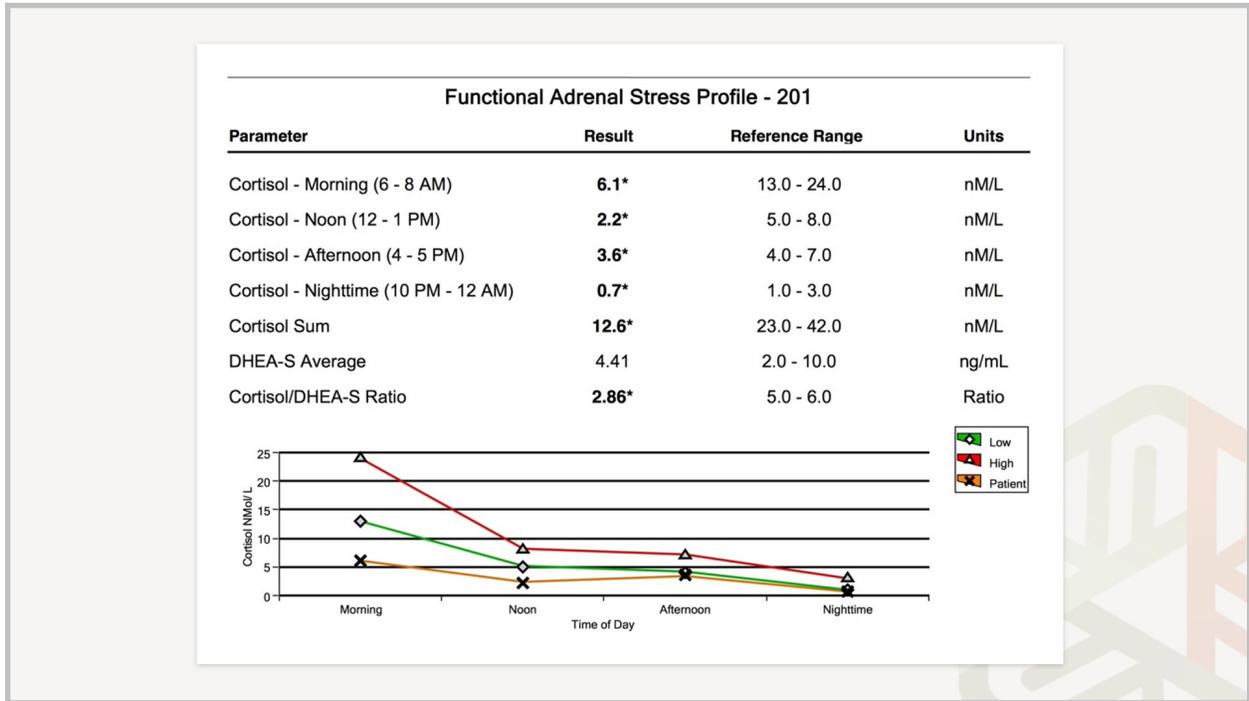


HPA-D Diagnosis - Part 4

Comparison of HPA axis assessment methods

	Serum	Saliva	Urine (24hr)	Dried Urine
Adrenal Hormones	Yes	Yes	Yes	Yes
Diurnal Free Cortisol Pattern	No	Yes	No	Yes
Cortisol Metabolism	No	No	Yes	Yes
Sex Hormones	Yes	Yes	Yes	Yes
Sex Hormones Metabolites	Yes	No	Yes	Yes
Easy Collection	No	Yes	No	Yes
Can Captures CAR	No	Yes	No	No*

I've put a table comparing the various methods of cortisol assessment on this slide, and the criteria for comparison, as you can see, are adrenal hormone measurement, whether it measures diurnal free cortisol pattern; whether it measures cortisol metabolism or metabolites; and sex hormone metabolites, which isn't crucial for HPA axis assessment, but is certainly useful information to have; how easy the collection is; and whether it can capture CAR. As you can see, the dried urine test answers yes to every one of these questions except for the last one, which is can it capture the CAR. The answer there is no, but I put an asterisk after the no, because some of the internal research at Precision Analytical that's ongoing suggests that the morning cortisol value correlates pretty well with the cortisol awakening response.



