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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Antipsychotics Update

Learning Objectives
After reading these articles, you should be able to:

1. Identify ways for clinicians to manage antipsychotic use in patients.
2. Discuss the benefits of using clozapine for treatment-resistant schizophrenia.
3. Describe the pros and cons of Abilify MyCite.
4. Summarize some of the current findings in the literature regarding psychiatric treatment.

Clozapine: A Fresh Look

Several trials show it to be a superior treatment option, yet clozapine remains the "red-headed stepchild" of antipsychotics. Even though large studies reveal clozapine has impressive efficacy, particularly with treatment-resistant schizophrenia, many of us are reluctant to use it.

According to one study, of the 30% of patients who have treatment-resistant schizophrenia, just 5% are put on clozapine (Olfson M et al, *Psychiatr Serv* 2016;67(2):152). And, before turning to clozapine, some psychiatrists will try a dozen other atypical antipsychotics and antipsychotic polypharmacy.

So, why is there reluctance to prescribe this highly effective antipsychotic?

In Summary

- Clozapine is a superior option for your patients with treatment-resistant schizophrenia.
- Use it as a third-line option while properly monitoring the side effects.
- Don't be intimidated by the monitoring requirements, since the latest changes make prescribing the drug easier.

There's likely more than one reason. Many of us are justifiably concerned about clozapine's serious potential side effects, which can include neutropenia,

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Q&A With the Expert

Prescribing and Managing Antipsychotics

Thomas Schwartz, MD

Professor and Interim Chair of Psychiatry and Behavioral Sciences, Upstate Medical University, Syracuse, NY.

Dr. Schwartz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

TCPR: Dr. Schwartz, there are so many antipsychotics available. How do you choose in your own practice?

Dr. Schwartz: Any drugs that have an FDA indication for a particular diagnosis are likely to be effective. I especially like to use those that have less risk of metabolic complications, such as ziprasidone, lurasidone, etc. If we are discussing effectiveness with schizophrenia, none are better than clozapine (Clozaril), so I am willing to move to this drug when initial medications fail to help. For me, though, it comes down to side effect profile, so my personal preference is to avoid risperidone, olanzapine, paliperidone, and quetiapine.

TCPR: Why do you avoid those medications?

Dr. Schwartz: Because they are the most metabolically unfriendly products we have. There's a hassle factor—more blood draws, more calls to the family practice doctor, more help managing diabetes and lipids. So, I like to start with a safer drug with less metabolic risk. That said, my inpatient colleagues really like olanzapine and risperidone, and with difficult inpatients, they tell me those drugs "cut the mustard" and work better. But my inpatient colleagues only manage these patients for 10 days. I work with the patients for 10 to 20 years, and must manage those metabolic issues. A lot of trials seem to indicate that maybe generic risperidone and generic olanzapine are better in schizophrenia, but because of their side effect profile, I like to hold them in reserve.

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Clozapine: A Fresh Look

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myocarditis, seizure, fecal impaction, and cardiomyopathy. We may also hesitate to choose clozapine because of the extra time and perceived inconvenience involved in lab monitoring, patient education, and extra required training (REMS certification) for prescribers.

For those reluctant to make clozapine their go-to antipsychotic for certain patients, this article will provide information to help you decide when it's right to prescribe.

How effective is clozapine?

In 1989, clozapine—which is also marketed as Clozaril—was the first FDA-approved atypical antipsychotic for schizophrenia. It is indicated for treatment-resistant schizophrenia, and for reducing the risk of suicide in patients with schizophrenia and schizoaffective disorder.

