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LETTER TO THE EDITOR

The realities of salivary cortisol sampling in the real world: Reply to the Letter to the Editor from Belaya and Melnichenko

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I agree with most of the comments made by Drs. Belaya and Melnichenko in their Letter to the Editor [1] in reply to my original commentary [2] about their original research article and will not belabor most of the points I made. I certainly hope that, because of their research using a platform immunoanalyzer [3], that the use of late-night salivary cortisol (LNSC) becomes commonplace and ubiquitous.

Variability in cut-offs is a fact of life when performing hormone assays. In fact, it is not uncommon for different laboratories to have differences in reference ranges even using exactly the same method. That is why accrediting organizations (like the College of American Pathologists) require each reference laboratory to establish and periodically verify their own reference ranges. This, of course, does not explain the magnitude of the differences in cut-offs described by Drs. Belaya and Melnichenko. The only reliable solution to this is for each clinician to carefully examine the results from their reference laboratory against the reference ranges specific to that laboratory.

One important caveat that I do want to clarify is in regard to my point about topical corticosteroids contaminating the saliva samples. The authors' reply to this in their letter is as follows: "We emphasized that patients should not eat or brush their teeth at least 30 min before sampling." This, I am afraid, is a non-sequitur that requires some discussion. Other than non-compliance with sampling time, the chief "Achilles heel" of salivary sampling is contamination during home sampling. We have found that topical hydrocortisone (authentic cortisol) on the lips or hands can render the sample useless [4]. A trip to any pharmacy or supermarket in the United States will reveal many, many choices of over-the-counter anti-itch ointments or creams containing up to 1 % cortisol! One can imagine the even a tiny bit of this material contaminating the saliva sample will falsely increase the cortisol concentration regardless of the assay method. The only reliable way to detect this is to show a normal cortisone concentration in the saliva sample [4]. We recommend that patients (a) avoid using any creams of any sort in the 24 h before sampling, (b) wear examination gloves or even sandwich bags on their hands while sampling, and (c) avoid touching the cotton sampler throughout the process of at all possible. We had one patient whose salivary cortisol was persistently elevated and denied use of anything suspicious—this was before the availability of LC–MS/MS to measure cortisol and cortisone. I had the patient come to our clinic and, wearing exam gloves, I placed the cotton sampler in the patient's mouth and retrieved it after it was soaked with saliva. The salivary cortisol concentration was completely normal. It turns out the patient was using a cream that he was unaware contained hydrocortisone. We have since had many patients with dramatically increased salivary cortisol in whom contamination was verbally verified and others in whom it was necessary to biochemically verify the contamination [4]. We even had one patient with contaminated, falsely elevated salivary cortisol who was applying a cream to the skin of her pet dog with eczema. She did not know that the cream was loaded with hydrocortisone. Therefore, one must be very suspicious of very high salivary cortisol concentrations in the absence of significant clinical symptoms and in the presence of other normal tests (like the overnight

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dexamethasone suppression test eloquently described by Drs. Belaya and Melnichenko [1]).

In summary, I very much appreciate the excellent study performed by Drs. Belaya and Melnichenko [3], and I hope that it will encourage clinicians around the world to demand the availability of salivary cortisol measurement using the platform immunoassay available in their own clinical laboratories.

References

1. A. Belaya, G. Melnichenko, Practical evaluation of late-night salivary cortisol: a real-life approach (Letter to the Editor). Endocrine. doi:10.1007/s12020-012-9709-9
2. H. Raff, Salivary cortisol and the diagnosis of Cushing's syndrome: a coming of age. Endocrine **41**, 353–354 (2012)
3. Z.E. Belaya, A.V. Iljin, G.A. Melnichenko, L.Y. Rozhinskaya, N.V. Dragunova, L.K. Dzeranova, S.A. Butrova, E.A. Troshina, I.I. Dedov, Diagnostic performance of late-night salivary cortisol measured by automated electrochemiluminescence immunoassay in obese and overweight patients referred to exclude Cushing's syndrome. Endocrine **41**, 494–500 (2012)
4. H. Raff, R.J. Singh, Measurement of late night salivary cortisol and cortisone by liquid chromatography tandem mass spectrometry to assess pre-analytical sample contamination with topical hydrocortisone. Clin. Chem. (2012). doi:10.1373/clinchem.2012.182717