Dr. McPherson: Hello, this is Dr. Lynn McPherson, and welcome to Palliative Care Chat, the podcast brought to you by the Online Master of Science and Graduate Certificate program at the University of Maryland. My guest today is Dr. Leah Sera, an assistant professor at the University of Maryland School of Pharmacy, and a faculty member in our master's program, also, by the way. And what we'll be discussing today is a project that Dr. Sera and I worked with one of our students, now a graduate, Dr. Annie Williams, on her project on anticholinergic burden in hospice patients. Welcome, Dr. Sera.

Dr. Sera: Thanks. I'm happy to be here.

Dr. McPherson: Yeah. We're very excited. So, what do you think? You think this is a real problem, this anticholinergic burden?

Dr. Sera: I think that there is definitely a lot of prescribing of anticholinergic medications for hospice patients, which we found from the study.

Dr. McPherson: We did find that. And I think you and I have chatted about why is this an important thing. I was just at MD Anderson giving a presentation on drug interactions, and I talked about the cumulative effects of anticholinergics and this burden that we've been talking about, and it really can be substantial. So I do think it's a really prevalent pharmacodynamic drug interacting where you see this additive or synergistic effects of drugs, and not in a good way, in this case. And when I gave that presentation, I started talking about how many muscarinic receptor subtypes we have. And I'll bet most people don't know that we have at least five muscarinic receptors, and they're spread throughout the central nervous system and the periphery. But blocking these receptors gives rise to the side effects. So we can certainly talk about the peripheral side effects of anticholinergic therapy, which is the dry eyes, urinary retention, dry mouth, constipation, which we all know how it was taught here, don't we? The can't see, can't pee, can't spit, can't ... Have a bowel movement, however you'd like to remember that.

Dr. Sera: Right.

Dr. McPherson: And then other peripheral effects are heat intolerance, tachycardia, decreased sweating. I always think of cholinergic stimulation as SLUDG. Do you remember that? The salivation, lacrimation, urination, defecation-

Dr. Sera: Urination, defecation-

Dr. McPherson: Yeah.

Dr. Sera: ... and GI effects. Yep.
Dr. McPherson: Yes. And then I think of anticholinergic as dry stuff, so it's gonna be the dry eyes, the urinary retention, the constipation, and so forth. But I think the most important ... Which is not to be undervalued in hospice, it's so important. But I think the thing that really strikes me are the central adverse effects with anticholinergics, so forgetfulness, agitation and confusion, delirium, paranoia, dizziness, drowsiness, and falls. I can't fit that into a little poem, but we see an awful lot of delirium in end-of-life care. Would you agree, Dr. Sera?

Dr. Sera: Absolutely. A lot of delirium, and a lot of secretions, also-

Dr. McPherson: Yeah.

Dr. Sera: ... which is one of the reasons that prescribing of antimuscarinic medications is so prevalent.

Dr. McPherson: Yeah. So when we talk about treating delirium, I think one of the first things we say is, "Look for drugs that could be causing the delirium," and I think anticholinergics are a perfect example of that. So I think people don't realize how many drugs have an anticholinergic side effect profile. So, certainly, the ones like the drugs that we use for overactive bladder, like Ditropan and Detrol, and these are the oxybutynin and tolterodine and things like that. And with those medications, they're more likely, statistically, to cause harm than benefit. And I think one of the things that makes me craziest in hospice care is ... And it just happened yesterday. If someone is on one of these drugs for overactive bladder and they're catheterized. That just makes me insane!

Dr. Sera: Right.

Dr. McPherson: So silly. Certainly, the anticholinergics we use for Parkinson's disease, such as trihexyphenidyl, benztropine, amantadine, those are all the strong anticholinergics. And I know that I try to discourage the use of Transderm Scop, how about you? What do you think about Transderm Scop?

Dr. Sera: Yeah. I always try to discourage the use of that scopolamine patch, as well, because it doesn't work fast, and it's long-acting, and so if you're trying to treat symptoms emergently for somebody who needs them on comfort, I just think that's ... Both of those things are points against it.

Dr. McPherson: I agree. And it plays peek-a-boo with the market. Sometimes it's on the market, sometimes it's not. And then, of course, continuing on, we have the GI antispasmodics, such as Lomotil and Bentyl, which I do like Bentyl for urinary spasms, bladder spasms, but strong anticholinergic. And as you mentioned earlier, these drugs for oral secretions, this is an example of where we're trying to cause a side effect to treat a symptom. So we're giving a drug that's a strong anticholinergic to cause drying of the mouth, and I know sometimes my nurse friends get upset with me that I try to discourage them, and I say, "If somebody has a deep pulmonary secretions, an anticholinergic really is not gonna dry
those up," and they really are not even particularly effective with the oral secretions. So which are your favorites of these antisecretory drugs, Leah?

Dr. Sera: What I use most are the atropine eye drops, but also, glycopyrrolate, because that doesn't seem to have as much cognitive effects.

Dr. McPherson: Right, because it doesn't cross the blood-brain barrier. That's a good point. I like that. We still see Levsin being used quite a bit and, sadly, the scopolamine. And I read a Cochrane review recently that said some of the drugs really don't even work to treat secretions, but it's so deeply ingrained in our culture we're probably gonna keep on doing it. And then, of course, my favorite is using Benadryl as a sleeping agent, which is a terrible idea because there's a strong anticholinergic, and hydroxyzine, which, good lord, that could drop a moose.

