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Challenging the Status Quo in Schizophrenia Treatment

Announcer:
You're listening to *On the Frontlines of Schizophrenia* on ReachMD. And now, here's your host, Dr. Shelina Ramnarine.

Dr. Ramnarine:
This is *On the Frontlines of Schizophrenia* on ReachMD. I'm Dr. Shelina Ramnarine, and joining me to discuss pharmacological and non-pharmacological approaches to improving outcomes in schizophrenia is Dr. Stephen Marder.

He's a Professor at the Seminole Institute for Neuroscience and Human Behavior at UCLA. He also serves as the Director of the Section on Psychosis. Dr. Marder, thanks for being here today.

Dr. Marder:
I'm glad to be here.

Dr. Ramnarine:
So let's begin by talking about emerging therapies or research directions that may shape how we treat schizophrenia in the coming years. Can you share more about those?

Dr. Marder:
Yes, and thanks for that question. I believe that we're really at an exciting time in the treatment of schizophrenia, where a new generation of drugs will give us an opportunity to really improve outcomes. Up until now, since the early 1950s, all of the antipsychotics have blocked dopamine receptors, and that is a mechanism which has been very useful to the field. Patients have had better outcomes. But there wasn't an alternative mechanism, and we've kind of been stuck with all of the disadvantages of D2 blockade.

These drugs have important adverse effects, which every psychiatrist is aware of—whether it's weight gain, neurological side effects, or endocrinological side effects. All of these are serious problems with these drugs, but also, the mechanism of action of the D2 blockade actually has other effects which psychiatrists really haven't talked about with patients. And that is that they tend to diminish how we evaluate rewards.

And by doing that, many people on antipsychotics feel somewhat diminished. It takes away a little bit of the sweetness of life. And we've asked patients to live with those effects. And I think now, with new medications, that may go away. These drugs, the first of which was introduced about a year ago—a combination drug, xanomeline-trospium—doesn't block dopamine receptors. It acts on dopamine through a different mechanism, where it sort of suppresses overactive dopamine. It still has very powerful antipsychotic effects, and it does seem, at least from preliminary reports—it hasn't been adequately studied—to not have that effect on seeking rewards, as evidenced by the fact that it seems to improve negative symptoms and may improve cognition.

And when I talk about this transformation, I'm not talking just about this drug, because an important effect of the approval of this drug is it's caused an awakening within the pharmaceutical industry. And xanomeline-trospium is probably the first of a new generation of antipsychotic drugs that aren't dopamine blockers.

And that's why I'm hoping that this will be the most important transformation in treatment, really, since the introduction of clozapine—which to me was one of the most exciting parts of my career, that suddenly we had a new drug that helped with the population. So that's why I think we're at this exciting time in drug treatment. And I'm hoping that in the very near future, the drugs that we've used—which, by the way, are probably some of the least popular drugs in psychiatry by the patients who need to take them—will actually be replaced by a new generation of better agents.

Dr. Ramnarine:
That's fascinating. So, when it comes to long-acting injectables, what role do they play in improving treatment adherence and outcomes in schizophrenia?

Dr. Marder:
Long-term studies have shown that patients who receive long-acting antipsychotics actually have better long-term outcomes. For example, studies done in Scandinavia, where large populations of patients are followed for years, have found that those who were assigned to long-acting anti-psychotics actually have better outcomes as determined by fewer hospitalizations.

I think these drugs have been greatly underutilized over the years. Until recently, there were very few choices of LAIs. And now, there are new ones that are being introduced. Some of them are subcutaneous, whereas, up until recently, the only alternatives we had were paliperidone, aripiprazole, and haloperidol—and in some places fluphenazine. So I think that we're going to have other alternatives in the very near future.

For example, risperidone is now available in a subcutaneous form. Olanzapine is being developed as a better LAI than the one that currently exists. So I think there are going to be more alternatives, and that will hopefully allow more patients to have access to these drugs.

