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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Women's Psychiatry

Learning objectives for this issue:
1. Describe characteristics and diagnosis of premenstrual dysphoric disorder (PMDD).
2. Explain available treatments for PMDD. **3.** Detail considerations when treating psychiatric illness in pregnant and lactating women.
4. Evaluate some of the current findings in the literature regarding psychiatric treatment.

PMS and PMDD: Mood Changes During the Menstrual Cycle

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Dr. Novosolov has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Of all the factors that contribute to mood, hormonal variations, such as those found in premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) can have a particularly strong effect. I've heard some people, for instance, describe PMS as a "powerful spell" that women are put under once every month.

But while it might feel like a mysterious force to women—and to their significant others—we now know much more about its biological basis. And since most of our patients are women, it's important for us to be asking about these symptoms, as it can dictate our treatment.

In Summary

- PMDD is a severe form of PMS that includes mood swings, depressed mood, irritability, and other emotional and physical symptoms that are bad enough to intefere with life, work, and relationships
- PMDD may be related to certain women's sensitivity to the drop in hormone levels of progestone and allopregnanolone during the luteal phase of their cycles
- SSRIs and oral contraceptives are the most effective treatments for PMDD; benzodiazepines, other antidepressants, and some non-drug options like therapy and supplements can help, too

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Q&A With the Expert

Treating Pregnant and Lactating Women

Madeleine Becker, MD, FAPM

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Dr. Becker has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

TCPR: Dr. Becker, from a practical point of view, when a woman of childbearing age is on psychiatric medications and either is trying to get pregnant or is pregnant, what is your general approach to treatment?

Dr. Becker: The general approach starts with a good history. Ultimately, the decision as to whether or not this patient needs to be on a psychiatric medication depends on her risk for psychiatric events during the perinatal period. When treating a pregnant patient, I weigh the risks of exposure of the fetus to medication, versus the risk of relapse of depression. If risk of relapse is high, and there is a need for medication,

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PMDD versus PMS

So what's the difference between PMS and PMDD? PMS is very common, affecting 80% of women with regular menstrual cycles. These are usually mild to moderate emotional fluctuations. When I ask women about premenstrual symptoms and they shrug it off and tell me, "I'm a little more moody the week before my period, but it's not a big deal," then it's probably PMS.

PMDD, on the other hand is a severe form of PMS. The symptoms of PMDD are similar to those of PMS, but are severe enough to interfere with work, social activities, and/or relationships. PMDD affects 3% to 8% of women and feels like a "hell on earth" period.

The typical story I hear is that for one to two weeks before menses, a woman's life is dramatically derailed: fights with her significant other, missing work or school, suicidal thoughts. Then, right when her period starts, these symptoms are suddenly lifted and she feels "great" again. In fact, a lot of women I see for a PMDD evaluation come to see me prompted by their significant other, with the couple on the verge break-up or divorce.

Diagnostic Criteria for PMDD

PMDD involves severe mood swings, depressed mood, irritability or anxiety, and four other emotional or physical symptoms occurring exclusively during the luteal phase (the one to two weeks before menses) and lifting within a few days of the onset of menses. To meet the PMDD diagnostic criteria, the symptoms must cause clinically significant distress or interfere with work, school, usual social activities, or relationships.

PMDD was made an official diagnosis in *DSM-5* in 2013. Although diagnostic criteria may look complicated and overwhelming, I find it helpful to think of PMDD as a woman meeting criteria for a MDE (major depressive episode) one to two weeks before menses (with or without physical symptoms like breast tenderness, cramps, or bloating), but then feeling 100% normal the other two or three weeks.

Pathophysiology

So what is going on here? There's good evidence that biology plays a key role. For starters, more women are admitted to psychiatric hospitals in the week immediately prior to menses than on any other week. In one study, 47% of admissions occurred during this week (Targum SD et al, *J Affect Disorders* 1991;22(1–2):49–53).