But is clozapine really more effective than other antipsychotics? Clozapine was first shown to be superior to chlorpromazine (Thorazine) in patients who had inadequate response to at least 3 first-generation antipsychotics (Kane J et al, *Arch Gen Psych* 1988;45(9):789–796). At the end of 6 weeks, 30% of patients randomly assigned to clozapine (n = 126) responded, as opposed to only 4% of those randomized to chlorpromazine (n = 142). That's a large difference, and since then other trials have gone on to report clozapine's superiority in treatment-resistant schizophrenia compared with other antipsychotics, such as haloperidol, olanzapine, quetiapine, risperidone, and ziprasidone. In addition, large effectiveness trials and population-based registry studies have demonstrated clozapine's superior efficacy and increased patient adherence compared with both FGAs and SGAs.

Clozapine is one of only a few drugs proven to decrease suicide risk. In a 2-year randomized controlled trial comparing clozapine with olanzapine (Zyprexa), clozapine was shown to significantly decrease suicide attempts, hospitalizations due to suicide, and suicide prevention treatment and interventions (Meltzer HY et al, *Am J Psychiatry* 2003;60(1):82–91).

Clozapine (Clozaril)—At a Glance	
Indications	Treatment-resistant schizophrenia (consider using after 2 failed trials of other antipsychotics)
Dosages available	25 mg, 100 mg
Dosing	• Start with 12.5 mg–25 mg daily • Increase by 25 mg–50 mg every few days • Target dose: 300 mg–450 mg daily for healthy adults, 150 mg–300 mg daily for older adults
Lab monitoring	ANC (absolute neutrophil count) every week for 6 months, then every other week for 6 months, then monthly
Comment	FDA requires training at www.clozapinerems.com

Which patients are right for clozapine?

All treatment guidelines for schizophrenia recommend clozapine after inadequate response to at least 2 antipsychotics. For patients who are extremely aggressive or suicidal, the APA treatment guidelines state a trial of clozapine may be reasonable as a first- or second-line antipsychotic.

How to prescribe clozapine

Educate your patients. The first step is achieving buy-in from your patient and the family. You'll need to give adequate disclosure about potential side effects, but this doesn't have to be a long speech.

Introduce the use of clozapine with a discussion about how other medications haven't been completely effective. Tell patients, "I know the medications you've tried haven't completely helped you. Clozapine is a medication that is more effective for people when other antipsychotics haven't worked. It has a bunch of side effects, but we can monitor for them. Should we try it for a little while? If it works, I think you might decide that the side effects are worth putting up with." Then, review the specific side effects and monitoring process (see table on page 3).

How to dose clozapine. Start with a low dose of 12.5 mg–25 mg a day to minimize side effects. Increase the dose by 25 mg–50 mg every few days. Dividing the dose into twice or 3 times daily can help minimize sedation and orthostasis. The initial target dose is 300 mg–450 mg daily in healthy adults, and 150 mg–300 mg daily in older adults. Once the titration is complete, all or most of the clozapine can be given at night to help with adherence.

Some experts believe that following clozapine serum levels is helpful in titrating the dose. Guidelines vary, but one common approach is to shoot for a serum concentration of 250 ng/mL–350 ng/mL of clozapine. If a patient isn't responding at that dose, aim for a serum level of 350 ng/mL–450 ng/mL. Since the seizure risk increases with higher clozapine concentrations, avoid going above doses of 600 mg/day (Xiang YQ et al, *Schizophr Res* 2006;83(2-3):201–210), or consider adding divalproex sodium.

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Mailing Information

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Many patients with schizophrenia smoke cigarettes, and smoking decreases clozapine levels by inducing the main enzyme that metabolizes the drug, CYP450 1A2. For patients who smoke, the doses recommended above are still reasonable for an initial target dose, but higher doses may be necessary. Also, smokers who are stabilized on a dose in the hospital may need an upward dose adjustment once they are discharged and resume smoking.

Clozapine monitoring and prescriber training

Don't be intimidated by the monitoring requirements for clozapine. The latest changes make prescribing the drug easier, not harder.

Before 2016, you had to order a WBC and ANC. You also had to keep track of the absolute values and changes in WBC and ANC over time. Since then, monitoring has become much easier. Now you need to monitor only the ANC every week for 6 months, then every other week for 6 months, and then monthly thereafter. Continuation of clozapine is based on the absolute ANC value, not changes in ANC over time.

