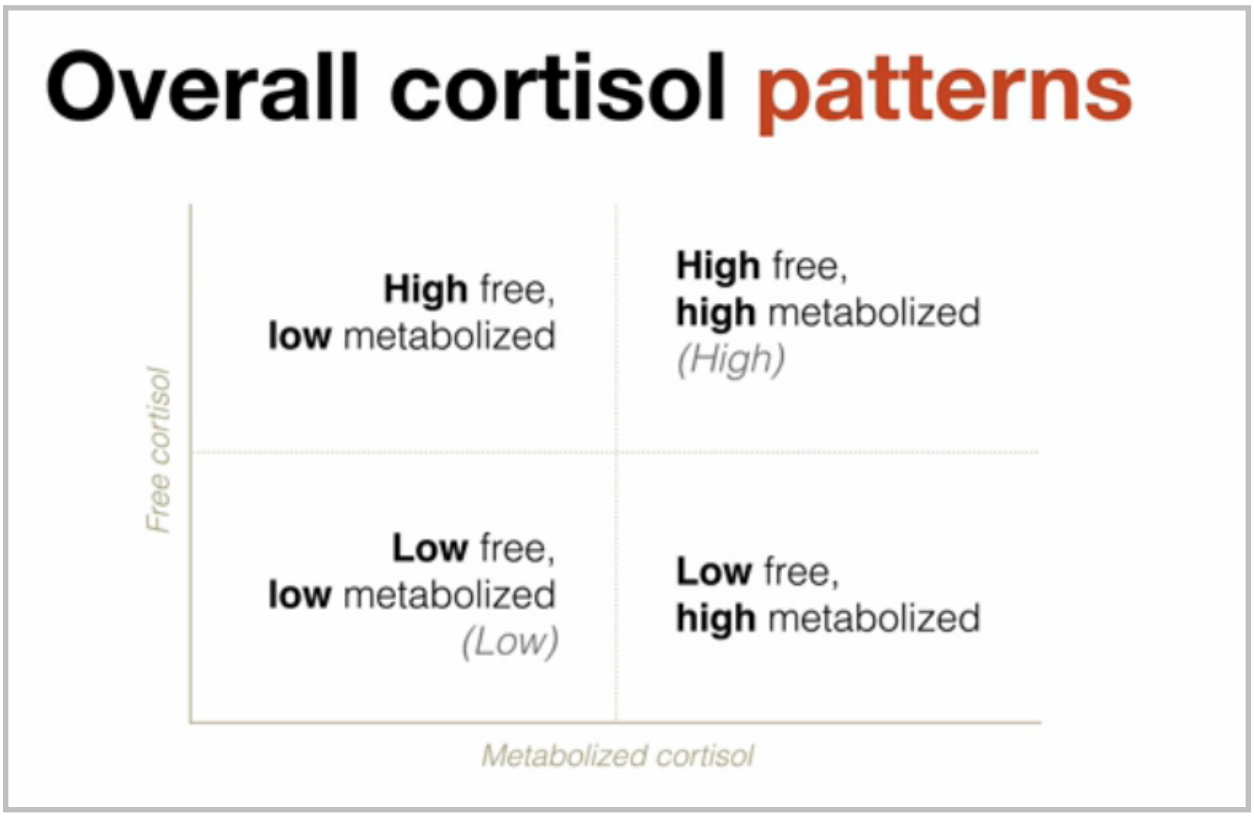
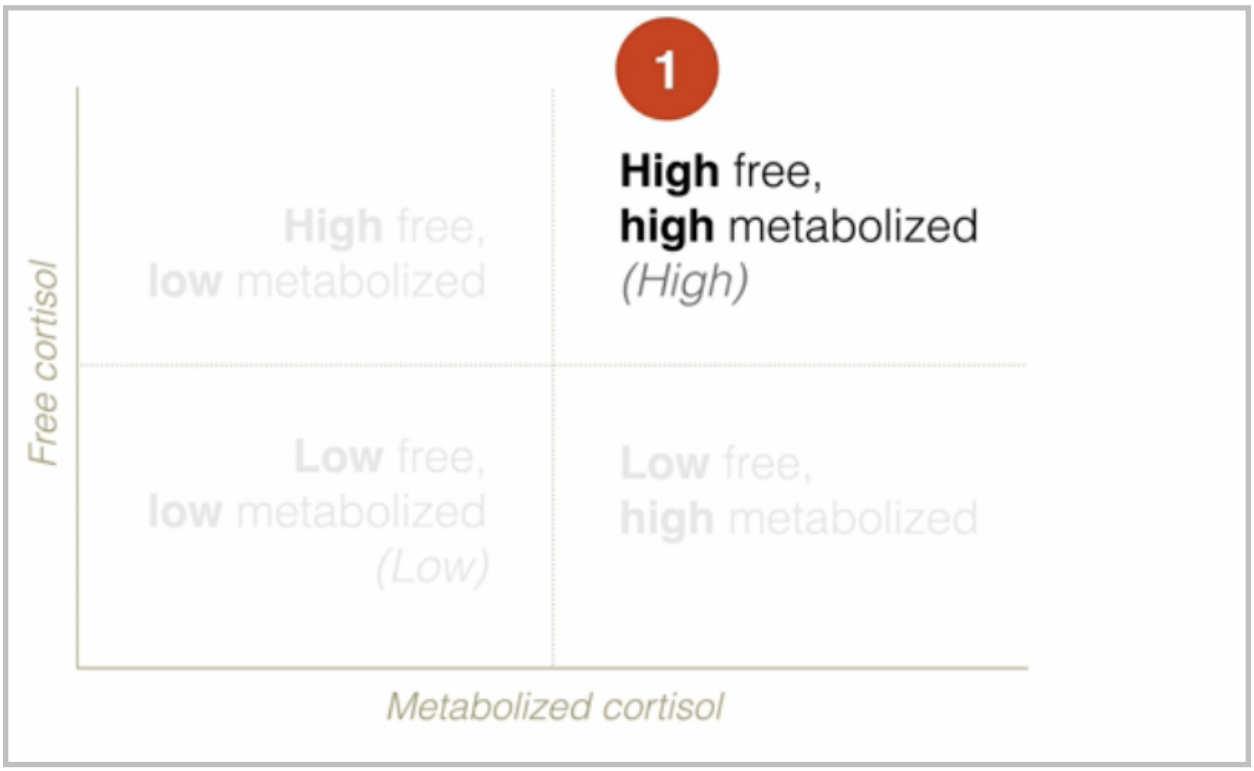
KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

