[MUSIC PLAYING]

ROY CHENGAPPA: Hello, everyone. My name's Roy Chengappa. I'm a professor of psychiatry at the University of Pittsburgh School of Medicine and also the service chief for a service line called the Comprehensive Service Recovery Line at the Western Psychiatric Hospital at the University of Pittsburgh's Medical Center. Welcome to the presentation, the title of which is, "De-prescribing Anticholinergic Medications in People With Severe Mental Illness." This is part one of the presentation, and I'll give you a background as to why I think this is a good idea. And Dr. Lupu, who is my colleague at the School of Pharmacy here and works as a clinical pharmacist with us, will do the presentation on the programs that we've had so far to decrease these medications and the success that we've had.

And so with that, I'd like to talk a little bit about the disclosures. Neither Dr. Lupo nor I have any disclosures to make that are relevant to this presentation. And at that point, I'd like to talk a little bit about the objectives of part one and to some extent part two.

So the first part of this presentation will define what extrapyramidal symptoms are-- things that you and I learned in medical school, pharmacy school, PA school, or nursing school-- and how to identify them, and why we treat them. And then the last objective is to say, should we use them forever, or is it time to re-look at these to discontinue them.

All right, so the why. The why we use anticholinergic drugs in people with schizophrenia who are treated with antipsychotics, or people with any other condition that are treated with antipsychotics, are because these antipsychotic drugs produce extrapyramidal side effects. Most antipsychotics, in fact all approved antipsychotics today, are dopamine receptor antagonists. And in so doing, they grab what we would call the neurons, which is why the first generation antipsychotics were called neuroleptics, and so this is seizing the neuron, literally means neuro lapses. And in so doing, they cause their actions, which is they work for the psychotic symptoms of schizophrenia, the psychotic symptoms of several other conditions.

But in so doing they also imbalance the system. And so we need anticholinergic drugs to bring the balance back. Less commonly, antipsychotic drugs sometimes cause hypersalivation, so anticholinergic drugs, not just used to counter the imbalance that is created in the brain but to counter things such as hypersalvation. And so sometimes antipsychotic drugs cause hypersalivation, and anticholinergic drugs are used to counter that.

Now rarely in neurology practice, and in movement disorder practices, and neuropsychiatry, we might use anticholinergic drugs to treat tardive dystonia. I'll talk a little more about this once I get into the mechanism.

This particular slide talks about the balance to the lingergic and cholinergic system. And as I mentioned before, every approved and marketed antipsychotic drug causes dopamine allergic imbalance. And so the cholinergic excitation occurs. And in this process, we end up having to use anticholinergic drugs.

So what actually do I mean by extra parameters side effects? Commonly, we use the acronym EPS in psychiatry and in psychiatric practice. So let's just look at what these side effects look like, just to remind ourselves.

Acute dystonia, we see within hours. They're frightening to someone who's never had them, even to trainee, physicians, and allied health professionals. They're frightening. They look like you had a lockjaw or your eyes roll up. And we call them oculogyric crises. So these are frightening.

And if they occur, because you've been given an antipsychotic injection, but you know, you're not hospitalized, you go home, it could occur at home within hours. It's frightening for someone who hasn't seen them. And in the wards, if there's a new nursing group that hasn't seen dystonia, it could be very frightening.

Subacute are things that show up in hours to days. So typically, these would be parkinsonian features. So as the neurons are sort of seized, as I mentioned earlier, you begin to see parkinsonian side effects. Except they are occurring in people who are in their 20s and 30s and getting these antipsychotic drugs, either initiated or maybe titrated upwards.

So what we see is rigidity. And so that typically, if I took my arm here and did this, or I look for cog wheel rigidity in the elbow, I would see it. And just from practice, I would see this sort of show itself up in different patients. I might come across very wooden. The tone of my talk, as I'm doing now, would become wooden. And it would become sort of flat. And I would look parkinsonian.

And I would lose my swing, arm swing as I walk. So we would call this, you know, the loss of arm swing. Or the gate would become very shuffling, as you might see sometimes in elderly people in nursing homes. They shuffle. And they're parkinsonian. Except you're seeing it in a 20, 30-year-old, who's being treated with antipsychotic drugs.

