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Beneath the Surface: Understanding the Pathophysiology of Residual MDD Symptoms

Announcer:
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Dr. Goldberg:
Well, hello, everybody. Welcome. This is CME on ReachMD. I'm Dr. Joe Goldberg, and joining me today is my friend and colleague, Dr. Manpreet Kaur Singh.

Welcome, Manpreet.

Dr. Singh:
Thank you so much. I'm glad to be here, Joe.

Dr. Goldberg:
Ditto. We're going to do some rapid-fire thinking today. I'm going to give you our first question. Let's see what you think about this one. Manpreet, first, can tell us a bit about your sense of the pathophysiology of residual symptoms in major depressive disorder? And feel free to speak about the brain.

Dr. Singh:
You bet. Thanks, Joe. I love the invitation to talk about the brain. Recurrent major depressive disorder is not one entity, not one animal, not one species. Depression, in and of itself, is a very heterogenous condition, and so it's no wonder that if it persists, even after an acute treatment trial, there might be residual symptoms in a variety of flavors. There might be attentional problems that are related to prefrontal cortical function. There might be anxiety. Residual anxiety is a big ticket one that ends up being a problem for a lot of folks. That is based on fear-based circuitry that isn't targeted necessarily by certain agents that are used to treat an acute depressive episode.

We have to remind ourselves that these medications that are used pharmacologically to treat depression and even psychotherapy tend to be very targeted in some ways. And so when you have a heterogenous condition like depression, you find yourself experiencing some improvement in certain kinds of symptoms and potentially nonresponse or residuality of other types of symptoms.

And you know what happens as a consequence of that is that patients feel like they're unfulfilled, and that can lead to a variety of other potential problems, whether it's nonadherence to their first trial of a medication, "Ah, this isn't working. It didn't fully cover my depressive episode," or "It didn't fully bring me to baseline." One has to work really hard with the patient to inspire confidence and help them understand and identify what kinds of residual symptoms come up.

Joe, what other residual symptoms have you noticed patients experience after anxiety or ADHD?

Dr. Goldberg:
Sad to say, any and all. So here's an inconvenient truth: While we strive for remission, and we sometimes use the analogy that the brain

is on fire, and you don't want to say we've extinguished 70% of the flames because residual symptoms, well, worsen and amplify and make things hard. The reality, oftentimes, is that we don't always make it to remission.

And so I think you nicely point out, Manpreet, the domains that we think about, is there leftover cognitive impairment? Is there leftover sleep problems? Is there leftover low motivation or drive? And I think it's very useful to take that kind of a categorization approach. But I think we sometimes also just have global incomplete response. Now the relevance of this, in my mind, has to do with how would you then target residual symptoms? So if I'm lucky enough to say, “Wow, we knocked down your suicidality and your anhedonia, but your concentration still leaves something we desired,” maybe that'll motivate my thinking about a particular treatment choice to target that symptom of or, “Well, you've got residual insomnia, so let's go with something that might help there,” a drug like mirtazapine, for example, or something that's got, you know, one of the second-generation antipsychotics that would cover multiple bases.

So I'm grateful when I can say here's a particular domain that's left over. But what keeps me up at night clinically is when patients just have ongoing symptoms, and then we have to decide, have we really made inroads in the totality of the syndrome, or do we have to think about something more fundamental?

Dr. Singh:
One hundred percent. And I would just add to that the consequences of not being thoughtful about what happens after an initial treatment trial or when a patient comes back to you with residual symptoms in terms of treatment planning, because it is what's left over that ends up driving the next discussion. And it might be a switch; it might be augmentation; it might be co-treatment with something else; it might be an entirely different strategy altogether.

Dr. Goldberg:
Absolutely. Well, this has been a great bite-sized discussion. That's our time for now. So thanks for listening.

Announcer:
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