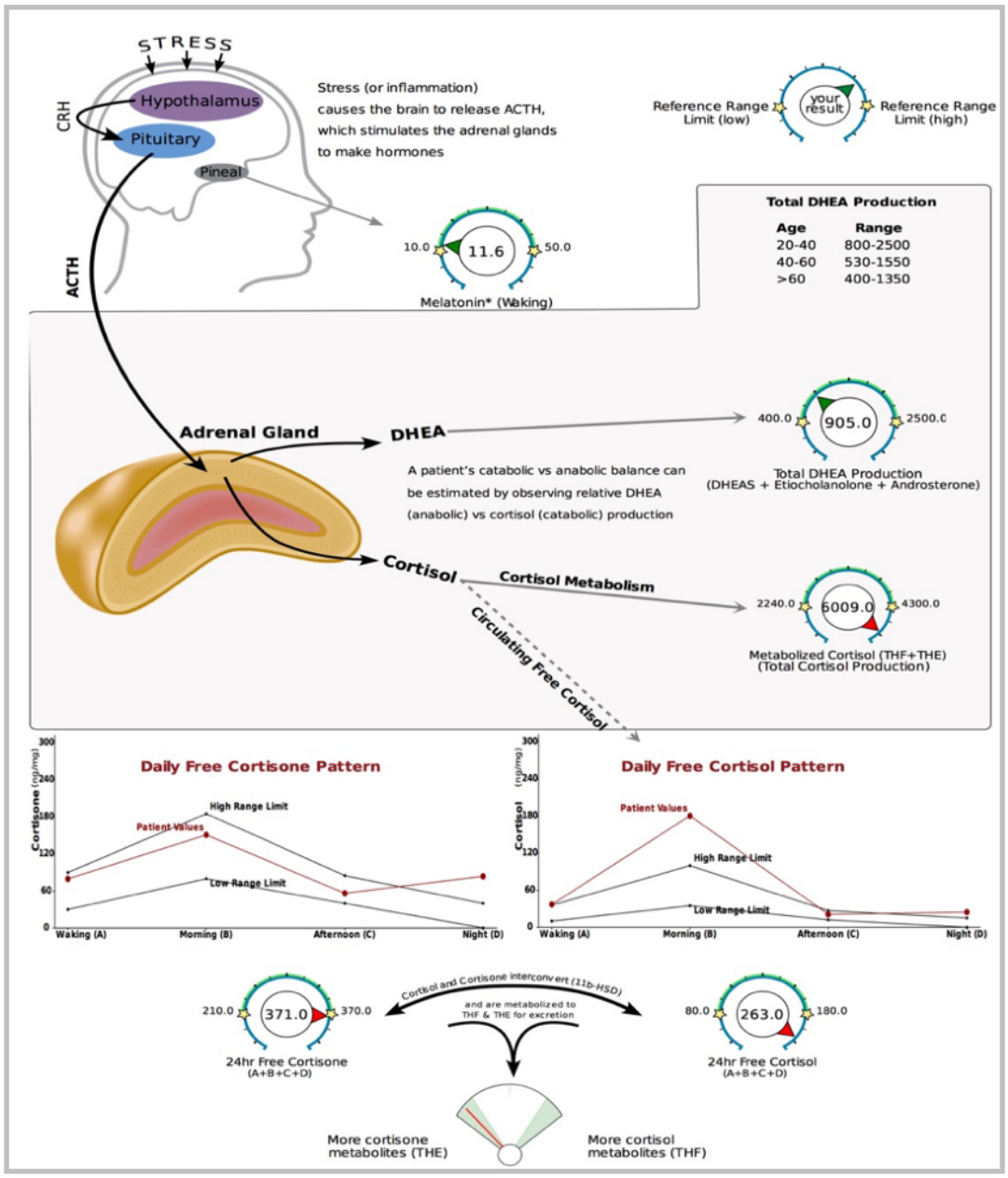
HPA-D: DUTCH Test I - Part 4



Okay, here are four key cortisol patterns that you're going to see, and this is where the DUTCH test really shines because we're able to differentiate between free cortisol and metabolized cortisol, and as you're about to learn, there are two patterns where free cortisol and metabolized cortisol are concordant, so they are the same. They track each other. Then there are two other patterns where free cortisol and metabolized cortisol are discordant, and these all mean different things, so it is really important to have those differentiated and separated out.



