit, you may recall that about 42 percent of patients taking corticosteroids over the long term do have adrenal insufficiency, so make sure that you pay attention during the intake to what medications your patients are taking, and look for things like prednisone, which is prescribed for autoimmune diseases like inflammatory bowel disease and rheumatoid arthritis, and even steroid inhalers for asthma in addition to opioids.