Before you can prescribe clozapine, you must complete an enrollment form, course, and quiz online, all of which can be found at www.clozapinerems.com. The entire process usually takes less than an hour.

Managing clozapine side effects

The most common side effects are weight gain, hypersalivation, sedation, orthostatic hypotension, and constipation. See the table on page 3 for some advice on how to approach these problems.

In addition to these common side effects, there are a few rare but serious side effects—neutropenia is one of them. Myocarditis/cardiomyopathy is very rare, and there is no agreed-upon monitoring for it, but some experts recommend that you get troponin and CRP (c-reactive protein) levels weekly for the first 8 weeks. This represents an abundance of caution and is not commonly done.

Seizures are rare and can be dose related, with doses greater than 600 mg daily associated with significant increased seizure risk: 4.2% vs 2.4% (Grove S, *East Asian Arch Psychiatry*. 2015;25(2):73–78). Having an anticonvulsant like divalproex on board helps minimize the seizure risk with higher clozapine doses.

Since clozapine can cause significant constipation, routine questioning about bowel habits is important. Consider initiating a preventive bowel regimen, including a stool softener, like those used with opioids. You should also make patients aware of other side effects, such as hyperglycemia, hypertriglyceridemia, and tachycardia. If sedation is a problem, the dose can be given mainly at night.

Sialorrhea is a particularly annoying side effect. Treatment approaches include sugarless gum, anticholinergics such as glycopyrrolate, sublingual ipratropium spray, and alpha-2 agonists

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Managing Clozapine Side Effects

Side Effect	Incidence	Monitoring	Treatment	
Bradycardia Orthostatic hypotension Syncope	9%–13%	• Pulse • Blood pressure • Orthostatic blood pressure • Dizziness	• Divided dose (2–3 times daily) • Start with low dose • Slow titration • Adequate fluid intake	• Behavioral changes (sit on edge of the bed with legs hanging down for a minute before getting up) • Fludrocortisone, if necessary
Constipation	15%–25%	• Clinical interview	• Drink fluids • Increase fiber • Exercise	• Minimize other anticholinergics (eg, benztropine, diphenhydramine) • Consider bowel regimen, similar to opioids (eg, docusate 100 mg–250 mg BID)
Drowsiness	Up to 45%	• Clinical interview	• Bedtime dosing	• Lowest dose possible
Hyperglycemia	27% increased to ≥ 126 mg/dL	• Baseline and quarterly fasting glucose or HbA1c	• Dietary intervention • Exercise	• If A1c > 6.5/7%, add metformin (6.5 for younger people with long life expectancy)
Hypertriglyceridemia	50% mean increase of ≥ 71 mg/dL	• Baseline, week 12, and annually	• Dietary intervention • Exercise	• Omega-3 fatty acids • Fibrates (caution with statins)
Myocarditis Cardiomyopathy	0.002%	• Troponin & CRP weekly for first 4–8 weeks	• Discontinue if CRP > 100 mg/L	• Troponin ≥ 2 x ULN
Seizures	2.4%–4.2%	• Clinical interview/contact from ER or hospital	• Use lowest dose possible (< 600 mg ideally)	• Concomitant valproate
Sialorrhea	15%–40%	• Clinical interview	• Glycopyrronium 2–4 mg at bedtime	• Botulinum toxin
Tachycardia	15%–25%	• Pulse	• Lower dose	• Beta blockers (eg, metoprolol)
Weight gain ≥ 7% from baseline	35%	• Baseline weight/BMI at weeks 4, 8, 12 and quarterly	• Dietary intervention • Exercise	• If gain > 5 lbs in first month or > 10 lbs from baseline, consider metformin

Abilify MyCite: Patient Care Breakthrough or Patent Extender?