Before going further, it helps to understand basic biology. In the first half of the menstrual cycle, a follicle grows into an egg (hence the term *follicular phase* for this part of the cycle). Then, after 14 days, the egg is released (ovulation). What is left behind is a structure called the corpus luteum (hence the term *luteal phase*), which then starts producing progesterone to thicken the uterine lining to prepare for implantation.

If the egg is not fertilized, then the corpus luteum stops secreting progesterone and decays. Thus, there is a drop in progesterone one to two weeks before menses, and this drop is what triggers the uterine lining to shed (menstruation). Recent research suggests that some women are more sensitive than others to this fall in progesterone, and this sensitivity causes the mood symptoms of PMDD.

A groundbreaking 1999 study found that progesterone gets converted into another hormone called allopregnanolone, which binds the GABA-A receptor—the same receptor to which benzodiazepines and alcohol bind—and acts as a powerful anxiolytic, anticonvulsant, and anesthetic agent that decreases anxiety and depression (Griffin L and Mellon S, *Proceedings Natl Acad Sci USA* 1999;96(23):13512–7).

Think of allopregnanolone as a soothing, calming hormone. When the progesterone level drops, the allopregnanolone level also falls. For women who are sensitive to this drop, it's similar to experiencing diazepam (Valium) or alcohol withdrawal.

You might be tempted to measure levels of progesterone or allopregnanolone, but such tests probably wouldn't tell you very much. They would most likely be normal, as would the rate of the progesterone or allopregnanolone drop during the luteal phase. PMDD is a clinical diagnosis and the current hypothesis is that it has to do with a woman's sensitivity to this drop in hormones—not to abnormal hormone levels themselves.

Treatment

SSRIs. So what can we do about PMDD? We all know the SSRI's mechanism of action related to the increase in receptor sensitivity to serotonin after four to six weeks. But it turns out that a second mechanism of action involves helping to accelerate the conversion of progesterone to allopregnanolone. Research has found that fluoxetine, sertraline, and paroxetine decrease the K_m (energy of activation needed for the reaction) of the enzyme 10- to 30-fold (Griffin *ibid*).

This means that progesterone is converted much faster into allopregnanolone and there is more of it around to act on GABA receptors. Imipramine (a tricyclic antidepressant) appears to have no such effect, and this effect seems to be specific to SSRIs alone.

Amazingly, this second mechanism of action works quickly, often within several days. In fact, many of my patients tell me

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that their symptoms completely go away within hours of taking an SSRI. Typically, only a low dose SSRI is needed (fluoxetine 10 to 20 mg daily or sertraline 25 to 50 mg daily, for example).

The SSRI can be started seven to 10 days prior to menses (or whenever your patient's PMDD symptoms come on), or daily if the woman is also depressed or anxious at baseline on the other days. Or, if there is baseline depression or anxiety that is exacerbated the week before menses each month, the SSRI dose can be increased just during the week before menses.

This is an important distinction: if a woman doesn't return to baseline during the other two to three weeks of the month, it's not true PMDD and would be considered premenstrual exacerbation (PME). I often record this as MDD with PME, or GAD with PME, for example.

Some women really like the idea of intermittent dosing, especially if they are weary of side effects. Surprisingly, I have never seen withdrawal or discontinuation symptoms with intermittent dosing, likely due to the low doses needed for PMDD.

Hormones. Another possible treatment is hormones, specifically oral contraceptive pills (OCPs). OCPs work by "flattening out" the body's hormone levels (keeping the levels consistent without any peaks or troughs), as the patient takes the exact same dose of progesterone and estrogen daily.

Some women are fine with the standard placebo week (the week in which the daily pill contains no active hormone), while others get a mood drop shifted to the placebo week when there is a drop in hormones. These women do best by taking the active pill continuously and cutting out the placebo week altogether.

