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Chris Aiken, MD
Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
How to Talk about Medication

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

1. Evaluate the current role of mirtazapine augmentation in depression.
2. Describe the benefits of the Medication Interest Model (MIM) for engaging patients in treatment.
3. Minimize the risk of complex sleep behaviors in patients taking z-hypnotics.
4. Summarize some of the current research on psychiatric treatment.

Mirtazapine Augmentation: Running Low on Rocket Fuel

Thomas Jordan, MD and Chris Aiken, MD.

Dr. Jordan and Dr. Aiken have disclosed that they have no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Adding mirtazapine (Remeron) to a serotonergic antidepressant is a popular augmentation strategy. When added to venlafaxine, the combo was thought to possess a particularly potent synergy that Stephen Stahl called "California Rocket Fuel." However, the strategy has failed in a handful of new studies, some of them much larger than the original data. Is it time to stop using it?

How does mirtazapine work?
Mirtazapine is in a class of its own

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Highlights From This Issue

Mirtazapine augmentation does not work when patients don't respond to antidepressant monotherapy

Shawn Christopher Shea, MD has been fine-tuning the art of doctor-patient communications for over 30 years. He shares his tips on talking about medications.

Serious injuries have prompted new warnings on hypnotics. We'll show you how minimize those risks.

Paxil has a reputation as the best SSRI for anxiety, but head-to-head trials suggest the opposite.

Q&A With the Expert

A New Way to Talk to Patients about Medication
Shawn Christopher Shea, MD

Director of the Training Institute for Suicide Assessment and Clinical Interviewing. Internationally recognized innovator in the fields of clinical interviewing and suicide prevention and author of seven books, several of which are included in Doody's Core List of the most important books in psychiatry and medicine.

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

TCPR: We all want to communicate better with patients, particularly around medications. You've lead workshops on this for several decades. Tell us about the model you developed out of that work.

Dr. Shea: The Medication Interest Model (MIM) is a set of over 100 interview techniques that create shared decision making regarding all disease states from psychiatric illnesses to diabetes, congestive heart failure and AIDS. The MIM techniques were created to help experienced clinicians maximize patient interest and follow-through with medications in their day-to-day practices. The model is designed for psychiatrists, as well as general medical providers and trainees—anyone who talks with patients about their medications. It addresses everything from creating motivation to uncovering

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Mirtazapine Augmentation: Running Low on Rocket Fuel

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pharmacologically. Like venlafaxine and other SNRIs, it increases norepinephrine and serotonin transmission, but it does so through a different mechanism. Instead of blocking the reuptake of these neurotransmitters as SNRIs do, it enhances their release by binding to alpha-2 adrenergic receptors. Theoretically, mirtazapine has a synergistic effect with serotonergic medications, enhancing their benefits and—through post-synaptic serotonin blockade—reducing common side effects like nausea and sexual dysfunction.

Mirtazapine's main drawbacks—weight gain and sedation—derive from its antihistaminergic effects at H1. About 30%-75% of patients gain significant weight on mirtazapine (Uguz F et al, *Gen Hosp Psychiatry* 2015;37(1):46-48).

EDITORIAL INFORMATION

Publisher: **Daniel Carlat, MD**

Editor-in-Chief: **Chris Aiken, MD**

Deputy Editor: **Talia Puzantian, PharmD, BCPP,** professor, Keck Graduate Institute School of Pharmacy, Claremont, CA

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A promising beginning

Beginning in the 1990's, a series of open label trials suggested that mirtazapine (30-45 mg/night) is an effective augmentation agent in treatment-resistant depression. Placebo-controlled confirmation started to roll in with a small study in 2002. The results were impressive, with remission rates of 45% with mirtazapine vs. 14% on placebo, but the study was small (n=26) (Carpenter LL et al, *Biol Psychiatry* 2002;15;51(2):183-188).

The venlafaxine/mirtazapine "rocket fuel" combination was used in the STAR-D trial, where it was compared to tranylcypromine monotherapy after failure of 3 antidepressants. STAR-D was designed to test whether any of the popular augmentation strategies from the 1990's worked better than the others. The bottom line is that none of them did, including the rocket fuel, but because it lacked a placebo arm the study can't tell us if any of those strategies actually worked at all (McGrath PJ et al, *Am J Psychiatry* 2006;163(9):1531-1541). The other study to test this combination had promising results but very poor design. It was a retrospective chart review of 39 patients that found higher remission rates with venlafaxine/mirtazapine than venlafaxine alone (Aydemir O et al, *Bulletin of Clinical Psychopharm* 2009;19:347-352).