You've probably heard about a new "digital pill" called Abilify MyCite. The product, which was FDA approved in November 2017, is the first drug in the U.S. with a digital ingestion tracking system.

MyCite consists of an aripiprazole pill that contains an embedded tiny sensing device (about the size of a grain of sand) called the ingestible event marker (IEM). Patients swallow the pill like any other, and once it dissolves, the IEM comes in contact with gastric fluids—which triggers the device to emit a signal. This signal communicates with a wearable sensor contained in a small patch on the patient's abdomen. The patch then transmits a signal to a mobile application, allowing the patient to view compliance data on a smartphone. Patients can share these data with whomever they want—such as a physician or a family member. If your patients give you signed consent, you can access their ingestion data via a web-based portal or app.

The idea behind MyCite is that it will allow you to tell whether your patients are compliant with their medication. However, Otsuka, the manufacturer, has not presented any data showing that this formulation improves compliance, and the FDA indication explicitly states that "the ability of Abilify MyCite to improve patient compliance or modify aripiprazole dosage has not been established." The label also points out that the system is not foolproof, and that ingestion is not always detected.

Nonetheless, it's likely that this innovation will help you track your patients' compliance. This would be helpful for those patients who are either forgetful or ambivalent about taking their antipsychotic. Currently, our standard approach for such patients is to simply ask them if they are taking their meds, but patients are often inclined to please us and will usually say "yes" even if they have skipped doses. If they are doing poorly, we think about increasing doses or making a medication change. It would be nice if we could definitively verify whether the drug is actually getting into the patient's system before we opt for any change to medication.

Conversely, some patients admit that they don't take their meds because, for example, they don't think they need them or they are worried about side effects. Such patients will presumably toss MyCite into the trash just as they would regular aripiprazole. For these patients, a long-acting injectable antipsychotic might be more appropriate—assuming they consent.

As we wait for empirical data to guide us in our use of MyCite, here are some of the major potential benefits and drawbacks of the formulation.

Potential benefits

- It may help determine compliance, and therefore help us decide whether a poor response is due to the wrong medication or to skipped doses.
- It may decrease conflicts between patients and family members. Family members are often concerned that patients are not taking their medications, leading to conflict and nagging. Family conflict can sometimes cause patients to decompensate, leading to rehospitalizations.

Potential drawbacks

- Some have wondered if putting a computer chip in a pill will make schizophrenic patients more paranoid. But a 2013 study of 27 patients with schizophrenia or bipolar disorder found that such patients tolerated ingestible sensors well. None of the participants became paranoid about the technology, 19 of them found the digital pill concept easy to understand, and 24 said they believed the technology could be useful for them (Kane JM et al, *J Clin Psychiatry* 2013;74(6):533–540).
- There are some concerns about privacy of the compliance data. To address this, the system requires patients to give informed consent before releasing their data. In addition, each time patients ingest a pill, they can decide whether to continue sharing the data. If they decide to opt out, they can simply turn off the app at any time.
- Although there is no information on cost yet, MyCite will presumably be much more expensive than a regular aripiprazole prescription. It's unclear how many health insurers will cover it.
- Is ingesting computer chips safe? According to the manufacturer, ingesting the tiny chips didn't cause any adverse effects. The receiving patch can cause some minor skin irritation.

Specific rollout dates for Abilify MyCite have yet to be announced, but Otsuka says it will be available sometime in 2018. Initially, the company plans to conduct beta testing by rolling it out to a select number of health plans and providers "who identify a limited number of appropriate adults with schizophrenia, bipolar I disorder, or major depressive disorder." The company's goal with this small initial rollout is to ensure that the technology works and is bug free.

TCPR VERDICT: Abilify MyCite sounds creepier than it is. Depending on insurance coverage, it's worth trying for patients who are ambivalent about taking their meds.