Finally, another side effect that's very troublesome that also occurs in a matter of days to early in the treatment course within weeks is akathisia. Literally translated from the Greek, it means inability to sit. And there, what we are noticing is people who are fidgety, not sitting still, jerking. But it's not their natural tendency. This has come about because of treatment.

This, many psychiatrists believe has nothing to do with EPS, but some do classify it as EPS. But the issue of anticholinergic drugs, they don't work as well for this particular akathisia fidgetiness. Beta blockers do and benzodiazepines do, they work better than anticholinergics. But a few people might even respond to anticholinergic drugs.

So the argument is antipsychotic drugs are not like short-term use drugs typically. In conditions like schizophrenia or related psychosis, we use them for years, if not for life. So the argument for continuation is, if they work by blocking the dopamine receptor and they cause these side effects, would you have to use anticholinergic drugs also for life? And so this is the argument for continued use.

But we shouldn't forget the brain will adapt. The body will adapt. And many of these side effects will mitigate on their own or even naturally over a period of weeks to months. So the argument against using them is they themselves come with side effects. Meaning, the anticholinergics have a whole bunch of side effects, such as dry mouth, blurred vision, constipation, urinary tension, memory issues, a dry skin.

And these of course, will impact the quality of life of the patient and also their continued treatment, adherence to treatment. So this is the argument why we have gone about this particular project. And this leads me to introduce me. To introduce, not me, but Dr. Lupu, who will do the next part of the presentation, which are quality improvement projects. So at this point, I'll stop and hand over this presentation to Dr. Lupu, who is an instructor in the school of pharmacy and therapeutics and is a clinical pharmacist here at the CRS Oxford Clinic, so Ana.

ANA LUPU: My name is Ana Lupu. I'm a clinical pharmacist here at the comprehensive service recovery line at Western Psychiatric Hospital. And I also am an adjunct instructor at the University of Pittsburgh School of Pharmacy.

Now, I'm going to talk to you about an anticholinergic medication production quality improvement initiative that we were able to do here at the CRS Clinic back in 2014 and over the past few years. This project actually started with a referral from Dr. Chengappa, who just spoke earlier. And he noticed a patient in his caseload, who was on multiple anticholinergic medications and was having side effects.

And this really initiated a referral to our clinical pharmacy team. And we put our heads together and we're able to work with the patient to reduce her anticholinergic burden. And we found that with this success, perhaps other patients can benefit from such a medication reduction.

And so we decided to go about it a little bit more systematically. We created a quality improvement project, where we used our in-house pharmacy to generate a report of patients taking benztropine or trihexphenidyl for extrapyramidal symptoms. We also looked at some other medications that were anticholinergic, such as hydroxyzine or diphenhydramine, but we didn't see as many patients on those medications. So we decided to focus on specifically those patients that were taking benztropine or trihexphenidyl.

And once we pulled this report, we let the physicians know that their patients were taking these medications, just as a heads up and to make them aware. And then the physicians were able to-- when they saw the patient. To assess whether a change was possible. If the change was possible, there was a referral to the clinical pharmacy team. And the clinical pharmacist went ahead and did an assessment with the patient, which I'll talk about in a few moments. And we really saw excellent results in the first part of our quality improvement initiative, in terms of patient outcomes specifically and reducing side effects.

So this really inspired the next step, which is was an expansion of this project. We had more than double the amount of patients identified through our in-house pharmacy and through our psychiatrist. And we were really able, in the second part, to also reduce these medications, the anticholinergic burden, and improve our patients' outcomes. And the results of the first part were published in the *Journal of Clinical Psychiatry* back in 2016.

So just to talk a little bit about the pharmacist assessment, once a patient was identified for a potential medication reduction and was referred to a clinical pharmacist. The pharmacist reviewed all of the medications that a patient was taking, including you know, over-the-counter medications, medications that were not for their psychiatric disorders. We really reconciled their medication list to make sure we had a good picture of everything that they were taking. We characterized their anticholinergic burden by using the anticholinergic cognitive burden scale, which I'll talk about in a moment. And we also looked at anticholinergic side effects, their impact on the patient's quality of life, as well as cognitive impairment.