So, up until 2018 mirtazapine augmentation held a lot of promise, and a bit of hype, but little in the way of confirmation.

New conflicting data

In the past year, a series of well-designed studies have brought those early results to question. In the first large, placebo-controlled trial of mirtazapine augmentation, the medication failed to separate from placebo in 480 patients who had failed a six-week antidepressant trial in a primary care setting. Remission rates were 24% on placebo vs. 29% with mirtazapine (Kessler DS et al, *BMJ* 2018;363:k4218). Negative results like this are often blamed on an unusually large placebo response, but that was not the case here. Most studies of treatment resistant depression see about 25% of their subjects remit with placebo.

The next study was also randomized, but open-label and not placebo-controlled. It followed 112 patients whose depression had failed to respond to venlafaxine. They were randomized to augmentation with mirtazapine or a switch to imipramine. Although augmentation usually outperforms switching in most depression trials, here the remission rates nearly doubled when switching to imipramine (72% vs. 39%) (Navarro V et al, *J Clin Psychopharmacol.* 2019;39(1):63-66).

New, yet to be published data presented at the May 2019 APA annual meeting is continuing this trend. This study randomized 204 patients who did not respond to paroxetine monotherapy to three treatment arms: paroxetine/mirtazapine, paroxetine/placebo, and mirtazapine/placebo. Mirtazapine augmentation failed to separate from the two placebo arms after 8 weeks (Xiao L et al, APA Poster 2019).

Mirtazapine for specific co-morbidities

Although mirtazapine augmentation has yet to demonstrate efficacy, it may have a useful role in certain types of depressed patients. Its sedative qualities can help insomnia, and it also improves deep stage N3 sleep and reduces nighttime awakenings (Karsten J et al, *J Psychopharmacol* 2017;31(3):327-337). In small, placebo-controlled trials, mirtazapine augmentation has improved obsessive-compulsive disorder, depressive symptoms of PTSD, and negative symptoms of schizophrenia (Pallanti S et al, *J Clin Psychiatry* 2004;65(10):1394-1399)

TCPR VERDICT: "California Rocket Fuel" turns out to be no better than regular, unleaded gasoline. As is often the case, the positive studies are small and flawed, while the negative ones are large and well-designed. Nevertheless, mirtazapine augmentation may still be useful for depressed patients with insomnia and weight loss.

To learn more, listen to our 9/23 podcast, *"Remeron Runs Out of Rocket Fuel".* Search for "Carlat" on your podcast store.

A New Contraindication for Ambien and the Z-Hypnotics

Chris Aiken MD and Talia Puzantian, PharmD, BCPP

Dr. Aiken and Dr. Puzantian have disclosed that they have no relevant financial or other interests in any commercial companies pertaining to this educational activity.

"Complex sleep behavior" is a euphemism for various problems that can happen after ingesting a sleeping pill. They range from cooking and emailing to driving a car or even sexual assault, all done in an amnestic state that is not recalled upon awakening. In 2007 the FDA placed warnings about these behaviors on all medications approved for insomnia, and this year they moved that warning up to a black-box level for the z-hypnotics: zolpidem (Ambien), zaleplon (Sonata), and eszopiclone (Lunesta). The new warning also applies to zolpidem's various forms: CR, sublingual (Intermezzo, Edluar), and oral spray (Zolpimist).

The agency took this step to recognize the gravity of these parasomnias, which are too often the butt of jokes. They reviewed 26 years of adverse event reports and found 66 cases of complex sleep behaviors that resulted in either serious injuries (46 cases) or death (20 cases). Some of the cases involved accidental overdoses, falls, burns, near drowning, exposure to extreme cold temperatures leading to loss of limb, carbon monoxide poisoning, drowning, hypothermia, motor vehicle accidents with the patient driving, and self-injuries such as gunshot wounds and apparent suicide attempts.