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Clozapine: A Fresh Look

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(eg, clonidine). Keep in mind that all these medications can themselves lead to more side effects. One novel treatment to consider is botulinum toxin injections in the bilateral and submandibular glands. Some case reports indicate benefit for antipsychotic-induced sialorrhea (Steinlechner S et al, *Psychopharmacology* 2010;207(4):593–597). For some additional resources, including discussions by patients who take clozapine, see: http://practiceinnovations.org/Consumers/Medication-and-Medication-Side-Effects.

TCPR VERDICT: About a third of your patients with schizophrenia will be treatment resistant and should have a trial of clozapine—make sure it happens!

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Expert Interview

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TCPR: That makes a lot of sense. But what happens when your patient doesn't respond to other drugs and you need to consider using olanzapine? There are various guidelines for what we're supposed to do in terms of monitoring, but what do you do, and what do you tell your patients?

Dr. Schwartz: With every atypical, there are class warnings for weight gain, hyperlipidemia, increased blood sugar, abdominal girth, tardive dyskinesia, and extrapyramidal symptoms (EPS). I have a conversation in layman's terms with the patient and say, "You might gain weight. Your cholesterol, your blood sugars might go up, you may get muscle shakes, muscle twitches, and some of those will be permanent (Wei Xin Chong J et al, *Mental Health Clinician* 2016;6(4):178–184)." I tell them that their risks with these drugs are greater than some of the other drugs. That's how I pitch it in the end, and I think that does get me through an informed consent process. For monitoring with all of the atypicals, we get vital signs—blood pressure, height, and weight. We check labs for sugars and lipids.

TCPR: Earlier, you mentioned clozapine in the context of saying none of the other antipsychotics are better. Do you have any advice on how to make the process of prescribing it a little less scary?

Dr. Schwartz: Yes. Good question. As we are finding more people with schizophrenia that are treatment-resistant and treatment-refractory, I think clozapine is making a comeback. I think if you march through the 11 or 12 atypical antipsychotics, spending 3 months on each, you have someone who might go 3 or 4 years with unmitigated psychosis. To me, that is too much of a delay and can worsen the patient's prognosis. I would say that, if you fail with 2 or 3 antipsychotics and you still have psychosis going on, go with clozapine. It's a great drug. [Ed note: See this month's article on clozapine on page 1]

"My personal preference is to avoid risperidone, olanzapine, paliperidone, and quetiapine because they are the most metabolically unfriendly products we have. There's a hassle factor—more blood draws, more calls to the family practice doctor, more help managing diabetes and lipids."

Thomas Schwartz, MD

TCPR: Do you find that you're doing the same monitoring with all the medications? And how do you manage the problematic issue of weight gain for patients?

Dr. Schwartz: Most of my patients have a scale at home, and I'll say, "I might not see you for 90 days, and if you gain more than 5 pounds I want you to call me, since I know that some people can gain 15 pounds in 3 months." So, I do try to empower my patients to self-monitor with their scale, but I don't necessarily bring them in every couple of weeks just to measure their weight. I tell them, "If you're consistently above 5 pounds, I'm going to give you a speech about diet and exercise. If that fails, I'm going to probably put you on weight loss meds."

TCPR: I'm guessing that first conversation about weight doesn't always work for your patients. When it doesn't, what else do you say to them?

Dr. Schwartz: What works the best in my practice is that I tell patients, "You don't have to count calories. You actually don't have to exercise." I start by telling them all the things they don't have to do, and their defenses drop some. It's about portion control, and my quick speech is: "You can eat everything that you normally eat, but I want you to take 25% of the food off your plate." And I joke about it by saying, "You can feed it to your dog. You can give it to your spouse. You can save it for another time. But you're not going to eat a quarter of what's on your plate. You can eat a candy bar, but eat three-quarters of it." That's portion control. A very simple explanation about portion control dieting has been my most effective approach. After that, if the portion control approach doesn't work, I move to weight loss methods.

TCPR: Which weight loss antidotes do you recommend?

