Perinatal depression: What you can do to reduce its long-term effects

New data show that a woman's antenatal depression can affect her child 18 years later, suggesting that early intervention is critical. Here, a look at how ObGyns can help.

Janelle Yates, Senior Editor

IN THIS ARTICLE

We've come a long way in our understanding of depression—and that's a good thing. Consider the treatments popular in the late 18th and early 19th centuries, for example, which included water immersion (short of drowning), spinning (to reorder the contents of the brain), and the induction of vomiting and administration of enemas, not to mention institutionalization.[1] These modalities wouldn't attract many patients (or clinicians) today.

And yet, even our distant forebears had some inkling of the potential for depression to continue from one generation to the next. As Trotula of Salerno noted around the 11th Century:

> If the womb is too moist, the brain is filled with water, and the moisture running over the eyes compels them to involuntarily shed tears.[2]

In other words, melancholy (aka depression) sometimes has its origins in the womb.

From our 21st Century vantage point, we understand this conclusion in more scientific terms. Data suggest than 14% to 23% of pregnant women will experience depressive symptoms during pregnancy,[3] with the potential for long-term effects in the child. In the largest study to date on the effects of antenatal and postnatal parental depression on offspring, Pearson and colleagues found that children of mothers who are depressed during pregnancy are likely to experience depression themselves at age 18.[4] Specifically, for each standard-deviation increase in the antenatal maternal depression score, offspring were 1.28 times more likely to have depression at age 18 (95% confidence interval [CI], 1.08–1.51; $P = .003$).[4]

Maternal depression in the postnatal period also was found to be a risk factor for depression in offspring, but only among mothers with "low education" (defined as either no education or compulsory education ending at or before age 16).[4] For each standard-deviation increase in the postnatal maternal depression score in this population, offspring were 1.26 times more likely to have depression at age 18, compared with the children of nondepressed women (95% CI, 1.06–1.50; $P = .01$).[4]

Although antenatal depression in fathers was not associated with an increased incidence of depression in offspring, *postnatal* depression was—but only when the fathers had low education.[4]

As for the mechanism of transmission of depression from parent to child? Although Pearson and colleagues did not attempt to identify it, they did observe that the

CONTINUED ON PAGE 53

CONTINUED FROM PAGE 48

differential effects of maternal and paternal *antenatal* depression—with only maternal depression having an impact on offspring—suggest that, in pregnancy, maternal depression may be transmitted to her child "through the biological consequences of depression in utero."[4]

Clearly, if it goes unchecked during pregnancy, maternal depression has the potential to ravage the life of both mother and child. In this article, I review guidance on the management of depression in pregnancy from the American College of Obstetricians and Gynecologists (ACOG) and the American Psychiatric Association (APA), and I offer insights from a perinatal psychiatrist on how ObGyns might adjust their practices to reduce the impact of depression on both mother and infant.

Complications of perinatal depression

In a joint report on depression and pregnancy from ACOG and the APA, Yonkers and colleagues noted that low birth weight, neonatal irritability, and diminished neonatal activity and attentiveness are among the adverse reproductive outcomes that have been associated with untreated maternal depression.[3] Reproductive outcomes are more dire if maternal depression is severe or if the mother has bipolar disorder or postpartum psychosis, potentially including infanticide or death from suicide.[5]

Pregnancy complications such as vomiting, nausea, hyperemesis gravidarum, and preeclampsia appear to occur more frequently in depressed women than in nondepressed women, according to the ACOG/APA report,[3] although this finding is based on limited data, notes Leena P. Mittal, MD, director of the Reproductive Psychiatry Consultation Service at Brigham and Women's Hospital in Boston and instructor in psychiatry at Harvard Medical School.

"The trouble with those studies in general is the difficulty of controlling for both the severity of depression and the effects of treatment of depression—or the effects of treatment versus effects of the illness itself," she says.