Although severe events are very rare, complex sleep behaviors are fairly common and occur in 3%-15% of people on z-hypnotics. Zolpidem is the most notorious only because it is the most frequently prescribed—its risk is actually no different than the others in its class. With all z-hypnotics, the risk goes up as the dose goes higher (Chen LF et al, *Neuropsychiatr Dis Treat* 2013;9:1159-1162).

The most important part of this warning is the word "contraindication." The FDA now recommends discontinuing z-hypnotics in anyone who has had a complex sleep behavior after taking them, however mild. Patients may protest that there's nothing dangerous about microwaving popcorn at 2 a.m., but there's always a risk that the problem might lead to a fractured skull or burnt arm.

Part of the reason for the absolute tone in this contraindication is that the benefits of z-hypnotics are so meager that it's hard to justify their use in the face of these risks. On average, they cause people to fall asleep 22 minutes faster than a placebo by polysomnographic measures, and only 7 minutes faster by subjective report, according to a meta-analysis of the FDA-registration trials (Huedo-Medina TB et al, *BMJ* 2012;17;345:e8343). They do nothing to improve quality of sleep or long-term health outcomes. Patients seem to find these drugs more helpful than the research suggests, in part because there is a large placebo effect. People fall asleep 20-30 minutes faster with a placebo. The amnestic qualities may also explain why these drugs are so well liked: patients forget how poorly they slept.

Preventing Complex Sleep Behaviors

1. Lower zolpidem in women

Women eliminate zolpidem slower than men, resulting in higher rates of complex sleep behaviors and more impairment of morning driving. The FDA changed the starting dose of zolpidem in women from 10mg to 5mg in 2013 (or 6.25mg for Ambien CR). Among the z-hypnotics, zolpidem has the highest risk of morning impairment, so the FDA recommends that we aim for lower doses in men as well and that patients avoid driving the next day after taking Ambien CR.

2. Watch for drug interactions

Zolpidem and eszopiclone are metabolized through CYP3A4, so inhibition of this enzyme can result in higher levels of the hypnotic (strong inhibitors: nefazodone, -azole antifungals, antiretrovirals, erythromycin, and clarithromycin; weaker inhibitors include: verapamil, pimozide, cimetidine, and grapefruit juice). Zaleplon is not significantly metabolized through the p450 system and is less prone to pharmacokinetic interactions.

3. Avoid other $GABA_A$ agonists

Complex sleep behaviors are more likely to occur when z-hypnotics are taken with other $GABA_A$ agonists, which include alcohol, benzodiazepines, barbiturates, and some herbs that are used for sleep and anxiety like valerian, kava, and skullcap. Gabapentin does not seem to share in this pharmacodynamic interaction, but valproate, which has $GABA_A$ activity, can (Dolder CR & Nelson MH, *CNS Drugs* 2008;22(12):1021-1036).

4. Don't eat before bed

Food delays the effects of zolpidem and eszopiclone by 1 hour and zaleplon by 2 hours. Delayed onset of sleep medicines is a risk factor for complex sleep behaviors and morning impairment. Patients should be advised not to eat within 30 minutes of taking these hypnotics.

5. Switch to a different class

The FDA recommends avoiding z-hypnotics if any complex sleep behaviors occur on them. Although all sleep medications have a blanket warning about these behaviors, it is mainly the $GABA_A$ agonists cause it: z-hypnotics and benzodiazepines. Suvorexant (Belsomra) has a slight risk (0.6%), while ramelteon, doxepin, hydroxyzine, trazodone, and melatonin appear free of the problem.

6. Behavioral approaches

Behavior therapy is recommended first-line for insomnia, before hypnotics (self-guided apps include CBT-i Coach and Restore CCBT; see *TCPR* Feb 2019).

Expert Interview
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side effects and collaboratively matching medication choice to the unique cultural needs of the patient.

TCPR: How do we need to shift our mindset to do this work?

Dr. Shea: Here's a good place to start: If patients don't want to take a particular medication, they probably have a logical reason for not doing so. They are not being resistant; they are actually making the decision that we ourselves would make if we believed what they believe. There are usually three beliefs that a person generally needs to have in order to stay on a medication.

TCPR: What are those?

