NIGHT-TIME SALIVARY CORTISOL TESTING

Doctors are using salivary testing as a way of checking for diurnal rhythm variations of hormones. For many hormones, salivary levels do not correspond to blood levels and their measurement cannot be recommended. However, for cortisol, there is a very good correlation between blood and saliva levels. Diurnal rhythm, our inner clock, tells us when to wake up and when to go to sleep at night. In healthy individuals, the largest dose of cortisol is released in the early morning. This tells our body to wake up and get ready for the day.

In people with Cushing's disease, this diurnal rhythm is inappropriately high in the evening and night hours. Cushing's patients may have high levels of cortisol after the sun goes down and the rest of the world is ready for rejuvenating sleep. This alteration in the diurnal rhythm is a very important piece of the puzzle when trying to establish the proper diagnosis of a patient who is suffering from Cushing's symptoms.

What is episodic Cushing's disease and why is it important for testing?

While most Endocrinologists think that Cushing's disease needs to be severe and present on all tests, Dr. Friedman was one of the first Endocrinologists to recognize that most patients with Cushing's are episodic in that they have some high cortisol values mixed in with normal ones. He prefers the term "episodic" or "periodic" over "cyclic" which implies regular patterns of high and low cortisol. He published an article entitled "High Prevalence of Normal Tests Assessing Hypercortisolism in Subjects with Mild and Episodic Cushing's Syndrome Suggests that the Paradigm for Diagnosis and Exclusion of Cushing's Syndrome Requires Multiple Testing" published in *Hormone and Metabolic Research* in 2010 found that found that 65 of the 66 patients with Cushing's syndrome had at least one normal test of cortisol status and most patients had several normal tests. Therefore, to diagnose Cushing's disease if you are episodic, you need to do multiple tests when high. Late-night salivary cortisol testing is the most convenient way to test for high cortisol and complements 24-hour urinary cortisol testing.

When to collect when in a high:

Patients describe the following issues as things they tend to experience in a "high" phase:

- Wired at night
- Weight gain
- Acne
- Anxiety increase/mood swings/irritability
- Euphoria/more energy than usual
- Very few aches and pains
- Tasks seem easier
- Insomnia/inability to stay or fall asleep.
- Energy levels that "perk up" after sunset.
- "Speed talking" – mind is going faster than your brain can process the thoughts to speak them.
- Water weight gain – edema
- High blood pressure
- High blood sugar if having diabetes
- Although Dr. Friedman uses continuous glucose monitors (CGMs) for his patients with diabetes, he hasn't found them to be that helpful to determine highs and they

aren't covered by insurance for those without diabetes. Instead, you can get Stelo or Lingo that are over the counter and look for a high glucose at night.

It may take a while to learn your cycles, so do not be discouraged if you do not produce positive results right away. It often takes people weeks or months to accurately diagnose their cycles. For this reason, we suggest keeping a diary of how you feel when you do each test. In this way, if we get an abnormal result, we can ask you to do further testing at times when you feel the same and perhaps expedite getting more abnormal results to back up your diagnosis.

PROTOCOL FOR COLLECTING SALIVA SAMPLES (the protocol varies slightly whether you use LabCorp or Quest)

You need to pick up a salivary kit with salivettes from your LabCorp or Quest pickup station. Pickup 4 blue-top salivettes at Quest or 4 white LabCorp. The pickup station is required to stock these. Have them order them if they say they are out. Do not use Quest salivettes for LabCorp or LabCorp salivettes for Quest.

LabCorp

Quest

Preparation for testing (both LabCorp and Quest)

1. **Twenty-four hours before collection** - do not use any creams or lotions that contain steroids such as hydrocortisone, and do not use any steroid inhalers. These products can contaminate the Salivette and interfere with results.
2. **Do not drink water for 10 minutes prior to collection.**
3. **Avoid activities that may cause your gums to bleed** - do not brush or floss your teeth for one hour before collecting saliva.
4. **Thirty minutes before collection** - do not eat or drink anything at least 30 minutes before collecting saliva.
5. **If your gums or the inside of your mouth are bleeding**, do not collect the sample
6. Wash your hands and dry them thoroughly before collection
7. Collect the salivary sample between 11 PM and 12:30 AM. Dr. Friedman does not recommend doing it after that.
8. Dr. Friedman usually recommends collecting 4 samples at night, only rarely will he recommend other times.
9. Make sure you have your name, date of birth and date and time of collection on each sample.
10. Put in the refrigerator and bring it to your local pickup station.

11. They can also be frozen.

Procedure for **LabCorp.**

1. Open the top cap/stopper and place the cylindrical cotton pad in your mouth.
2. Roll the cotton pad in your mouth for a minimum of 90 seconds or until you can no longer prevent swallowing excess saliva (pad should be saturated).
3. If you cannot roll the cotton pad in your mouth, place the cotton pad under the tongue for a minimum of 90 seconds or until it is well saturated.
4. Once the pad is saturated, it should be put back into the insert (internal smaller vessel) and firmly closed with the top cap/stopper. The Salivette should now look exactly as it did when you started, with the cap, insert, cotton pad, and centrifuge tube.

Procedure for **Quest.**

1) Without touching the Salivette, remove the top of the plastic container and remove the swab from the Salivette.
2) Put the swab into your mouth, e.g. in your cheek, where it should remain for 2 minutes without chewing. If an extremely small amount of saliva is produced, leave the swab in the mouth for longer.
3) Return the swab with the absorbed saliva to the Salivette.

Quest Specimen Stability

- Room temperature: 72 hours
- Refrigerated: 21 days
- Frozen: 6 months

LabCorp Specimen Stability

- Room temperature: 14 days
- Refrigerated: 14 days
- Frozen: 5 months
- Freeze/Thaw cycles X3

Note: Dr. Friedman will instruct you on how many salivary cortisol tests to do (usually 4). LabCorp and Quest require that the number of salivary cortisols needs to have the correct code checked off on the requisition. Therefore, you could freeze your samples and bring them in together. Tell the lab that their instructions all the sample to be frozen and if they don't understand that, they can talk to their supervisor.

Approximately 10-14 days later, we will receive the results at the office. Dr. Friedman will use these results to help assess your condition.