Dr. McPherson: The tricyclic antidepressants, antipsychotics all have anticholinergic side effects. And just looking at other phenothiazines such as promethazine, which is Phenergan. I always tell the story about my sister, who's also a pharmacist, and when she gets nauseated, boy, she goes running for the Phenergan. And I have accused her of ... That doesn't make sense. It's such a dirty drug. It really is not a very targeted drug. It's just a really hugely strong antihistamine anticholinergic drug. And she said, "Well, you're right. It knocks me out, but I wake up two days later and I'm not nauseated anymore," so I guess different strokes. Some antiarrythmics, such as disopyramide, and muscle relaxants. Are there others that you can think of, Dr. Sera. That I haven't mentioned, that you think we should point out? Some that, perhaps, people don't even think about.

Dr. Sera: I think that you've covered most of the big offenders that I see in my practice.

Dr. McPherson: Yeah. Bit it's interesting, looking at this paper that Dr. Williams was the first author on. Some of the drugs, like we use the scoring system of one, two, or three. Some of the drugs that would score even one point, we wouldn't even thing of, like beta blockers, for example, or H2 blockers, or some of the opioids, for example, even, would count into this whole mix. So there's a lot to consider there. So, tell us a little bit about this study. Why Dr. Williams chose to do this, and how we went about doing it, and the results.

Dr. Sera: We wanted to look particularly at a population of hospice patients who had an admitting diagnosis with dementia, and then look at the anticholinergic burden, particularly of medications with an ACB or anticholinergic burden score of two or three, that really have an established effect on cognition and increase the risk of delirium. So we did this at ... This was a retrospective study. We obtained information from Seasons Hospice and Palliative Care. They're a national hospice organization with many locations in the US. We looked at patients who were admitted to hospice with an admitting diagnosis of dementia on or after January 1st of 2016 and who were discharged by death on or before December 31st 2016. And we looked at particular medications, so we looked at anticholinergic burden, so drugs that had a score of two or three. We added up
the scores of all those drugs and came up with a total anticholinergic burden score for each patient.

Dr. McPherson: And what did it show? What were the results?

Dr. Sera: So, this study showed that about almost 30% of patients who are included on our study, so patients with dementia, were prescribed at least one drug with anticholinergic properties. And the most common drugs with anticholinergic properties in this study were atropine, Levsin, scopolamine, and then quetiapine and olanzapine, and there were a number of others, as well, but those were the most common drugs that we saw in this study, in this population.

Dr. McPherson: Which is kind of a red hot mess right now, trying to decide how to treat delirium in people with dementia with all of the brouhaha about the antipsychotics. So perhaps this is another nail in the coffin of the antipsychotics in that clinical situation. But it can be a tough clinical situation to deal with, wouldn't you agree?

Dr. Sera: Yeah. I mean, I think that the drug ... The most commonly prescribed drugs in this study, so the atropine, hyoscyamine or Levsin, and scopolamine, all those are typically prescribed to help control secretions at the end of life. And then Seroquel or quetiapine and olanzapine would be used ... They're prescribed for delirium. And both of those are, in different ways and for different reasons, but they're both really challenging for patients and caregivers at the end of life.

Dr. McPherson: Yeah. I'm looking into results here, and looking at the most common drugs with anticholinergic properties prescribed in this dementia population with a score of two or higher. 42% was quetiapine. So that's interesting.

Dr. Sera: Yeah.

Dr. McPherson: I know it makes me a little nuts when I see physicians or NPs or PAs write for quetiapine as a sleeping agent. It's really not indicated for that, and at that dose that you're using, 12 or 25 milligrams at bedtime, it's just very expensive Benadryl, because it's a very strong anticholinergic, particularly at the low doses. I'm excited that [Dr. Jason Webb 00:10:42] just agreed to do a podcast with me really focusing on quetiapine and some of the issues that go along with this medication. So I guess our conclusion is, I'll read from the paper here: "Due to the limited benefit and increased harms with the use of drugs with anticholinergic properties, providers should aim to maximize nondrug options," that makes sense, "By reducing the use of the top five, which," as you mentioned, "Are quetiapine, atropine, hyoscyamine, olanzapine, and scopolamine. The quality of life and care for end-of-life patients with dementia can potentially be improved." So even though we are pharmacists and we're all about the drugs, I think you and I spend as much time recommending stopping drugs as starting drugs. Would you agree?
Dr. Sera: Absolutely. I mean, I think that drugs certainly play a very important role in managing symptoms and improving quality of life, but part of knowing about drugs is knowing when you don't need them or whether the risk outweighs the benefit.

Dr. McPherson: Absolutely. So, if you want to read more about this study, which, of course, I think is a ... I love doing practical research, and this strikes me as such a practical thing. It was published in the American Journal of Hospice and Palliative Medicine in 2018. I think it was epubbed before hardcopy, so you can do a search on their webpage. And again, I'd like to thank Dr. Annie Williams, Dr. Leah Sera, for joining me here today in this podcast. This is Dr. Lynn McPherson and this presentation is copyright 2018 University of Maryland. For more information on our completely online master of science and graduate certificate program in palliative care, or for permission requests regarding this podcast, please visit graduate.umaryland.edu/palliative. Thank you so much.

Dr. Sera: Thank you.