It is also important to mention that women are sensitive to hormones in different ways—some to the hormone fluctuation, some to the amount, and others to the specific progestin type. Therefore, you might have to try a few different OCPs. Women who are sensitive to hormonal fluctuations should avoid triphasic OCPs. It usually takes about two cycles to see if an OCP will work.

The combination drospirenone/ethinyl estradiol (Yaz), the only OCP studied for PMDD, has shown good results for both physical and mood symptoms (Yonkers KA et al, *Obstet Gynecol* 2005;106:492–501). It shortens the placebo week to four days instead of the usual seven, which, in practice, could be done with any OCP. Keep in mind that OCPs, like SSRIs, can lower libido—especially Yaz, since the progestin it uses (drospirenone) has antiandrogenic activity.

I am often asked what it is better to try first, SSRIs or OCPs? It depends on the individual. Women who don't like the idea of hormones or have a history of worsening mood with OCPs might prefer SSRIs, while women who aren't keen about taking psychiatric medications might wish to try OCPs first. In my practice, I have found that it's usually easier to start with an SSRI since you know pretty much immediately if it will work or not.

Benzodiazepines. As you might imagine, benzodiazepines can also be an effective treatment for PMDD or PME since they work on the GABA receptor. Sometimes I'll give patients a small amount of both fluoxetine and lorazepam (Ativan), for example, and ask them to try both during their premenstrual week to see which is more effective for them (Freeman E et al, *Prim Care Companion J Clin Psychiatry* 2003;5(1):30–39).

Other antidepressants. Although SSRIs are the gold standard for PMDD, there has been some evidence that serotonin-norepinephrine reuptake inhibitors (SNRIs) and clomipramine (a tricyclic antidepressant) show some efficacy for PMDD (see, for instance, Mazza M et al, *Expert Opin Pharmacother* 2008;9(4):517–521).

Non-pharmacological treatments. It can be helpful to simply walk a woman through the pathophysiology of PMDD or PME so that she and her family are more aware of the biological explanation of her symptoms. I often have women track their symptoms on a mood chart for at least two months. This serves two functions: (1) it can ensure that we are dealing with a premenstrual pattern, and (2) it can often help decrease distress by predicting when the bad days are coming.

Although there is no consensus about the best tracking tools, two well-validated scales include the Calendar of Premenstrual Experiences (COPE) and the Prospective Record of the Severity of Menstruation (PRISM), both of which ask the patient to measure a variety of symptoms on each day of her cycle.

Other helpful things to try are diet and lifestyle changes: eliminating caffeine, sugar and sodium use, cutting out nicotine and alcohol use, getting good sleep and regular exercise (for more information, see http://bit.ly/KJrg1N).

In terms of psychotherapy, one study found that cognitive-behavioral therapy (CBT) was as effective as fluoxetine (20 mg daily) in the treatment of women with PMDD at the end of six months, as measured by a prospective daily diary (Hunter MS et al, *J Psychosom Res* 2002;53(3):811–817).

Certain nutritional supplements have also shown promise in various studies for physical and emotional symptoms of PMDD, including calcium (1,200 mg/day) and Vitamin B6 (50 to 100 mg/day). Make sure to caution patients that Vitamin B6 in doses above 100 mg/day can cause peripheral neuropathy. There is also some limited evidence that magnesium (200 to 360 mg/day) and Vitamin E (400 IU/day) can provide modest relief of symptoms.

Herbal remedies may also be helpful. Placebo-controlled studies have shown that extracts of *Agnus castus* fruit, also known as chasteberry, can significantly decrease emotional and physical PMS symptoms, and that *Gingko biloba* can also improve symptoms of PMS.

Light therapy has also been explored as a possible treatment for PMDD (see http://bit.ly/KJrg1N). More work must be done to determine optimal doses and treatment durations for these alternative interventions.