Dr. Shea: The first is that there is something wrong, or else they wouldn't need the medication. Second, they have to believe that a medication is a reasonable option, and third, that the pros of that medication outweigh the cons. We call this the "Choice Triad", and it fits with most patients, just as it would for us. Occasionally there are patients that might have characterological problems and don't take the medications because they are oppositional. But that is not what is going on with the vast majority of patients. It's not defiance. They legitimately do not think this medication is appropriate for them. And sometimes they are right.

"None of us would take a medication if we didn't believe that there was something wrong with us, especially if it causes side effects like tardive dyskinesia."

Shawn Christopher Shea, MD

TCPR: How does the Choice Triad play out in psychiatric patients?

Dr. Shea: Take schizophrenia. Many people who are in their first psychotic break do not think that there is anything wrong with them. Well, none of us would take a medication if we didn't believe that there was something wrong with us, especially if it causes side effects like tardive dyskinesia. When we understand that they are making a wise decision for what they believe to be true, it changes the interaction; the way it feels to be in the room with them. The problem is not the patient; the problem is that the patient has a belief that is different than our own.

TCPR: Sounds like you need to understand the patient's beliefs first. How do you get to that?

Dr. Shea: Ask how they feel on their medication right now and just take it from there. Often, they barely have to answer because it comes through in their body language. If it seems they're on a medication that they clearly love, I'd give it some real thought before recommending a change. Sometimes we assume, or are pressured by administration to think, that we need to do something different at the first meeting. But that's not always the case. Sometimes the *Continued on page 5*

Ask the Editor

Is Paxil the Best SSRI for Anxiety?

Dear Dr. Aiken: *Your review of Paxil's risks in the May issue failed to mention a benefit that's unique to this drug. Isn't it the best SSRI for anxiety?*

Dr. Aiken: Paroxetine's (Paxil's) reputation as the anti-anxiety SSRI got off to a running start. It was first launched for panic disorder in 1996, two years before its approval for depression, and went on to gain approval in 4 other anxiety disorders. A rumor began to percolate that paroxetine was a better choice for anxious patients, and it continues to be spread. For example, Stephen Stahl highlights it on his website: "In clinical practice, many clinicians use [paroxetine] for patients with anxious depression."

The data tells a different story. In head-to-head comparisons, paroxetine works as well as other serotonergic agents in anxiety disorders, and sometimes worse. That includes around a dozen large, head-to-head trials in generalized anxiety disorder, social anxiety disorder, panic disorder, and major depression with anxiety. It fared no better than sertraline, citalopram, venlafaxine, and clomipramine, and was consistently outperformed by escitalopram (Sanchez C et al, *Int Clin Psychopharmacol* 2014;29:185-196). Overall, paroxetine has only modest anxiolytic effects (effect size of 0.3), and anxiety does not predict whether a depressed patient will respond to it (Sugarman MA et al, *PLoS One* 2014;27(9):e106337).

Paroxetine does hold more FDA-approvals in anxiety disorders than most other antidepressants: panic disorder, generalized anxiety disorder, social anxiety disorder, PTSD, and OCD. Those approvals came with a license to market, and that marketing may be responsible for its clinical lore. Side effects may have also assisted in its reputation. Paroxetine causes more fatigue than other SSRIs, and sedative effects can be conflated with anxiolytic effects (Nevels RM et al, *Psychopharmacol Bull* 2016;46:77-104).

Paroxetine does stand out in a few ways that aren't so desirable. It has higher rates of weight gain, sexual dysfunction, withdrawal problems, anticholinergic effects, congenital malformations, and CYP2D6 drug interactions than other SSRIs (Marks DM et al, *Expert Opin Drug Saf* 2008;7:783-794). Our May 2019 issue added another risk to that list: dementia. There may be patients who respond uniquely to paroxetine, but anxiety is not a reliable guide to finding them.

Expert Interview

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medication regimen a person is on is the best one for them, even if they're not getting total relief (see box below for MIM sample questions).

TCPR: How do you approach side effects?

Dr. Shea: I'll ask, "What does it mean to you that you get lightheaded? What impact does that have on your life?" I'm looking for their perception, their fears. That's what causes people to stop their medications; not simply the side effects but their beliefs about them. If it was just about the severity, no one would take chemotherapeutic agents for cancer, but they do. For a teacher or an actor, a "simple" dry mouth may be viewed as job-threatening, and they may feel that they need to stop the antidepressant no matter how much relief from their depression it is providing. In contrast, a patient who is no longer sexually active may find serious sexual side effects to be of no concern whatsoever.