Dr. Schwartz: The one with the most evidence is metformin. It's off label; it's a $5 generic. There are at least 20 trials, and this is almost a standard of care. It clearly knocks off 5 to 10 pounds in our patients. It does not make people hypoglycemic like insulin would (Zheng W et al, *Journ Clin Psychopharm* 2015;35(5):499–509). There's nausea and diarrhea, and you must watch out for acidosis. You need a basic metabolic panel once a year to make sure the bicarb isn't too low. But in my practice, it is a very well-tolerated drug.

TCPR: And what dosing of metformin do you use?

Dr. Schwartz: I start off at 500 mg twice a day, and I give that 2 to 3 months to settle in. After that, if there's no significant weight loss, I will go up to 1,000 mg BID, and I'll give that another couple of months. If it works and the weight is staying off, I may keep the patient on the metformin.

TCPR: What labs do you recommend before starting an atypical antipsychotic?

Dr. Schwartz: I'll get baseline labs. Before I start the drug, I'll get a lipid panel and either a fasting glucose or a hemoglobin A1C. Because I'm doing a blood draw regardless for atypical monitoring, I usually get a CBC because there are general precautions about agranulocytosis. Then I'll titrate the drug, and once I'm up to a reasonable dose, which could be anywhere from 2 weeks to several weeks, I'll get a new blood draw. Then I'll wait 3 or 4 months, and then get another blood draw. After that, if the patient's labs are clean, I'm happy with once-a-year blood draws. If the patient shows some inkling toward more weight gain, and one of the labs has peaked a little bit, then I'll probably get blood every 6 months.

TCPR: That reminds me to ask you about labs in general. Clinicians are pretty good about ordering labs, but when we get a result that's flagged as abnormal, how should we respond?

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Research Updates IN PSYCHIATRY

DRUG SAFETY

QTc Prolongation Risk Management in Hospital Patients

REVIEW OF: Vandael E et al, *J Clin Psychopharmacol* 2017;37(5):540–545

Many of the medications we prescribe, most notably antipsychotics and antidepressants, have some risk of QTc prolongation. Since it's rare to have complications of a prolonged QTc interval—such as torsades de pointes (TdP) and sudden cardiac death—clinics and hospitals typically don't screen for it using electrocardiograms (ECG).

This study evaluated the impact of combining 2 medications that are known to cause QTc prolongation, and attempted to stratify patients based on a baseline risk score calculation. The study population consisted of 152 patients in 6 psychiatric hospitals who were already taking 1 or more QTc-prolonging medications. All patients received a baseline ECG to see whether their existing medication was causing QTc prolongation. These patients were then observed, and those whose clinicians added another torsadogenic medication were included in the study and were given another ECG within 14 days. The most common medications prescribed in the study were mirtazapine, quetiapine, escitalopram, and trazodone.

How did adding these medications affect ECGs? Across all patients, there was a statistically significant increase ($p = 0.032$) in mean QTc interval from a norm of 409.1 ms to 411.8 ms with a single QTc-prolonging medication. At follow-up ECG, after the addition of a second QTc-prolonging medication, only 3 participants (2%) developed a prolonged QTc (≥ 450 ms for men and ≥ 470 ms for women). Only 8 patients (6.6%) had an increase in their QTc ≥ 30 ms, and no one had an increase in QTc ≥ 60 ms. No study participants experienced TdP or sudden cardiac death.

The study also explored potential predictors of QTc prolongation by assigning a risk score at baseline. This score, called the "RISQ-PATH score," was computed using the patient's age, sex, cardiac risk factors, and number of QTc-prolonging medications currently prescribed.

According to the RISQ-PATH score, 58 patients (38.2%) were considered high risk at baseline, and these patients had a significantly higher QTc interval in the follow-up ECG compared to low-risk patients (420.7 ms vs 406.2 ms, $p < 0.001$).