TCPR'S VERDICT: Mood changes are common during the menstrual cycle and probably arise from fluctuations of hormones and their metabolites throughout the cycle. PMDD may result from sensitivity to rapid changes in estrogen and progesterone levels. Oral contraceptives, SSRIs, and other interventions can be effective treatments.

Expert Interview

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I involve the patient in the decision making process, discussing risks as well as benefits of treatment. The goal of treatment should be to maintain euthymic mood throughout the pregnancy, using the lowest effective dose of medication necessary to do so.

Patients with a history of severe depression or bipolar disorder are at high risk for relapse when medications are stopped during pregnancy

Madeleine Becker, MD

TCPR: So what kinds of questions would you ask to determine risk?

Dr. Becker: Important questions include: how serious has depression been in the past? Did she need to be treated with medications, and which ones? Was she ever suicidal? Is there a history of postpartum depression or postpartum psychosis? Is the patient on medications now? How long has she been on the current medications? What happened when she stopped medications in the past? If the patient is on medications, is her mood stable?

TCPR: So really we shouldn't assume that every woman that is on psychiatric medication needs to take medication throughout the pregnancy?

Dr. Becker: Not necessarily. Some patients have been on medications for a mild to moderate depression in the past, but have been stable in mood for years. In some cases, if depression was not severe, it may be worth a trial of psychotherapy, and discontinuing medication during the pregnancy with close monitoring of mood. I also try to avoid polypharmacy during pregnancy, because there's some evidence to show that being on more than one medication during pregnancy is associated with more adverse outcomes (Byatt N et al, *Acta Psychiatr Scand* 2012;1–21). Optimizing one medication rather than using multiple medications is preferable. However, if it is determined by history that a patient needs to stay on a psychiatric medication while pregnant, and she is stable on her current medication, it is best to continue her current medication. Pregnancy is not the time to experiment with different medications.

TCPR: For a first pregnancy, are there any features of past episodes of psychiatric illness that might indicate a worse course during pregnancy?

Dr. Becker: Patients with a history of severe depression or bipolar disorder are at high risk for relapse when medications are stopped during pregnancy (Cohen LS, *J Clin Psychiatry* 2007;68). There is also a high risk of postpartum psychosis in patients with bipolar disorder, occurring in up to 40% of women with bipolar disorder (Chaudron LH and Pies RW, *J Clin Psychiatry* 2003;64(11):1284–1292). For a patient with a history of severe depression who is stable on medication, I usually recommend that they remain on their current medication during the pregnancy.

TCPR: How prevalent is psychiatric illness during pregnancy?

Dr. Becker: Depression is common during pregnancy. About 10% to 15% of pregnant women fulfill criteria for major depressive disorder, and up to 70% of pregnant women report depressive symptoms (Gottlib IH et al, *J Consult Clin Psychol* 1989;57:269–274). Postpartum depression, a major depressive episode that occurs within the postpartum period, is the most common complication of childbirth, occurring in about 10% to 20% of women (O'Hara MW & Swain AM, *Int Rev Psychiatry* 1996;8:37–54) and suicide accounts for about 20% of postpartum deaths (Lindahl V et al, *Arch Wom Ment Health* 2005;8(2):77–87). As I mentioned earlier, there is a high risk of relapse of bipolar disorder during pregnancy, and this risk is doubled when mood stabilizers are discontinued (Viguera AC et al, *Am J Psychiatry* 2007;164(12):1817–1824).

TCPR: When it comes to substance abuse or dependence, are there any general strategies you would recommend for a woman who abuses opioids or benzodiazepines?

Dr. Becker: Getting them into treatment is probably the most important thing to do. Opioid-dependent women can be entered into a methadone maintenance program or treated with buprenorphine, both of which provide better neonatal outcomes (Jones HE et al, *NEJM* 2010;363(24):2320–2331). Hospitalization can also offer a place to safely taper women who are dependent on benzodiazepines.