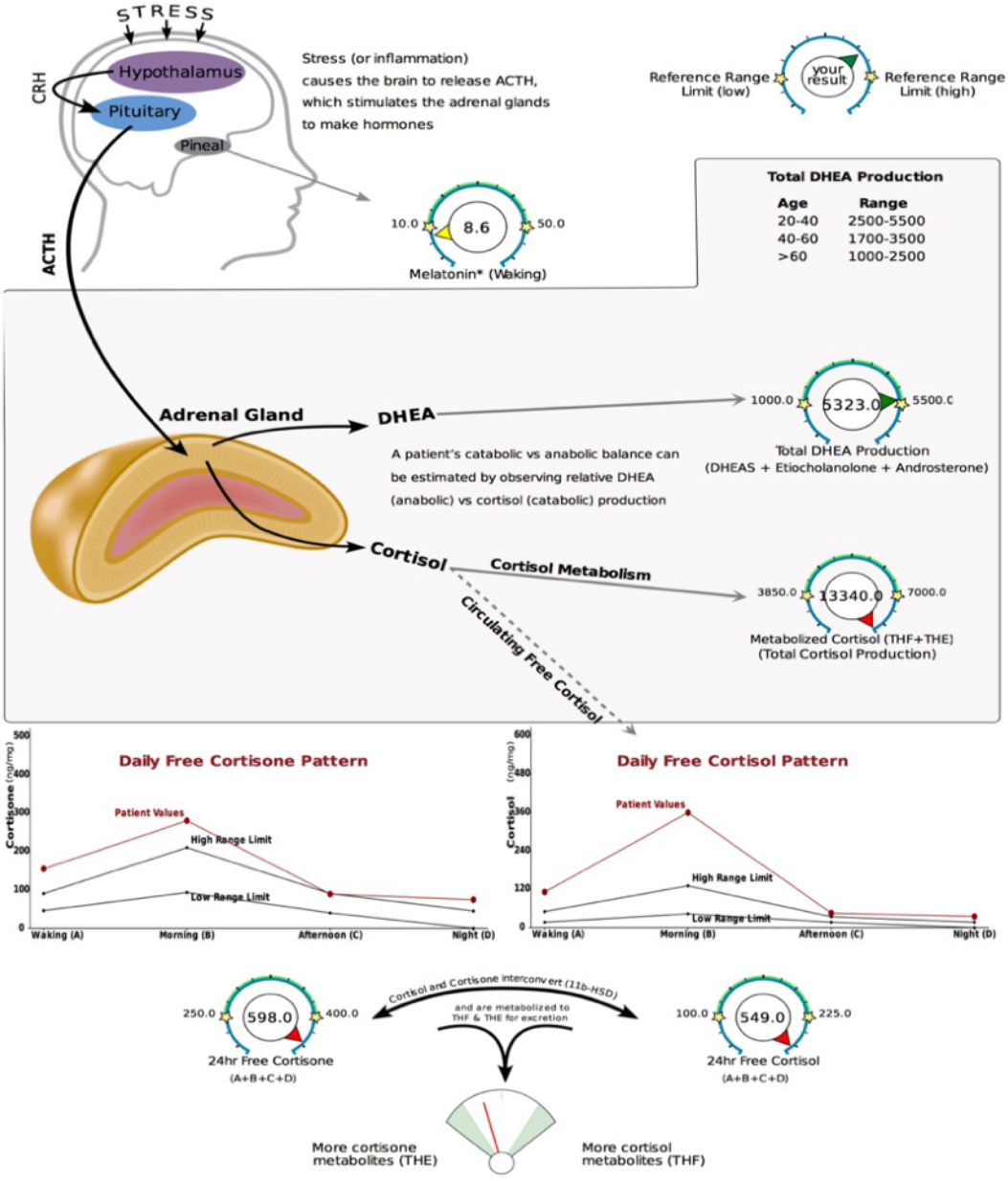
So the first pattern we're going to talk about is high free cortisol with high metabolized cortisol. This is most often seen in Cushing's disease or pseudo-Cushing's syndrome, high perceived stress, and inflammatory conditions like PCOS, IBD, depression, etc.



This patient is a 51-year-old female with PCOS and Hashimoto's. She had high free cortisol, high free cortisone, and high metabolized cortisol. Her tetrahydrocortisone was particularly high, and PCOS patients will often also see high DHEA as well as high estrogens and androgens in addition to high cortisol, although as you can see, this patient's total DHEA production was normal.