TCPR'S TAKE

There is a direct correlation between the number of QTc-prolonging medications and a longer QTc interval. However, for most patients in this study, the absolute increase in QTc interval was very small, with only 2% of patients developing a prolonged QTc. And, regardless of the QTc prolongations, none of these patients developed any clinical symptoms attributable to the ECG changes. A risk score, such as the RISQ-PATH score, would be helpful in choosing which patients need ECG monitoring, but this test needs further validation before being used in the general psychiatric population. Also, despite these "reassuring" data, the problem may be greater among the elderly. For a geropsychiatrist, these data may not be reassuring.

The bottom line is that while combining QTc-prolonging medications does indeed affect QTc intervals, the magnitude of the effect is likely to be tiny, with a very low probability of clinical consequences. While prudence would dictate avoiding such combinations, if the patient's symptoms require these medications, go ahead and prescribe them while monitoring the ECG.

—Thomas Jordan, MD

Dr. Jordan has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Expert Interview

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Dr. Schwartz: I recommend asking for training from a colleague who's a family medicine doctor or an internist. Get 30 minutes of the person's time and ask, "What do you look for in a lipid panel, and how do you test for elevated blood sugars?" Also ask, "What scares you in a lab profile, and what should I worry about?" That's what I did—I talked to my uncle, who's an endocrinologist. If you don't feel comfortable interpreting labs yourself, you can always shoot off a quick letter to your patient's primary care doctor to ask for help.

TCPR: Using that approach, what are some of the things that you've learned that we should take note of in the labs?

Dr. Schwartz: Fasting glucose is one area that comes to mind, and it should be below 100. If patients are between 100 and 120 twice, they're prediabetic. If they're above 120 twice, they're diabetic. When somebody gets in that 120 range, I start getting worried, and that's my cue to get help. In terms of lipids, I focus on triglycerides, which in my experience usually spike first in a metabolic disorder. When triglycerides spike above 150, I get worried. At that point I'll prescribe fish oil, but I'll also refer the patient to primary care.

TCPR: When you use fish oil, is there any particular brand that you favor?

Dr. Schwartz: Lovaza and Epanova are the only FDA-approved ones, but it can be hard to get coverage, so over-the-counter fish oil works as well. I usually use about 4,000 mg per day. And there's some data regarding fish oil helping ADHD and depression, so every now and then I get lucky and it helps the other medications that are on board.

TCPR: Switching gears a little, let's discuss some of the relatively new antipsychotics. Many of us have very little experience prescribing them. What are some of their advantages?

Dr. Schwartz: Let's start with cariprazine (Vraylar) and brexpiprazole (Rexulti). These are sometimes called third-generation antipsychotics. They're very similar to aripiprazole. These 3 drugs have a different mechanism than other

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CME Post-Test

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatReport.com to take the post-test. You must answer 75% of the questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be completed within a year from each issue's publication date. As a subscriber to *TCPR,* you already have a username and password to log onto www.TheCarlatReport.com. To obtain your username and password, please email info@thecarlatreport.com or call 978-499-0583.

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For those seeking ABPN Self-Assessment (MOC) credit, a pre- and post-test must be taken online at http://thecarlatcmeinstitute.com/self-assessment/

Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning Objectives are listed on page 1.

1. One of the drawbacks to using lurasidone includes: (LO #1)

[ ] a. It must be dosed three times per day
[ ] b. Lipid abnormalities often increase with extended use
[ ] c. Rapid weight gain can occur during the first 6 months
[ ] d. It must be taken with food for effectiveness

2. To avoid the risk of _____, clinicians should avoid prescribing clozapine in doses above 600 mg/day. (LO #2)

[ ] a. Sleep paralysis
[ ] b. Reduced blood clotting capacity
[ ] c. Seizure
[ ] d. Stevens-Johnson syndrome

3. One concern about using Abilify MyCite for schizophrenic patients is a small but significant increase in paranoia surrounding the technology. (LO #3)

[ ] a. True
[ ] b. False

4. According to a study, what percentage of patients with treatment-resistant schizophrenia are prescribed clozapine? (LO #2)