TCPR: Let's switch gears for a moment and talk breastfeeding. What are some of the known benefits of breastfeeding itself for both the mother and for the infant, and when is it not recommended?

Dr. Becker: There are many reported benefits of breastfeeding for babies, including lower infection rates, lower rates of SIDS, and lower infant mortality rates. Additionally, breastfeeding promotes attachment and is more economical than formula, just to name a few benefits (Gartner LM et al, *Pediatrics* 2005;115(2):496). I encourage women to breastfeed if this is their preference. There are a few medications that are best avoided in nursing mothers. Preferred medications are those that are known to be secreted in very low concentrations into breast milk. These include SSRIs, benzodiazepines, and other medications with shorter half-lives. It is best to avoid medications like lithium in nursing moms because they are metabolized through the kidneys and they can easily accumulate in babies. Neonates can easily become dehydrated and suffer from lithium toxicity.

TCPR: Please tell us about psychotherapy in pregnancy and postpartum.

Dr. Becker: Psychotherapy should be the initial treatment for mild to moderate depression. Both cognitive behavioral therapy and interpersonal therapy can be effective for depression in women in the perinatal period. Therapy can be especially useful for women with mild depression, or women who are reluctant to use psychotropic medication. Therapy is also a helpful adjunct to medication treatment (Zlotnick C et al, *Am J Psychiatry* 2001;158(4):638–640).

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FDA PREGNANCY CATEGORIES	
Category A	* no evidence of fetal risk in well-controlled human studies
Category B	* no evidence of fetal risk in animal studies * well-controlled human studies do not exist
Category C	* evidence of fetal risk in animal studies * well-controlled human studies do not exist
Category D	* evidence of fetal risk in humans, but benefits may outweigh risks
Category X	* evidence of fetal risk in humans; risks outweigh benefits