So these visits were a sort of a longer baseline assessment visit. And then some patients required multiple follow-ups. And then all of the assessments were done at the end of the taper, or when medication could no longer be decreased, in terms of the dose.

So some patients required only about a month for a medication to be stopped. They were very on board. And it was very successful discontinuation. And other patients really required a lot more follow-up and monitoring and education. And in this particular case, really collaborating with the physicians even the therapists, the pharmacists, you know, and sometimes the patient service coordinators really delivering that message and helping the patient feel comfortable with the medication changes or identifying any problems that were coming up was really essential to helping the patient get on board and to making sure the patients were safe and still adhering to their medications.

So now we'll talk a little bit about the anticholinergic cognitive burden scale, which we used to help sort of quantify the burden that our patients were experiencing from their medications. This is a widely used and validated scale, which categorizes the potential of medications to cause anticholinergic adverse effects. So a score of zero means, no anticholinergic activity, all the way down to a score of three, which means, established and clinically relevant cognitive anticholinergic side effects and the potential for delirium. So these are the medications that we are most concerned about.

And most of the literature looking at anticholinergic burden has identified a score of three as being clinically significant, especially in terms of cognition. And in the elderly, we've also found that a total score of three or more can increase the risk of death and also can cause a decline in MMSE scores over the years. So this is a very important point to remember.

And I'd also like to talk a little bit about the medications on the anticholinergic burden scale and just point out a few examples to you. So if you look on the right hand column, an anticholinergic burden score of three, we have medications such as benztropine and trihexphenidyl, of course, that we talked about. But we also have multiple antipsychotics, including clozapine, quetiapine, and perphenazine. And we also have some of our bladder anticholinergic.

And then I do want to point you to the left hand column, some of the medications with a score of one, include medications such as even metoprolol or atenolols or blood pressure medications, ranitidines and medications for acid reflux, as well as some of our antipsychotic medications, such as aripiprazole or risperidone and haloperidol. So really you can see how easily in some of our patients, especially those patients with comorbid psychiatric and medical comorbidities, it can add up. And it can really cause an impact on their quality of life.

We use the memory impairment screen as well, just to kind of get a picture of cognitive impairment in our patients. We did this at baseline. So at the first visit, they had to look at four words, repeat them. And after a few minutes and some distraction, they had to try to remember those words. And they receive points, more points if they were able to remember them on their own. And they did receive a point if they were able to remember them with a cue. And so on this particular screen, score of four or less is considered possible cognitive impairment. And a score of five to eight usually means no cognitive impairment.

And then finally, I want to talk about the Pittsburgh Anticholinergic Symptom Scale, which we also use. This was a scale developed by Dr. Chengappa in clinical practice years ago. And we adapted it for this project in order to make it more patient friendly and really in order to help the patients see what some of the side effects that anticholinergic medications can cause.

And so you can see on the left hand side that we list things like dry mouth, blurred vision, fast heartbeat, difficulty urinating, constipation, confusion, or memory problems as the side effects. We did try to make them as patient-friendly language as possible. And patients were able to look at this scale and circle a number, in terms of how often they feel like they're experiencing these symptoms. And the last two questions were an opportunity for patients to tell us the significance that these symptoms or side effects had on their quality of life. So you know, how often it was really impacting their ability to get out of the house or to not be able to do something that they really wanted to do.

We did find that using the scale was pretty very quick as all the other scales were. None of them really took longer than three or four minutes to administer. Perhaps this scale a little bit longer, because it generated a lot of discussion and questions. But it really helped patients connect the side effects that they were experiencing and which medications in particular might be causing these side effects. And it highlighted the importance of why we were really working with them to reduce their anticholinergic burden.

A lot of times patients were nervous or uncomfortable with a medication change, because they really were concerned about decompensation, about their psychiatric symptoms becoming worse. And so being able to provide this education and to use some of these tools was really helpful in these cases.

So now I'd like to talk about the results of these projects. So in part one, we identified 29 patients. And of those, 19 patients were recommended to the pharmacist for a medication change. 66%, overall, had an actual medication change. So all 19 patients either had a medication discontinued-- so 13 had a medication discontinued. And six had dose reduction. So we did see a good amount of success here. And really on our scales, we found that patients reported 50% improvement in their anticholinergic drug side effects, 40% improvement in their quality of life or the impact that these side effects were having on their quality of life, and a 20% overall improvement in memory recall we saw.