TCPR: Empathy sounds very important here.

Dr. Shea: Yes. It's all too easy to minimize side-effects. One thing that's helped me avoid that is the realization that side effects are actually a disease. They fit Webster's definition: A disease is something that causes pathophysiologic changes in the body. So, when we cause side effects, we are giving the patient a disease. We're asking people to swap diseases. Is the disease that I have worse than the disease that these medications are causing? They are also struggling with the financial costs of the medicine and its psychological toll. What does it say about me that I have to take this medication?

TCPR: Patients often lose interest in medications when they are on them for prevention. How do you work with that?

Dr. Shea: Let's say a person with bipolar disorder is euthymic on a combination of lithium and Depakote, and they are thrilled. They truly believe that the medications have helped. But with the passage of years that patient might still have a very normal human question: "Do I still need these meds?" They're unlikely to share that doubt with me unless I ask them to: "You've been doing really well on your lithium and your valproate for the past two years. Some of my patients have told me that they start to wonder at this point, 'Do I actually need these medications?' Sometimes, they even have thoughts like 'Maybe I should stop them or lower the dose', and I'm just curious, have you had any thoughts like that?"

TCPR: And if they intend to stop them?

Dr. Shea: After gently reviewing the pros of staying on the medication in a non-defensive fashion I might say: "You know, I will always tell you what I believe. My personal belief is that I really think you should stay on these medications. On the other hand, if you definitely are going to stop them, then I think we ought to do it together. It's usually not wise to stop a medication suddenly. It is safer to taper off slowly, one at a time, and I'd be willing to do that with you." It's important that the patient understand I'm on their side. "I hope you are able to stay well off the Depakote. The less medication one needs the better. My fear is that the bipolar disorder will come back. Let's hope it doesn't. Let's do this together and let's agree that you will call me if you get any of your early warning signs of mania or depression."

TCPR: When is it better to step in more actively and challenge the patient?

Dr. Shea: For that to work they need to understand your philosophy around medications first. I usually explain that in the initial meeting. Here is just one example of a MIM technique for doing

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The Medication Interest Model: Sample Questions

Opening up Discussion

- "Do you feel that you are on too little, too much, or just the right amount of this medication?"
- "Since the last time we met, what have you thought about the risperidone we started?"
- "Do you have a medication in mind that you might want to try for your depression?"
- "Do you know anyone who has taken lamotrigine? What did they think of it?"
- "How do you think your spouse will feel about you starting an antidepressant?"

Engaging Motivation

- "Is there anything that your OCD is causing you to not be able to do that you really wish you could do again?"
- "If I had a magic pill—and I don't—but if I did, and it could take away one of your symptoms, which is the one you most want help with?"
- "What would you like this medication to do for you?"

When Interest in Medication is Low

- "Well, we probably disagree about whether or not you have schizophrenia, but you know, people are entitled to their own opinions, and I respect yours."
- "I'm getting the feeling that you are just a bit hesitant to start duloxetine. Which is okay, but I just have a hunch here (well-timed pause) you're not going to take this thing, are you?"
- "Many patients tell me that it's easy to forget to take their medications. In the weeks since we last met, how many doses do you think you might have missed, just roughly: 10 doses, 15 doses, 20 doses?"

Side Effect Inquiries

- "Are you having any problems that you are wondering whether or not they might be a side effect?"
- "Are any side effects interfering with your relationships?"
- "Would you want to stay on this medication if we could get rid of your side effects by cutting your dose in half?"
- "Is taking the medication inconvenient for you in any way?"
- "It can be tough for anyone to pay for medications; how much of a burden do you think this will be for you and your family?"

Source: Adapted from Shea SC, The Medication Interest Model, 2018

Research Updates IN PSYCHIATRY

CANNABIS

Is There a Case for Cannabis in the Treatment of Pain?