TCPR: How do you approach herbal and natural treatments in pregnancy?
Dr. Becker: Because there are few data to show their safety or efficacy during pregnancy, I do not prescribe herbal remedies during pregnancy.
TCPR: Please tell us a little bit about the FDA's pregnancy risk categories.
Dr. Becker: FDA pregnancy risk categories (A, B, C, D, and X) are based on published evidence and expert opinion. This system doesn't consider the potential benefits of treatment of mental illness, which we do consider when we treat pregnant patients. Combining the published data with a specific risk/benefit assessment for each individual patient is a good way to approach a case.
TCPR: So, for instance, with atypical antipsychotics, the majority of them are Class C, but clozapine (Clozaril) and lurasidone (Latuda) are Class B. Does that make them more attractive drugs for a pregnant patient?
Dr. Becker: Not necessarily. In the case of lurasidone, it's a newer medication and there much less information on its safety and use during pregnancy. Good data on medications in pregnancy are hard to come by, as there are few case-controlled studies done with pregnant women. Most data consist of case reports. Thus, the safety data on atypicals during pregnancy are limited, but those which have been around for a while are generally considered to have few adverse effects. Again, the use of medications during pregnancy should always be considered on an individual basis and a risk benefit assessment (ACOG Committee, *Obstet Gynecol* 2008;111(4):1001–1020, also reprinted on the APA site at http://bit.ly/1dAXDqC).
TCPR: Since they are the most widely studied and prescribed drugs in pregnancy, can you tell us about the use of SSRIs?
Dr. Becker: Most SSRIs are Category C. As a class, the SSRIs are not considered to be major teratogens—that is, they have no specific, consistent pattern of congenital malformations (Byatt N et al, *op.cit*). Paroxetine (Paxil) is category D, and has been inconsistently associated with an increase in cardiac malformations (Einarson et al, *Am J Psychiatry* 2008;165:749–752). The SSRIs have been associated with persistent pulmonary hypertension in the newborn (PPHN) (Kieler H et al, *BMJ* 2012;344:d8012). There is also evidence that other factors associated with maternal depression can contribute to the risk of PPHN, such as preterm birth and smoking (Wichman KL et al, *Am J Perinatal* 2010;28:19–24). SSRIs have also been associated with preterm delivery, lower birth weight, and slightly lower Apgar scores (Ross LE et al, *JAMA Psychiatry* 2013;70(4):436–443). Neonatal behavioral syndrome is a spectrum of symptoms including irritability, respiratory distress, tachypnea, decreased feeding, and lethargy. This cluster of symptoms are seen in 10% to 30% of babies exposed to SSRIs late in pregnancy (Chambers CD et al, *NEJM* 1996;335:1010–1015). The mechanism may either be one of drug toxicity or a withdrawal syndrome associated with the SSRIs. Symptoms generally occur after birth to days after delivery and tend to resolve in days to weeks (Moses-Kolko EL et al, *JAMA* 2005;293:2372–2383).
TCPR: When the fetus is exposed to medications in the mother, are there any long term behavioral or psychiatric consequences?
Dr. Becker: A few recent studies have associated the SSRIs with autism spectrum disorders (Croen LA et al, *Arch Gen Psychiatry* 2011;68:1104–1112), but this has recently been challenged (Hviid A et al, *NEJM* 2013;369(25):2406–2415). Few studies have looked at the long term effects on children exposed to SSRIs during pregnancy. One recent study that looked at IQ and behavioral measurements of kids who have been exposed to SSRIs and depression found that kids who were exposed either to untreated maternal depression or to psychiatric medications had similar IQs, which were lower than children of healthy mothers who were not depressed, and similar behavioral measures (Nulman I et al, *Am J Psychiatry* 2012;169:1165–1174). More studies need to be done on this topic.
TCPR: This brings up the important point that untreated mental illness is clearly associated with adverse pregnancy outcomes, right?
Dr. Becker: Yes. Untreated depression, has been associated with premature births, low birth weight, and postnatal complications in babies. It is also associated with poor prenatal care and increased use of drugs and tobacco (Wisner KL et al, *Am J Psychiatry* 2000;165(5):557–566), as well as increasing risk for postpartum depression. So, it is important that women receive treatment for depression throughout the perinatal period.
TCPR: Thank you, Dr. Becker.

Research Updates IN PSYCHIATRY

Section Editor, Glen Spielmans, PhD

Glen Spielmans, PhD, has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

MEDICATION

Should We Prescribe Meditation to Our Patients?

Many people claim that meditation helps them reduce stress, anxiety, or depression, but little quality evidence exists to support those anecdotes. Add to that the difficulty in designing a controlled trial of meditation—eg, how can people be blinded to their treatment group?—and it's hard to know how to counsel patients on the effectiveness of this strategy.

A recent meta-analysis examined 47 trials with a total of 3,515 participants to see if meditation was truly efficacious for a variety of conditions. Researchers included studies of various types of mindfulness and transcendental, or "mantra," meditation for their influence on positive and negative affect, health-related behaviors, and outcomes like pain level or body weight.

All studies included a control group, defined as a program "matched in time and attention" but not involving meditative practice. Most trials were for short-term interventions (between four and 15 weeks), while a few were conducted up to five years. Twenty of these trials specifically enrolled subjects with psychiatric or substance abuse disorders, while the rest enrolled patients with a range of other medical problems.

So what were the results? When meditation was compared with a specific active control intervention (such as an exercise program or progressive muscle relaxation), no type of meditation showed any advantage over the control condition. When meditation was compared with a nonspecific control like an educational program, subjects engaged in mindfulness meditation (but not "mantra"-based meditation) showed improvement in anxiety (effect size 0.38 at eight weeks), depression (0.30), and pain level (0.33), but not in other measures.

These effect sizes are comparable to those found in antidepressant trials, particularly for mild to moderate depression.

The majority of subjects in the meditation trials were drawn from a primary care, not psychiatric, population. Risks were virtually nil, as compared with the well-known adverse effects of medications (Goyal M et al, *JAMA Intern Med* 2014; online ahead of print).