This patient also complained of irritability, fatigue, and disrupted sleep, and check out her nighttime free cortisol and especially her nighttime free cortisone. You can see here she is making more cortisone compared to cortisol, and that will tend to happen when cortisol levels are very high. It is a wise attempt of the body to try to protect itself by converting as much cortisol to

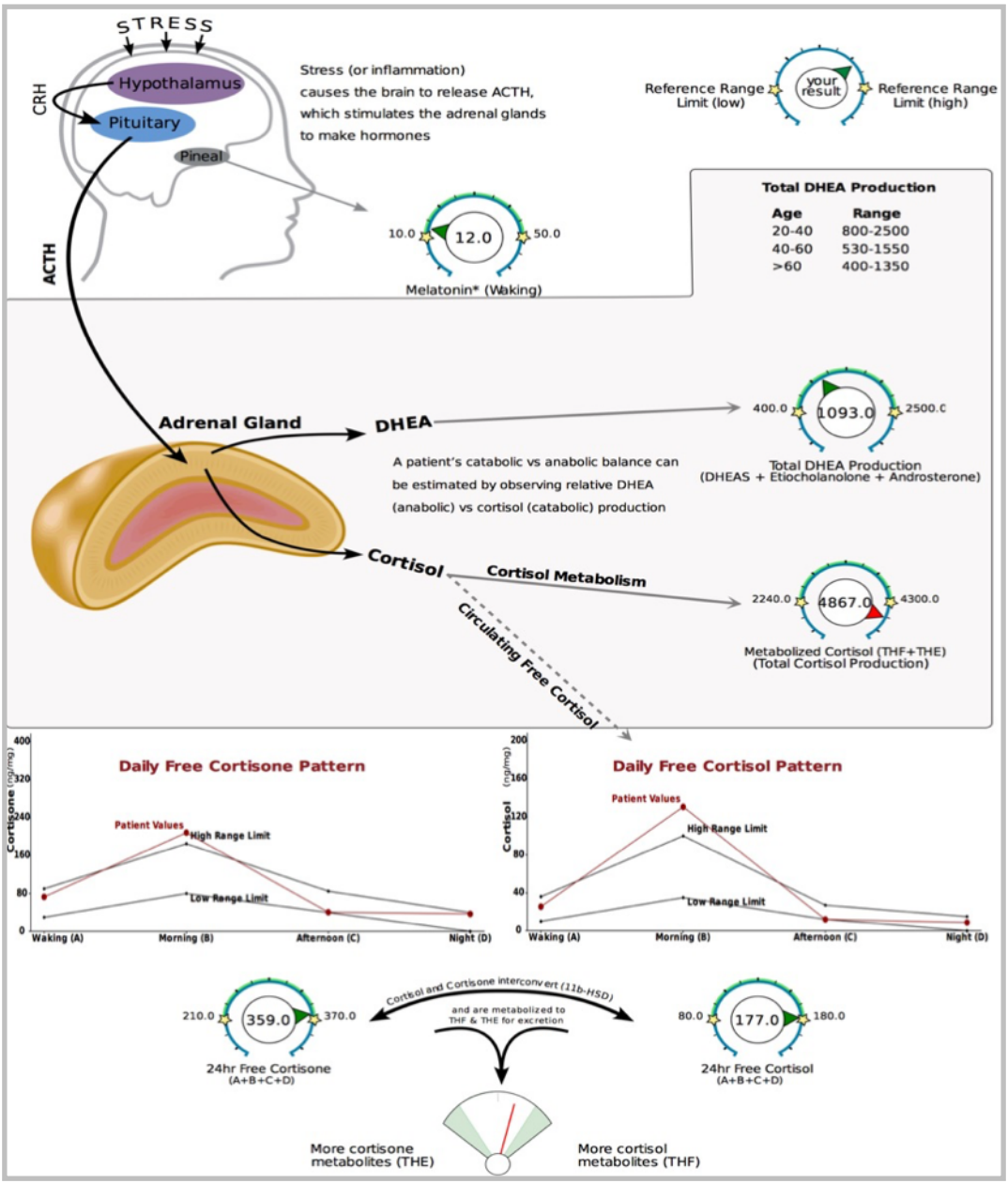
cortisone, which is less active, as it can. That's an appropriate response, but in this case, it is insufficient to protect against the effects of this very high cortisol picture.