We had similar success in the expansion part of the project from 2016 and 2017. We identified 51 patients who could benefit from a potential reduction in their anticholinergic medication. And 76% of them, so 3/4 actually had a medication change. 60% of them had a medication discontinued. So 31 out of 51 were able to stop their medication.

And we again, saw improvement in the anticholinergic drug side effects of 50%. 60% reported improvement in quality of life or how those side effects impacted their quality of life. We also saw improvement in memory recall.

We did look at antipsychotic prescriptions as well, to help us sort of get a sense of maybe which patients might be easier to reduce or stop these medications. And so we had 65% of our participants on one antipsychotic, 35% of our participants on two antipsychotics. And then in terms of first versus second generation antipsychotics, 80% of our patients were on at least one second generation antipsychotic, the most common of which was clozapine.

And we sort of postulated that most of those patients that were on an anticholinergic drug medications, may have been on them for drooling, secondary to clozapine. But we also saw a lot of patients on risperidone and paliperidone. So you know, these are potent D2 receptor blocking agents and do have the tendency to cause some perhaps stiffness, tremors, so EPS. And we did see, like I said, 43% of our participants on a first generation antipsychotic, with haloperidol being the most common.

We also looked at the demographic and treatment factors that might have influenced the ability or the likelihood of a patient to be able to successfully stop their anticholinergic medication. So we compared the first plus second generation group. There were 12 patients in that group. We saw 83% success, in terms of discontinuation or dose reduction in that group. Similarly, in those patients on second generation antipsychotics only, we saw an 83% reduction or discontinuation.

In our patients on first generation antipsychotics, we saw a 50% reduction. And even that was encouraging, because sometimes we think, oh, well, if a patient is on a first generation antipsychotic, they're very likely to experience EPS forever. And so we don't always attempt to remove them. But in this case, five out of 10 patients were able to stop that medication.

We compared the oral versus long acting formulations. And we did notice more success in those patients on oral antipsychotics only versus long acting antipsychotics. And then we also compared male and female. Those were very similar, in terms of the discontinuation rates. We had about 60% success. And we also noticed that we had more success in our non-Caucasian patients. So 83% we're able to stop or discontinue medication compared to our Caucasian patients.

So to summarize, the results of our projects we considered them very successful and encouraging, in terms of patient outcomes. We were able to see that patients on both first and second generation antipsychotics could potentially discontinue their benztropine or trihexphenidyl for EPS. And in most cases, EPS did not reoccur. But in a few patients, we did notice that some of the symptoms came back.

So we did have to restart those medications. And sometimes they were OK on a lower dose than before. And other times, we had to titrate all the way up, but these were just a few cases here and there. For the most part, we saw good, overall success, you know, for out to about six months in those patients that stopped their medications.

And so therefore, it's important to periodically reassess the need for these anticholinergic medications for EPS. And if we do determine that a reduction could be helpful, it's really helpful to develop a patient-centered strategy for medication discontinuation, to really review their history in the available documentation, to determine why a patient was on this medication in the first place, has that antipsychotic already been changed to another, and are there potentially better or safer approaches to manage some of the side effects that those patients are experiencing, for instance, propranolol, in the case of akathisia, instead of a medication such as benztropine or trihexphenidyl.

And we realize that not all clinics have the same resources or clinical pharmacy teams that we have here. But really being able to have anybody on the team, whether it's a therapist or a nurse or even service coordinators really support the patient during a medication change is essential. Patients will get nervous or sort of perhaps just wary of a medication change, because they do worry that they could decompensate. So having that extra support and having somebody else looking out for the patient, making sure they're not experiencing any exacerbations in their symptoms is very, very important.

And if you do have the time and the ability to use some of the objective assessments that we talked about today, we did find that those are helpful, in terms of patient counseling and education. And those are typically pretty quick and easy to administer. So with that, we want to just wrap up and say that hopefully you might consider reducing some of these anticholinergic medications for EPS in our patients, with the hopes that we'll have some long-term positive effects on both cognition and outcomes. Thank you.