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Cushing's Disease: Reassessing Recurrence Rates and Implications for Practice

### Announcer:

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#### Dr. Fleseriu:

This is CME on ReachMD, and I'm Dr. Maria Fleseriu, and here with me today is Dr. Richard Auchus.

It's important that clinicians have an accurate picture of recurrence so they can properly monitor their patients with Cushing's disease throughout their lives. Rich, what does recurrence mean for you and for the patients with Cushing's disease? And how we can monitor for it?

## Dr. Auchus:

Well Cushing's disease is hypercortisolemia due to an ACTH-producing pituitary tumor. So it means regrowth of the tumor. And I want to distinguish this from absence of remission. So it's very important after pituitary surgery that the patient goes through a phase of adrenal insufficiency. If they don't, and just become, quote/unquote, normal, that really means that they have some residual tumor, and at some point, they are very likely to recur.

The other predictors of recurrence would be people who have macroadenomas who have known incomplete resections and where people have resections done at a center that is not experienced at doing pituitary surgery. I would say, overall, the recurrence rate is about 50%, based on large studies. And the most sensitive way to pick up recurrence is the late-night saliva cortisol. Most of us now will do an annual late-night saliva cortisol or 2 or 3 to screen for recurrence particularly in people who we think are at higher risk. The sensitivity is 75% to 90%, much lower when you go to the dexamethasone suppression test and urinary free cortisol; those only become positive later on as the disease progresses.

Patients often suspect they know when they have a recurrence because they feel some of the symptoms that they had, either depression or poor sleep or agitation. And they usually can tell you that they're concerned that they're having a recurrence. And the important point here is not to wait until the urinary free cortisol is elevated to define someone as having a biochemical recurrence, because they will benefit from treatment as soon as you can identify this, whether this be repeat surgery or radiation therapy or medical therapy. And I think it's also important to consider what tests were abnormal at the start of the diagnosis in deciding how to work up people for recurrence.

So those are the main things that I would say are important. Recurrence is actually quite common. It should be screened for annually, urinary free cortisol being the most sensitive, and not waiting until some of those later tests are abnormal to proceed.

## Dr. Fleseriu:

Thank you, Rich. I completely agree. I think the most important thing would be that we need to follow patients that had successful treatment for Cushing's disease throughout their lives. The rates of recurrence are much higher than we used to think, in some studies

35% or even more, so it's important to be attuned to what the patients feel. If the patients tell me that, "I think, Doctor, my Cushing's is back," I believe them even if their urinary free cortisol is normal. I know that there are other tests that we can do. And the patient is always right for recurrence; they know when it's coming.

And then also the tests differ in between for some patients. They can do late-night saliva cortisol. Though I like it the most, as you said, it's the most sensitive and the earliest one for Cushing's. However, if they can do it, then I will do an overnight dex suppression test. However, if a woman is on oral estrogen, we can't do that. So it's very important to look. But the key point, do not wait for the urinary free cortisol to become abnormal. I had a patient recur after their urinary free cortisol became abnormal 3 years later, so we can't wait for that. Of course, we treat it earlier.

So I think that's the key. The patients need to know that the recurrence is very frequent, and they have to be followed forever, even if they move on a different coast.

Well, this has been a great discussion, too brief for us, as we have so many things to talk about. However, our time is up. Thank you for listening.

# Announcer:

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