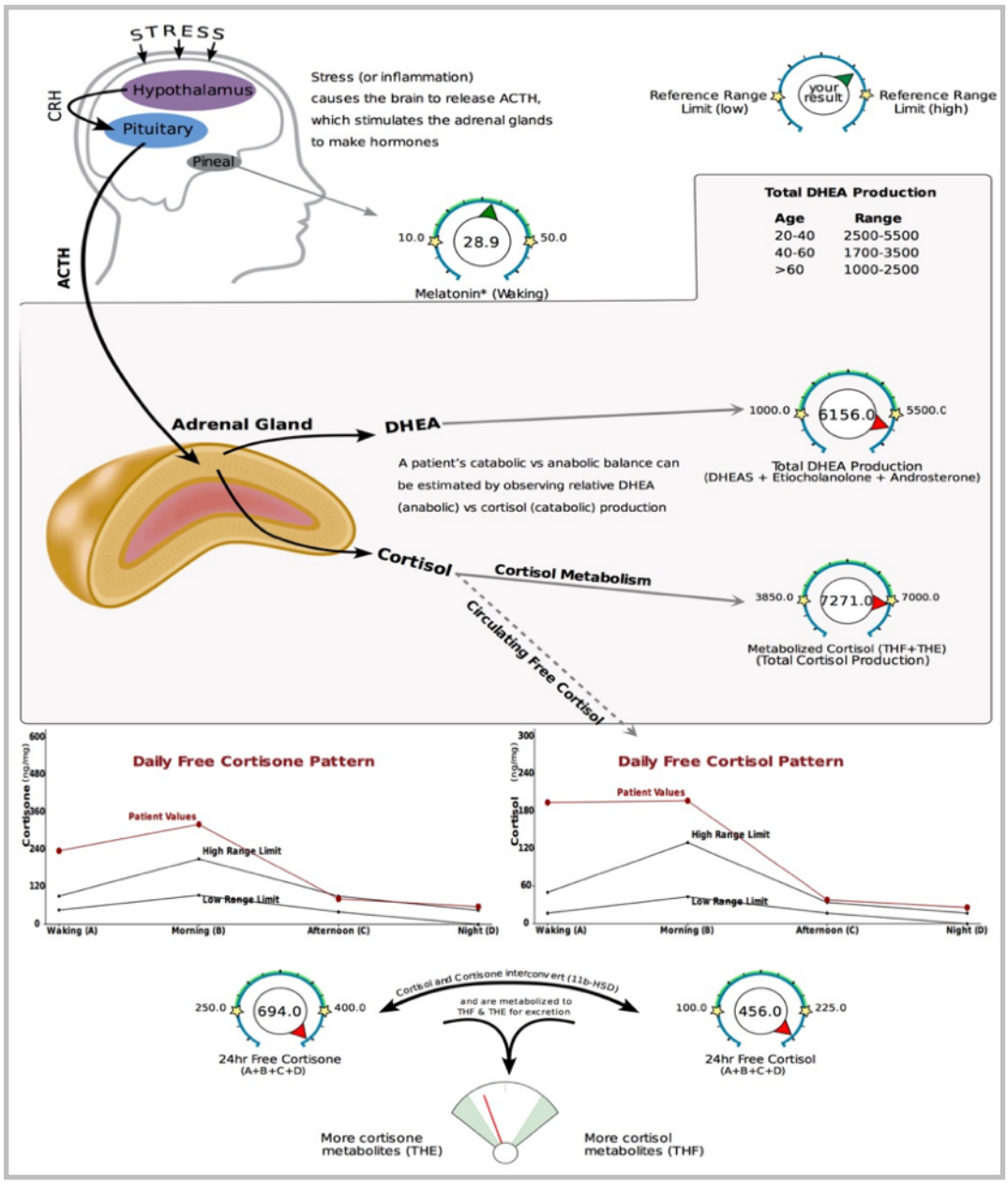
This result is from a 25-year-old with pre-diabetes, GERD, gut issues, and eye floaters. Other test results for this patient revealed severe gut dysbiosis, gut inflammation, dyslipidemia, vitamin D deficiency, impaired methylation, systemic inflammation and inflammation in the liver, high testosterone, and high estrogens. As you can see, her free cortisone, free cortisol, and metabolized cortisol are all very high. Metabolized cortisol is 13,340, nearly two times the upper end of the

range. The 24-hour free cortisol is 549, which is two times over the top of the range. Could this be pseudo-Cushing's syndrome? The literature would suggest metabolites should be four times the reference range, but that as a single marker is probably not as diagnostic as the high nighttime cortisol, and that is only slightly elevated in this case. Remember, we should expect to see that as three to four times the upper limit in Cushing's disease or pseudo-Cushing's syndrome. In this case, I think this patient's high cortisol levels are more related to being overweight.

As we'll talk about later, when a patient becomes obese, what we typically see is normal or even low free cortisol and very high cortisone metabolites, but according to the scientific literature, that doesn't tend to happen until the patient becomes actually obese. In overweight patients we more regularly just see high cortisol, both metabolized and high free cortisol, but this phenomenon where we see low free cortisol and high metabolites doesn't become statistically significant until the patient is actually obese. So overweight people are kind of similar to lean up to a certain point, and then it seems like a switch gets flipped once they pass a certain BMI, and we see that discordant pattern with low free cortisol and high total cortisol.