TCPR's Take: This meta-analysis supports the use of mindfulness meditation as slightly more efficacious than a nonspecific control, especially for mild or moderate depression or anxiety, but shows that it is no more effective than other therapeutic interventions. Furthermore, the authors emphasize that meditation is a skill to be "learned and practiced over time," and whose benefit cannot be readily assessed in a brief clinical trial.

SCHIZOPHRENIA

CBT for Schizophrenia: Is Talk Cheap?

Schizophrenia, a condition that is thought to affect 1% of the world's population, remains one of the most challenging psychiatric disorders to treat.

Lately there's been a resurgence of interest in cognitive behavioral therapy (CBT) for this disorder. Treatment guidelines in the United Kingdom, for instance, recommend the use of CBT for all patients with schizophrenia, as it can reduce the risk of hospitalization compared to treatment as usual.

A newly published study may put a damper on that enthusiasm for CBT. In a comprehensive meta-analysis of fifty international clinical trials of CBT for schizophrenia published between 1993 and 2013, researchers found that the effect of CBT on overall symptoms—and on positive symptoms in particular—may not be as high as once thought.

Specifically, when the researchers limited their analysis to studies which were not biased in favor of CBT, they found that the benefits of CBT seemed to vanish.

The most significant bias was found in the presence or absence of "blinding." When subjects' symptoms were rated by clinicians who didn't know what treatment the subjects were receiving (ie, the clinicians were "blinded"), CBT was found to be less effective than when the evaluators knew which group the subjects were in. Average effect sizes relative to placebo decreased from 0.62 (in unblinded studies) to 0.15 (in blinded studies) for overall symptoms, and from 0.57 to 0.08 for positive symptoms.

The authors did not identify any differences in outcome caused by other potential biases, such as a high dropout rate, the lack of a control group, or publication bias—in which positive results are more likely to be published than negative results (Jauhar S et al, *Br J Psychiatry* 2014;204:20–29).

TCPR's Take: This meta-analysis suggests that the efficacy of CBT for schizophrenia may be overstated and that evaluators in clinical trials may be biased in favor of outcome. In other words, when they know which patients are receiving CBT, the evaluators may be more likely to rate them as "improved." In practice, however, the outcomes we seek often have more to do with our patients' overall function than with symptom burden, and the integration of CBT principles with other supports—including medication—may pay off according to these outcome measures.

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CME Post-Test

This CME post-test is intended for participants only seeking AMA PRA Category 1 Credit™. For those seeking ABPN self-assessment (MOC) credit, a 13 question pre- and post-test must be taken online. For all others, 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 at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by February 28, 2015. As a subscriber to *TCPR,* you already have a username and password to log on www.TheCarlatReport.com. To obtain your username and password or if you cannot take the test online, please email info@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CME 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. Which hormone surges in the period after ovulation, before menstruation (Learning Objective #1)?
   [ ] a) Estradiol [ ] b) Progesterone [ ] c) Follicle-stimulating hormone [ ] d) Luteinizing hormone

2. Which of the following medications has not shown effectiveness in treating premenstrual dysphoric disorder (PMDD) (LO #2)?
   [ ] a) Fluoxetine (Prozac) [ ] b) Imipramine (Tofranil)
   [ ] c) Drospirenone/ethinyl estradiol (Yaz) [ ] d) Lorazepam (Ativan)

3. Up to what percentage of women with bipolar disorder may experience postpartum psychosis (LO #3)?
   [ ] a) 15% [ ] b) 20% [ ] c) 40% [ ] d) 50%

4. A 2013 meta-analysis of CBT for schizophrenia found that the effect size of CBT for overall symptoms fell from 0.62, when evaluators were not adequately blinded, to what level when they were (LO #4)?
   [ ] a) 0.08 [ ] b) 0.15 [ ] c) 0.30 [ ] d) 0.51