There are many reasons why psychiatrists have been reluctant to use these drugs. Some of them are not used to giving injections. They may not have nurses or other people to do injections. I think those problems have been solved in other countries. When one looks to Europe, long-acting antipsychotics are much more widely used.

The other thing is that LAIs have been limited to people who have clear histories of non-adherence and can't be expected to take oral medications. And I'm hoping that we'll find, in the very near future, that for larger populations, those who may not have a clear history of non-adherence—taking a drug every day for the rest of your life is kind of hard—for those people, clinicians and patients will see that this is sort of a better way to assure that somebody's able to stay on their antipsychotic.

Dr. Ramnarine:
For those just tuning in, you're listening to *On the Frontlines of Schizophrenia* on ReachMD. I'm Dr. Shelina Ramnarine, and I'm speaking with Dr. Stephen Marder about schizophrenia's evolving treatment landscape.

So, Dr. Marder, shifting now to non-pharmacological treatments, what are some of the most effective psychosocial interventions for this population?

Dr. Marder:
Again, I think that schizophrenia is probably an undertreated illness, because too many people only receive pharmacological treatment, and that's seen as an adequate treatment. But actually, one characteristic of schizophrenia is that it's an illness that affects multiple domains. People are affected both by reality distortions and psychosis, but also by decreased motivation and negative symptoms, as well as cognitive impairment.

And so we have a number of approaches. Again, many of them are underutilized. If one looks at just the psychosis itself, there are a number of effective treatments. Cognitive behavior therapy for psychosis has been found to be very effective. It's a very good treatment for patients where multiple drugs have been tried and patients still have treatment-resistant symptoms. And one adds CBT for psychosis, which really decreases the severity of psychotic symptoms and helps people live with their existing symptoms. I think there's a tendency among psychiatrists to think that the solution to psychosis is always going to be pharmacological. But in many cases, when one reaches the limit of pharmacology, CBT for psychosis can be effective.

There are also very good psychosocial treatments for delusions. Metacognitive approaches to delusions are available. They're actually websites that do that. If one goes beyond psychosis to some of the other symptoms, some of the most effective are family interventions, particularly educating families. Some of the largest effects on outcomes really occurred through interactions between clinicians who educate patients, families, or even set up groups where families are educated about the treatment and share their approaches.

For the cognitive impairments, there are a number of effective treatments, but cognitive remediation, which is available through different websites, actually helps patients to improve memory and executive function, and can be very effective, particularly since the current D2 blockers are, really, relatively ineffective for cognition.

Dr. Ramnarine:
Thank you so much for sharing that. So, given how important coordinated care and community support are in this space, how can multidisciplinary teams help shape outcomes for schizophrenia patients?

Dr. Marder:
Schizophrenia is an illness which exists on multiple domains, and there are different kinds of professionals who can help with those domains. For example, a team that includes both a prescriber and one who has to deal with the health problems of people with schizophrenia. In most clinics that treat a lot of schizophrenia, patients also have other medical comorbidities. A high portion of them have diabetes, pre-diabetes, or obesity, and those need to be addressed. Having a member of the team that can help address those problems is important. For example, one of the most effective interventions for schizophrenia is to help patients return to work or go back to school, for students.

It's been shown that particularly early in the treatment, it's important to have employment specialists or educational specialists that give individuals the supports they need to get back to work and to succeed at work, or to get back to school. One of the goals early in treatment, I think, is to really change the trajectory away from disability to better functioning.

And again, having individuals who are able to do that is important. The other thing is that some methods of coordinated care that include nurses or peer supports—who could actually go out into the community and see patients where they are—can be very helpful. For example, nurses can deliver long-acting injectable drugs. They can meet with families and help out. So I think the concept of coordinated care is really important in individuals with schizophrenia.

Dr. Ramnarine:
With those insights in mind, I'd like to thank my guest, Dr. Stephen Marder, for joining me to discuss how pharmacological and non-pharmacological approaches are helping improve care for patients with schizophrenia.

Dr. Marder, it was great having you on the program.

Announcer:
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