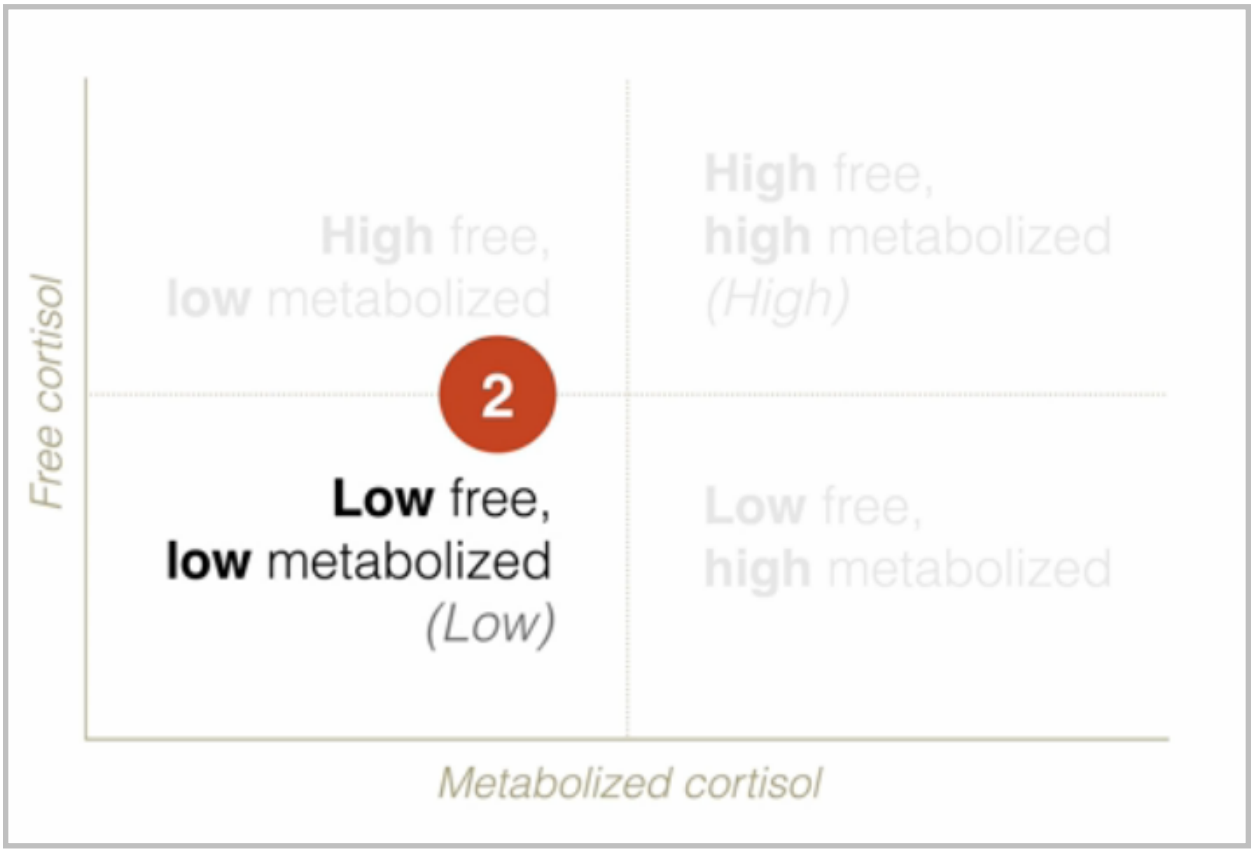


This patient is a 60-year-old female with chief complaint of recurring gastrointestinal issues and SIBO. She had high fasting blood sugar and hemoglobin A1c, which are signs of dysglycemia that we'll be talking about later. She also had low vitamin D, functional anemia, and markers for decreased mitochondrial function. These are all things that would activate the HPA axis and stress response, and it explains her high cortisol level. So, she had high metabolized cortisol, as you can see, and her free cortisol wasn't out of the lab range, but it was very close. The upper end is 180, and she was at 177. Upper end of the free cortisone range is 370, and she was at 359.



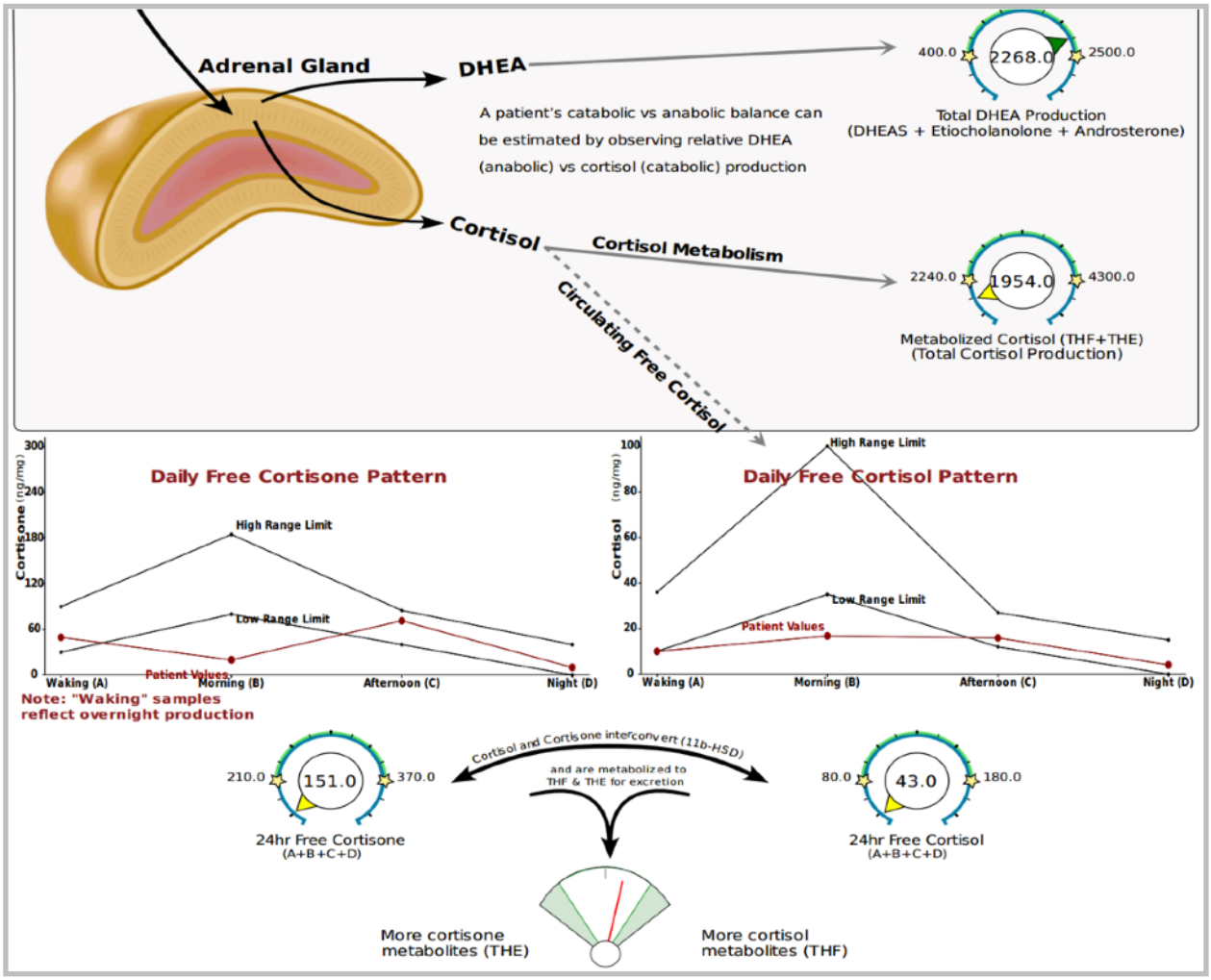
This is a 23-year-old male who has been diagnosed with postural tachycardia syndrome. The most common form is called partial dysautonomic, or PD, form. It's characterized by mild peripheral autonomic neuropathy caused by an inability of the peripheral vasculature to constrict in the face of orthostatic stress, like when they are standing up. The less common form is called hyperadrenergic POTS, and that is what he has. These patients tend to report a gradual and progressive onset of symptoms as opposed to an abrupt onset. They report significant tremor, anxiety, and cold, sweaty extremities when they're upright. Many will report a significant increase in urinary output after being upright for even a short period of time, and over half suffer from true migraine headaches. The hallmark of this form of POTS is that in addition to orthostatic tachycardia, they will often display orthostatic hypertension, so they will have significantly elevated