Now let's look at an example of how the different methods play out in clinical practice. This is from a 34-year-old male patient, this saliva test result on the slide. His main complaints were waking up tired, getting a second wind at night, IBS-like symptoms, and poor exercise tolerance. He's a software developer that works for a tech startup and was in the habit of using electronic media extensively at night, and he also sits a lot. So we did a split sample and had him do saliva tests from two different labs and DUTCH testing on the same day so we could compare the results, and here are his saliva test results from one lab. This is suggestive of adrenal fatigue; you can see that cortisol is low at all four time points and the 24-hour estimate of cortisol production is also low.

Tests Ordered					
TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Salivary Cortisol X4, Timed					
#1 Salivary Cortisol	0.020		ug/dL		01
Draw date/time: 11/09/15 - 00:01					
Reference Range:					
Children and Adults:					
8:00a.m.:	0.025 - 0.600				
Noon:	<0.010 - 0.330				
4:00p.m.:	0.010 - 0.200				
Midnight:	<0.010 - 0.090				
#2 Salivary Cortisol	0.141		ug/dL		01
Draw date/time: 11/09/15 - 08:00					
#3 Salivary Cortisol	0.058		ug/dL		01
Draw date/time: 11/09/15 - 12:00					
#4 Salivary Cortisol	0.123		ug/dL		01
Draw date/time: 11/09/15 - 16:00					

Here's another saliva test result from a different lab, and as you can see here, all of his values are actually within the normal range, unlike the previous result.

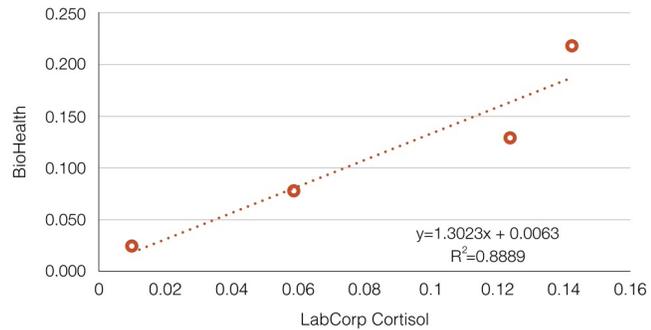
Saliva Comparison

BioHealth

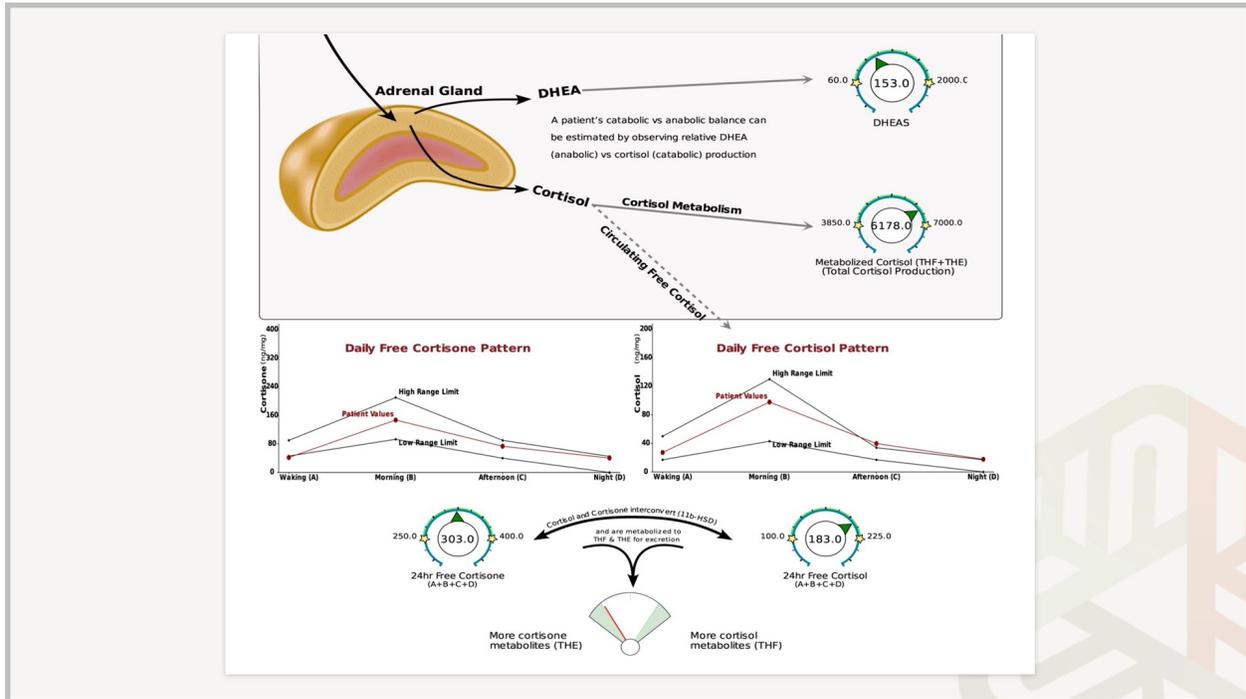
	Low	High	Sample value
8am	0.472	0.871	0.221
Noon	0.182	0.290	0.080
4pm	0.145	0.254	0.131
Bed	0.036	0.109	0.025

