TD Pathophysiology and Drug-induced Parkinsonism Podcast

FEMALE SPEAKER: This podcast is for informational purposes only. The information provided herein is based upon the healthcare provider's clinical judgment and personal experience.

DR. LESLIE LUNDT: Hi, this is Dr. Leslie Lundt, medical director at Neurocrine. And with me today, we have Dr. Jonathan Meyer from San Diego.

DR. JONATHAN MEYER: Hello. Thank you for having me.

DR. LESLIE LUNDT: Dr. Meyer, can you tell us a little bit about your practice setting, please?

JONATHAN MEYER: So I'm a clinical professor of psychiatry at UC San Diego. So there I do mostly teaching. I'm also a psychopharmacology consultant for the state hospital system in California. So that's 6,500 patients, most of whom have schizophrenia spectrum disorder. So it's the largest state hospital system probably in the world.

DR. LESLIE LUNDT: So you're really the perfect person to talk about tardive dyskinesia.

DR. JONATHAN MEYER: We have a lot of people in the state hospital who are on chronic antipsychotics, many of whom require high doses.

DR. LESLIE LUNDT: So, Dr. Meyer, one of the things that people really struggle with out there is how to tell the difference among the various drug-induced movement disorders. Can you give us some tips on, say, drug-induced Parkinsonism versus tardive dyskinesia? How can you tell?

DR. JONATHAN MEYER: Well, part of it is just, from the appearance, Parkinsonism is often involved with rigidity, a certain type of rhythmic tremor. You'll see it in people who have either recently started a medication or subsequent to a dose increase.

Tardive dyskinesia tends to involve non-rhythmic movements. So, as opposed to a tremor, which is rhythmic, tardive dyskinesia involves non-rhythmic movements. Tends to be centered often in the facial region, but not always.

And the time course of onset is often very delayed by months-- in some cases, years-- from the institution of the drug. In terms of response to treatment, Parkinsonism is often made better by anticholinergic medication. Whereas, because of the underlying pathophysiology of tardive dyskinesia, anticholinergics will make the tardive dyskinesias worse.

The other thing people might do is lower drug dosages. You get them below their threshold for Parkinsonism. Whereas for tardive dyskinesia, often sometimes we don't realize it exists until the person, let's say, abruptly stops their medication and we have an unmasking of the problem, which was not evident previously.

DR. LESLIE LUNDT: OK, so just to clarify things, so the medicine we're really talking about would be antipsychotics.

DR. JONATHAN MEYER: Yes.

DR. LESLIE LUNDT: So if you lower antipsychotics, Parkinsonism should get better.

DR. JONATHAN MEYER: That's correct.

DR. LESLIE LUNDT: But TD might get worse.

DR. JONATHAN MEYER: It often will. And this has to do with the pathophysiology of tardive dyskinesia. Essentially, we think what's going on there is that the chronic exposure to postsynaptic D2 blockade causes both upregulation and super-sensitivity of these postsynaptic receptors.

While you're on active drug, you may be able to block enough of these postsynaptic receptors that you don't realize there's an issue. But if you take away some of the drug, now all these super-sensitive receptors have access to dopamine. And you see this exaggerated dopamine signal in the motor part of the striatum. And so what dyskinesia represents is actually an exaggerated dopamine signal related to the process, which I described previously.

As I said, you can mask that by blocking enough of these super-sensitive receptors. And that's why sometimes we don't realize there's a problem until the person stops their meds. Or we lower the dose and we realize, hey, they're having some abnormal mouth movements, which are consistent with tardive dyskinesia.

DR. LESLIE LUNDT: So that being said, if you increase their antipsychotic, what would happen?

DR. JONATHAN MEYER: Well, temporarily, you might suppress the movements.

DR. LESLIE LUNDT: OK, thank you. Thank you so much for your time today. I hope that the audience learned as much as I did.

DR. JONATHAN MEYER: Oh, my pleasure.