serum catecholamine levels with serum norepinephrine levels over 600 ng/mL, along with very high cortisol and DHEA, so as you can see here, 24-hour free cortisol was over two times the upper end of the range. The 24-hour free cortisone was significantly elevated. Metabolized cortisol was elevated, and DHEA was elevated.



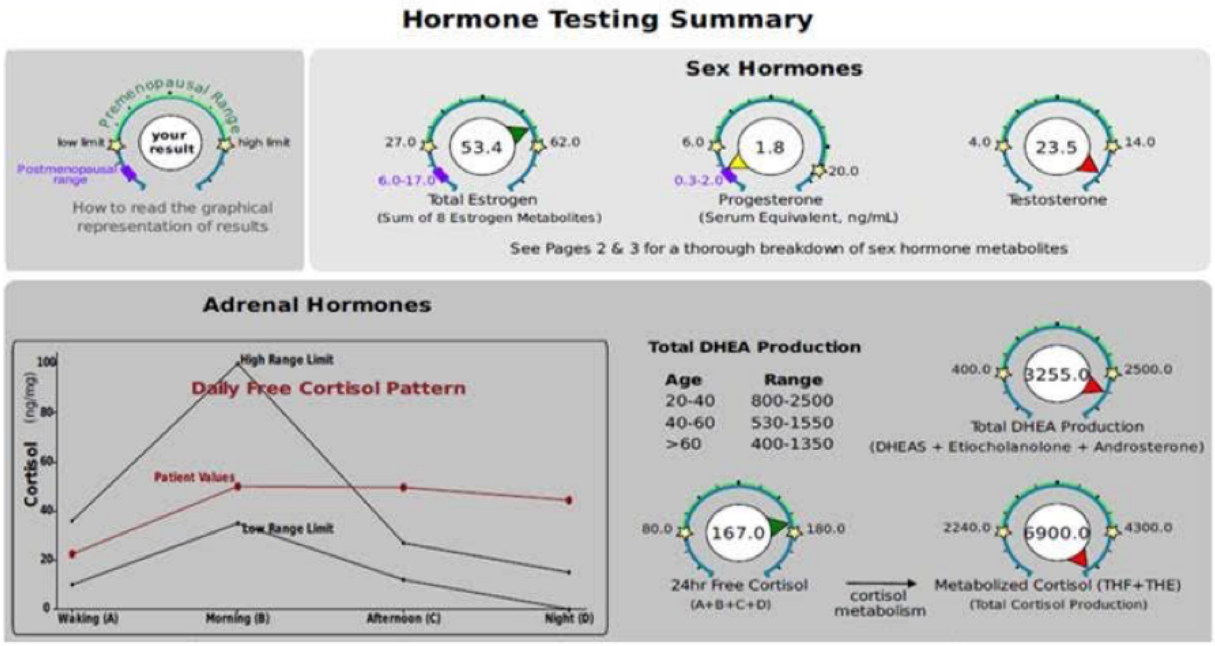
Okay, the next pattern is the second concordant pattern where free cortisol and metabolized cortisol are the same, but in this case low instead of high. This is most often seen in Addison's, medication-induced adrenal insufficiency, trauma, PTSD, and possibly chronic fatigue syndrome, though most studies actually of chronic fatigue show low free cortisol with normal metabolites.