5. In the 2014 Goyal et al study of meditation, those practicing mindfulness meditation showed improvement in which of the following measures (LO #4)?
   [ ] a) Anxiety [ ] b) Negative affect [ ] c) Health-related behaviors [ ] d) Body weight

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News of Note

New Schizophrenia Drug Fails Two Phase III Trials

Roche Pharmaceuticals' potential new medication for schizophrenia, bitopertin (RG1678), failed its first two phase III trials. In both trials, adding bitopertin to antipsychotics for 24 weeks failed to improve persistent negative symptoms of schizophrenia as measured by PANSS (Positive and Negative Symptoms Scale) scores when compared to placebo, according to a report released by the company in January.

Despite this setback, the manufacturer is continuing several other phase III trials. A third trial is under way for persistent negative symptoms, while three additional trials are studying bitopertin for positive symptoms—such as hallucinations and delusions—that do not resolve with standard antipsychotic therapy. All in all, Roche is conducting six phase III studies, enrolling more than 3,600 people in 32 countries.

Currently, no medications are approved specifically for the treatment of negative symptoms of psychosis, such as social withdrawal and lack of motivation. Bitopertin is a glycine reuptake inhibitor that is thought to improve NMDA receptor function and, if approved, would be the first glutamate-based pharmacological treatment for schizophrenia.

J&J Starts Sharing Clinical Trial Information

Johnson & Johnson will begin providing all clinical trial data gathered through its Janssen pharmaceuticals arm to Yale School of Medicine's Open Data Access (YODA) Project. Physicians and researchers will be able to request access to the anonymized data through YODA, and not the drug company.

According to J&J, "under the agreement, YODA will independently review and make final decisions regarding all requests for the company's clinical trial data, including clinical study reports (CSRs) and de-identified patient-level data."

These are the raw data that researchers report in the published literature, and that the drug company interprets to justify the superiority of its product. Presumably, independent researchers will be able to use these data to identify which patients may benefit more from a drug than others, or to reevaluate the risks of drugs.

Outside of the FDA, it's no easy feat to obtain raw clinical trial data. Scientists and doctors have always had the option of requesting data directly from the drug company, but the decision as to whether data would be shared lay in the hands of the drugmaker. The argument for the benefit of YODA is that it is not biased in any way to the interests of the pharmaceutical company in making these decisions.

CDC: Only 1 in 6 Has Ever Talked about Alcohol with Doc

A January 2014 report from the Centers for Disease Control and Prevention says that alcohol screening and brief counseling by physicians can significantly reduce weekly alcohol consumption and binge-drinking episodes, but that only one in six people has ever talked with their doctor or other health professional about alcohol use.

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The report says that at least 38 million Americans drink too much, defined as binge drinking (five or more drinks for men and four or more drinks for women in one sitting), high weekly use (15 or more for men or 8 or more for women), and any alcohol use by pregnant women or those under age 21.

Drinking too much is associated with heart disease, breast cancer, sexually transmitted diseases, unintended pregnancy, fetal alcohol spectrum disorders, sudden infant death syndrome, motor-vehicle crashes, violence, suicide, and other health problems, according to the CDC.

The CDC recommends that all physicians screen patients for alcohol use through an "alcohol screening and brief intervention (ASBI)." This process can be as easy as asking about drinking, explaining in plain language the dangers of drinking too much, and providing next-step options for people who want to reduce their drinking. The Affordable Care Act requires new health insurance plans to cover ASBI and compensate providers for the service, according to the report.

While psychiatrists may be more on top of this issue than some other physicians because of the nature of our work, this serves as a reminder to ask everyone—including pregnant women and those under age 21—about their drinking habits and their motivation to change them. The report can be found at http://1.usa.gov/1aYcRLY.

Next month in *The Carlat Psychiatry Report*: Schizophrenia

This Month's Focus:
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