REVIEW OF: Da Vita et al, *JAMA Psychiatry* 2018;75(11):1118-1127

STUDY TYPE: Meta-analysis of placebo-controlled trials

In the midst of the opioid epidemic, researchers are looking for new ways to treat chronic pain. Interestingly, states that have legalized medical marijuana have fewer opioid prescriptions but no clear reduction in mortality over time (Shover CL et al, Proc Natl Acad Sci U S A. 2019;116(26):12624-12626). Opioid users who smoke marijuana are less likely to drop out of maintenance treatment programs, while benzodiazepine use predicts worse outcomes in this population (Powell et al, *J Health Econ* 2018:58:29-42; Socías ME et al, *Addiction* 2018;113:2250-2258). Could marijuana have direct benefits in the treatment of pain?

To address this question, researchers analyzed 18 placebo-controlled trials of cannabinoids as a treatment for mechanically-induced pain in otherwise healthy subjects. A total of 442 participants were included. Mean age was 27 with equal numbers of men and women. Two-thirds of the studies involved synthetic tetrahydrocannabinol (THC), the cannabinoid responsible for the "high" in marijuana, or schedule-III analogues of THC, such as dronabinol and nabilone. The other third used plant-based cannabis. The majority (89%) used a cross-over design where subjects received both cannabinoids and placebo with a washout period between the doses.

Compared to placebo, cannabinoid administration was associated with a small increase in pain threshold and a small-to-medium increase in pain tolerance. However, it did not change overall pain intensity. Cannabinoids made people better able to withstand a greater pain burden, but only to a certain point. They also made the experience of pain less unpleasant (small-to-medium effect size), and this effect was strongest with plant-based cannabis. *Unpleasantness* is important because it may influence the progression from chronic pain to depression. No significant association was found between cannabinoid administration and hypersensitivity to pain. Gender did not significantly impact any of the outcomes.

The biggest limitation to the study is the lack of blinding as most subjects could probably guess whether or not they were "high." Furthermore, it is unclear how well mechanically induced pain approximates real, chronic pain. Lastly, cannabidiol (CBD) was not included in the study. CBD is often praised by enthusiasts for its properties and was recently approved in a prescription form for intractable seizures (Epidiolex; see *TCPR* Jan 2019). Unlike THC, CBD produces no "high" and may have added antipsychotic effects.

TCPR'S TAKE

Despite the widespread use of THC for a variety of ailments, little data exist to support its many claimed benefits. Additionally, the risks, including psychosis, are too large to recommend it to patients as an alternative analgesic.

—Adrienne Grzenda, MD, PhD. Dr. Grzenda has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Expert Interview

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this called Introducing Shared Expertise: "I'd like to make sure you're comfortable with my approach to using medications, because you are the one who's putting them in your body; not me. My own feeling about medications is that they can be invaluable and even save lives. But I'm aware they can also cause bad side effects. This is a shared journey and we are both experts. I view myself as an expert on medications and their side effects, but you are the only person that knows what you are feeling on them. If for any reason, you decide there is a problem with a medication, please tell me. I'll always want to know. Don't stop it immediately; call me and I'll try to help you figure out what's going on." Another thing I'll say is: "I view it as my responsibility to let you know whether a medication seems to be working. If I see a problem with it, I'm gonna tell you that I think we should stop the medication." The message that I am a watchdog for problems with medications—not a pill-pusher—means an enormous amount to patients.

TCPR: You explain what can happen if patients stop their meds, but can that ever backfire? Like when fear is used to motivate?

Dr. Shea: Yes, in the MIM we teach that one has to be careful with fear. Humans usually can't tolerate high amounts of fear for long periods of time. Their defense mechanisms may kick in and they will either deny it's a problem or rationalize it away. It is important for a person to legitimately be aware of the risks of the disease, including death in some instances, but without causing a terror that can backfire. But there are exceptions. There are patients that actually respond well—and require—being frightened. Like a coach, the art is figuring out when to do that and when not to.

TCPR: How do you work with patients who feel—accurately or inaccurately—that they are sensitive to medications?

Dr. Shea: At some point in the first meeting, when the patient is telling me what meds they're on, I might say, "You know I'm really curious, do you think you're particularly sensitive to medications?" If they hesitate, they probably are sensitive, or think they are. Then I'll ask for examples. And if I think their examples are just common, benign side effects like nausea on SSRIs, I don't challenge them on that. In an initial encounter such a challenge may set back the alliance

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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 (LO) are listed on page 1.