LabCorp

	Low	High	Sample value
8am	0.025	0.6	0.141
Noon	0.01	0.33	0.058
4pm	0.01	0.2	0.123
Bed	0.01	0.09	0.01



Now, it's difficult to directly compare results from saliva labs, as I mentioned before, because different labs use different measurement units, but I went ahead and converted the results from these two different labs and put them in a table on this slide, and then I plotted the results on a graph. As you can see, the 8 a.m. and noon samples are extremely close. The afternoon and evening are not quite as concordant, but they're still close. The biggest difference we see here is in the lab range itself, particularly the lower end of the range in the morning and at noon. The lower end of the range is 0.025 for LabCorp, which was the second result, but 0.472 for BioHealth, which was the first result. That's almost 20 times higher lower end of the range for BioHealth than LabCorp, and it's a similar story for the noon reading lab range. Now of course, it's possible that BioHealth's ranges are correct and LabCorp's are not, and I would be the first to argue that conventional ranges are often inaccurate, but the difference between the functional and conventional range is rarely if ever twentyfold. I can't think of a single example where the functional range is twenty times tighter than the conventional range. I'm not sure how BioHealth determines their ranges, but it's possible that their ranges have been influenced by the adrenal fatigue concept and the idea that low cortisol is a common pathology, and it's possible that they adjusted the lower end of their ranges upwards to catch more adrenal fatigue patients.



Here are the same patient's test results on the same day from DUTCH, and as you can see, cortisol is definitely not low here. In fact, free cortisol is a touch on the high side in the afternoon and evening, which fits well with this patient's symptoms of getting a second wind at night. If we compare this to LabCorp, they use a more classic reference range of plus or minus two standard deviations. If you take LabCorp's morning range as an example, the high end is 25 times higher than the low end, but for DUTCH and Precision Analytical, the difference between the high and the low end of the range is three to four times. DUTCH is looking more at the 20th to the 80th percentile as normal, which would be consistent with a functional medicine approach, whereas LabCorp is looking at anyone in the 5th to the 95th percentile as normal. Look also at metabolized cortisol level; here, it's at the high end of the range, the range is 3850 to 7000. He's at 6178, so this is definitely not a low cortisol presentation, which is what was suggested by the BioHealth saliva test.

So given all this, what should you choose? Saliva has been the default, but DUTCH has only recently become available, and not as many practitioners are aware of it. Saliva is still valid and useful, but a growing number of clinicians, myself included, now prefer the DUTCH testing. HPA axis and the regulation of cortisol are incredibly complex, as you know from basic physiology and adrenal fatigue sections we've already covered. One way to look at this is as a house of mystery with about 10 windows; seven of the windows are boarded up, and saliva allows us to look into two windows. Urine testing allows us to look into one of those two windows, which is overall free cortisol, and a third window which is total production. DUTCH gives us all three windows: the diurnal pattern, the overall free cortisol levels, and total cortisol production, but we still can't see into the windows of tissue sensitivity, receptor response to both cortisol and ACTH, etc. The best of

both worlds, as I mentioned before, would likely be DUTCH test plus a saliva cortisol awakening response, and that's not currently offered by anyone, but as I mentioned, that may be a possibility in the future.

Okay, that's it for now, and in the next presentation we're going to finally start looking at some test results. Sorry if this has been a little overwhelming, but as I mentioned before, due to the prevalent misunderstandings about so-called adrenal fatigue and the HPA axis, I felt like we needed to really cover the basics in detail before we dive into looking at test results. Okay, see you then.