So we just saw an example of low free cortisol and low metabolized cortisol in the previous section, which was the guy with knee pain. I actually had trouble finding other examples of this, and it's illuminating how few examples I could find in my case files given how many of these tests I've done, and it supports what we've already discussed in the HPA unit, which is that low cortisol overall is a lot less common than high cortisol.

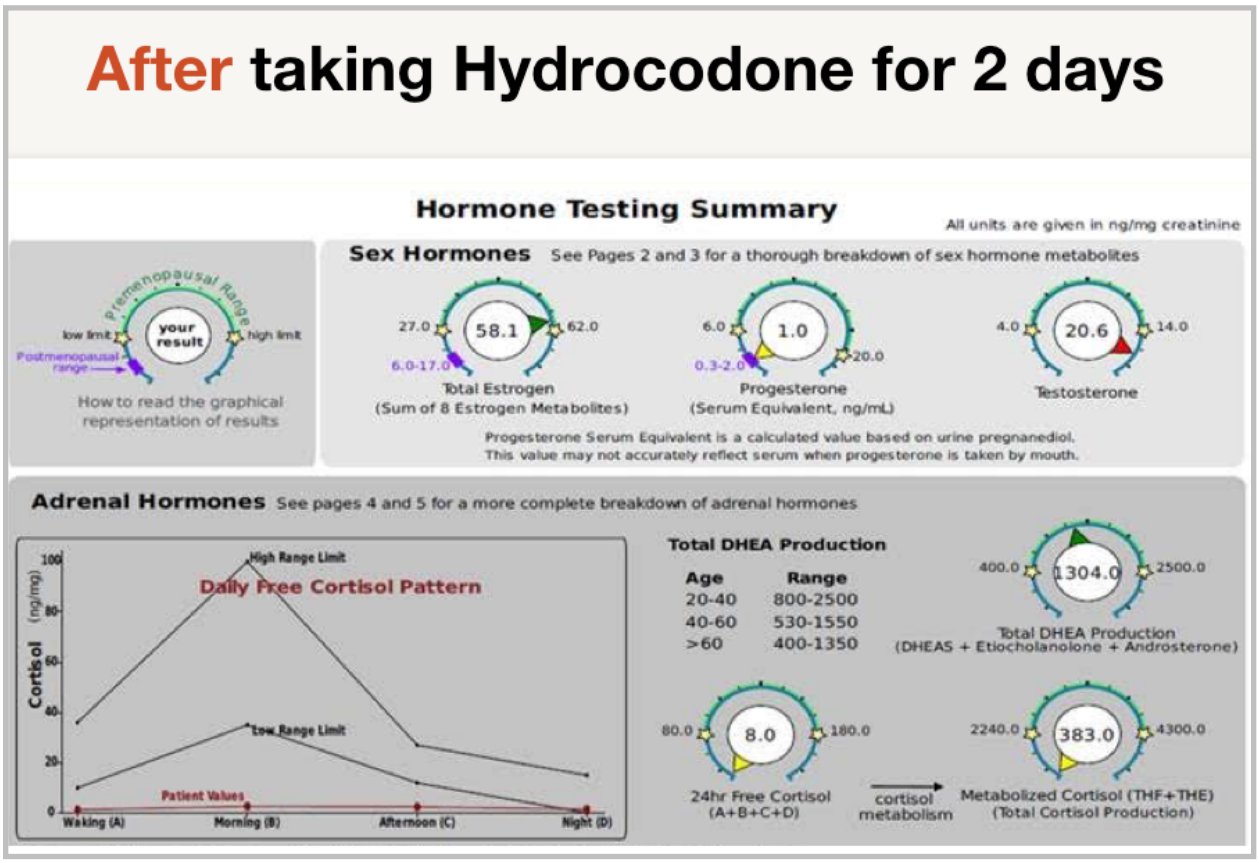


So this patient on this slide here is a 36-year-old female with a chief complaint of food sensitivities and recurrent UTIs. Her stool test results indicated SIBO, significant pathogenic and insufficiency dysbiosis, and gut inflammation. Other results indicated borderline B12 deficiency and hypothyroidism. Cortisol helps resolve the inflammatory response, so when cortisol is low, the patient can't turn off the inflammation, and that could be contributing to her gut issues and food sensitivities as well as her UTIs. On the other hand, her gut issues are likely contributing to low cortisol levels, so this is a classic example of the vicious cycle that we've talked about so many times.

Before taking Hydrocodone



After taking Hydrocodone for 2 days



Here is an example of low free and total cortisol that is caused by opioid use. This is a 23-year-old woman who got her wisdom teeth removed, and she collected presurgery examples on the 14th and 15th of the month. Then she had surgery on the 16th and was on hydrocodone after surgery and took one pill every four to six hours from the 16th to the 19th of the month. Then she collected the after-surgery samples beginning on the 18th in the evening and then on the 19th. You can see the very dramatic difference between her results. Her presurgery example is on the left, and she actually had high metabolized cortisol and high total DHEA, and she had very high free cortisol, particularly in the afternoon and the evening. Then after taking hydrocodone for two days, her free cortisol dropped to 8, so that is again in Addison's range, and she has a completely flat-line cortisol curve at the very bottom of the graph, so this is a really good indication of what opioids can do to a patient's cortisol production.