1. According to Dr. Shea, which of the following statements is reflective of the Medication Interest Model (MIM) technique called "Introducing Shared Expertise"? (LO #2)
   - [ ] a. "Since we disagree about whether or not you think this medication will be helpful, let's start at half the recommended starting dose and go from there."
   - [ ] b. "Do you know anyone who has experienced the same side effects as you're having on this medication?"
   - [ ] c. "I know it's easy to forget to take medication—can you tell me if you've missed any doses in the past week?"
   - [ ] d. "I view it as my responsibility to let you know whether a medication seems to be working and if I see a problem I will tell you that I think we should stop the medication."
2. In the past year (2019), several large, placebo-controlled trials found significant remission rates with mirtazapine augmentation in patients who failed to respond to antidepressant monotherapy. (LO #1)
   - [ ] a. True
   - [ ] b. False
3. Complex sleep behaviors occur in _____ % of people who take zolpidem (Ambien). (LO #3)
   - [ ] a. Under 3%
   - [ ] b. 3%-15%
   - [ ] c. 17-25%
   - [ ] d. Over 25%
4. According to a recent metaanalysis, cannabinoids improved pain tolerance but had no effect on overall pain intensity or hypersensitivity to pain in subjects with mechanically induced pain (LO #4)
   - [ ] a. True
   - [ ] b. False
5. Common side effects of mirtazapine include _____ (LO #1)
   - [ ] a. Fatigue and dry mouth
   - [ ] b. Nausea and sialorrhea
   - [ ] c. Weight gain and sedation
   - [ ] d. Tardive dyskinesia and headache

Expert Interview

Continued from page 6

because if I challenge them I am essentially saying, "I don't believe you; you're wrong." Not exactly a good way to start off a therapeutic alliance.

TCPR: Any techniques for sensitive patients?

Dr. Shea: After I start to write the prescription, I'll stop, and the patient will notice that I've stopped. And I will look at them and say, "You know what, if it's okay with you, I would like to start this at half the recommended starting dose. I want to let your body get a chance to see what this feels like. And if everything is okay, we can then start to raise it to help with your symptoms. At this tiny dose it might not even help, but I just think it is a smart way to start up with this medication because of your history with sensitivity to medications. Would that be all right with you, to start that low?" The patient may very well go home and tell their spouse, "That's the first damn doctor that ever listened to me."

TCPR: Thank you for your time Dr. Shea.

Editor's note: Dr. Shea covers the MIM in more detail in *The Medication Interest Model* (Philadelphia, PA: Lippincott Williams & Wilkins; 2018). He has also written a version focused on psychiatric patients in the online supplement to *Psychiatric Interviewing: The Art of Understanding,* 3rd Edition (Toronto, ON Canada: Elsevier;2017).

To learn more, listen to our 9/9/19 podcast, *"A New Way to Talk about Psych Meds" with Shawn Christopher Shea.*

Podcast Special: "Top Psychopharm Myths". Our 9/30 podcast *features an expert interview with Nassir Ghaemi MD, who challenges many common practices in his new textbook,* Clinical Psychopharmacology *(Oxford University Press, 2019)*

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PSYCHIATRY
P.O. Box 626
Newburyport, MA 01950

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In Brief

Good News for Lithium in Children. The FDA lowered the approved minimum age for lithium from 12 to 7 years, based on a review of recent controlled trials that demonstrated safety and anti-manic efficacy in the lower age range. Shorty after this label change, a naturalistic study of 340 children with bipolar disorder was published comparing lithium to other mood stabilizers. After 4 years of treatment, children who took lithium had better functioning and lower rates of suicide, depression, and aggression.

Generic Pregabalin Released. Pregabalin (Lyrica) is now available generic at a monthly cost of $15-20. Pregabalin is FDA-approved in epilepsy, neuropathy, and fibromyalgia. In psychiatry, its off-label use is supported by large, randomized-controlled trials in generalized and social anxiety disorders (dose 300-600mg qhs). The main side effects are fatigue, dizziness, weight gain, and concentration problems.

Generic Latuda Delayed. Generic Latuda (lurasidone) was approved this year but its release has been delayed to 2023. The manufacturer's patent was extended because they obtained approval in a pediatric population, for bipolar depression.