[ ] a. < 1%
[ ] b. 5%
[ ] c. 9%
[ ] d. 14%

5. According to a recent study assessing risk of prolonged QTc during hospitalization, what percentage of patients developed this condition while taking QTc-prolonging medications? (LO #4)

[ ] a. < 1%
[ ] b. 2%
[ ] c. 5%
[ ] d. Between 7% and 9%

Expert Interview
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antipsychotics—they partially agonize D2 and D3 receptors. They're not full antagonists, so I put them into their own family. I think aripiprazole (Abilify) is a great drug. It's generic; it's $5; it has a lot of FDA-approved indications. So, I usually start with Abilify, and if patients can't tolerate Abilify, I then switch them to Rexulti. Vraylar is interesting to me; it is probably the best at manipulating the D3 receptor, which is one of the wakefulness and executive functioning receptors.

TCPR: What has been your experience with Latuda?

Dr. Schwartz: Because it rarely causes weight gain or lipid abnormalities, Latuda (lurasidone) is a fantastic drug, and it's approved for bipolar depression. The problem with Latuda is that, to be fully absorbed, it must be taken with food. I've had a couple patients who could not absorb it even after eating enough calories. I even had a gentleman—just to demonstrate that he was in fact taking it correctly—come to my practice each day to take his Latuda along with a donut, but he still could not absorb it. As for side effects with Latuda, you can see some EPS, some headaches and stomachaches; you get some fatigue. These are the kinds of constitutional nickel-and-dime side effects that you can get from several psychiatric medications.

TCPR: What about Geodon as an option to avoid metabolic effects?

Dr. Schwartz: From a metabolic point of view, ziprasidone (Geodon) is my second favorite behind lurasidone. The issue I have with ziprasidone is that, although it works for schizophrenia and bipolar mania, there are only a couple of small studies showing that it helps depression. The other problem is that dosing is unpredictable. I have some people who get sedated on low doses of around 20 mg twice a day with food; others get horrible akathisia. So, in terms of doing informed consent with patients, I tell them, "We are starting on a low dose, but I have no idea if you're going to get tired and sedated, or if you're going to feel like you are caffeinated with akathisia. You might get none of those side effects." But again, this is why I prefer Latuda, which seems to have fewer side effects and is more predictable.

TCPR: And when you do prescribe ziprasidone, what do you do about cardiac issues?

Dr. Schwartz: I follow the FDA guidance. Unless a person has previous heart issues or a family history of heart issues, I don't do an ECG. If I ever end up super-dosing it and going off label by pushing the drug higher, I will get an ECG.

TCPR: Thank you for your time, Dr. Schwartz.

THE CARLAT REPORT: PSYCHIATRY

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This Month's Focus:
Antipsychotics Update

Next month in *The Carlat Psychiatry Report:*
Neurofeedback

Note From the Editor-in-Chief

We publish an issue on antipsychotics at least once a year, and it's always a challenge to decide what to cover. There are dozens of antipsychotics, and most of them are approved for mood disorders as well as psychosis. I was lucky to be able to speak with Dr. Thomas Schwartz, whose wealth of clinical knowledge on neuroleptic use is astounding. He has some excellent advice on how to monitor and manage metabolic side effects—especially for the likes of olanzapine and risperidone. He also has some comments on when to consider using the newest neuroleptics. We then move to an oldie but goodie: clozapine, a potentially dangerous but extremely effective drug for treatment-resistant schizophrenia. We update you on how to safely prescribe it, along with a straightforward approach to monitoring side effects. And finally, we cover the "Big Brother" pill, Abilify MyCite, concluding that this digital pill sounds much spookier than it actually is. It's innovative and may be the forerunner of medications of the future, but it's hard to imagine too many patients for whom its expense will justify its use. All in all, I think this issue shaped up pretty nicely—let me know if you agree.

Best, Danny Carlat
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