That difficulty is compounded by the likely use of multiple medications—including nonpsychiatric agents—during pregnancy, "which makes it difficult to assess the impact of a single compound, such as an antidepressant, on maternal and fetal outcomes," according to ACOG and the APA.[3] (More than 80% of pregnant women take at least one dose of a medication.[3])

How the ObGyn can make a difference

Because of the potential for adverse short- and long-term effects of perinatal

What is perinatal psychiatry—and when is it necessary?

Perinatal psychiatrists have special training in women's mental health.

"We provide preconception counseling, advice and information oriented to pregnancy and the postpartum period, and help patients and providers understand the reproductive impact of psychiatric and psychotropic medications and psychiatric illness and symptomatology as they fluctuate throughout the woman's reproductive life cycle, from menarche to postmenopause," says Leena P. Mittal, MD, director of the Reproductive Psychiatry Consultation Service at Brigham and Women's Hospital in Boston and instructor in psychiatry at Harvard Medical School.

If a pregnant woman has severe depressive symptoms, should the psychiatrist have expertise in perinatal issues?

The answer to that question depends on the access to psychiatric services, says Dr. Mittal.

"I think everybody would prefer to have more perinatal psychiatrists available, but a general psychiatrist can be very helpful and important during those times as well," she says. "ObGyns certainly should think about when they can pull in a specialist in women's mental health—even outside the perinatal period—for help in assessing the reproductive impact of psychiatric illness and treatment," she says.

Two organizations can provide information on perinatal psychiatry and women's mental health issues:

- **The North American Society for Psychosocial Obstetrics and Gynecology** (NASPOG) (www.naspog.org) – a professional society of researchers, clinicians, educators, and scientists involved in women's mental health and health care
- **Postpartum Support International** (www.postpartum.net) – a group that provides support to women suffering from perinatal mood and anxiety disorders, including postpartum depression, and offers educational outreach to health-care providers.

depression, "there is a need to identify it and attempt to address it prior to the postpartum period," Dr. Mittal says. "If a woman has depressive symptoms during pregnancy, it is important to try to direct her toward treatment—either by initiating treatment yourself or referring her to a psychiatrist or psychiatric care provider before she enters the postpartum period." Once she's postpartum, she will be exposed to additional variables that will influence the severity and duration of her depression, Dr. Mittal says.

Managing perinatal depression: A summary of recommendations from ACOG and the APA

Preconception period

- If the patient is currently taking antidepressant medication and reports no symptoms or mild symptoms for 6 months or longer, tapering and discontinuation of medication prior to conception may be appropriate.
- Discontinuation of antidepressant medication may not be appropriate if the woman has a history of severe, recurrent depression; psychosis; bipolar disorder; other psychiatric illness requiring medication; or a history of suicide attempts.
- Refer women with suicidal thoughts or acute psychotic symptoms to a psychiatrist for aggressive treatment.

Pregnant women currently using antidepressant medication

- Psychiatrically stable patients who prefer to continue medication may be able to do so after consultation between their psychiatrist and obstetrician to assess risks and benefits.
- Women who want to discontinue medication may do so, depending on their psychiatric history, provided they are asymptomatic. When medication is discontinued, it should be tapered gradually. Women who have a history of recurrent depression are at high risk of relapse when their medication is discontinued.
- Women who experience recurrent depression or depressive symptoms despite medication may benefit from psychotherapy to replace or augment drug therapy.
- Women who have severe depression (ie, suicide attempts, psychosis, functional incapacitation, or weight loss) should remain on medication throughout pregnancy. If such a patient refuses to continue medication, alternative therapy and monitoring should be established before she discontinues it.

Pregnant women not currently using antidepressant medication

- Consider psychotherapy for patients who prefer to avoid medication.
- For women who prefer to take a medication, provide counseling about the risks and benefits of their treatment options, including information on how these risks and benefits vary by stage of gestation. Also explore the patient's history of depression and any other conditions and circumstances that may be relevant (eg, smoking, alcohol consumption, etc).

All pregnant women

- Any woman who reports suicidal thoughts or psychotic symptoms should see a psychiatrist immediately.

SOURCE: American College of Obstetricians and Gynecologists and the American Psychiatric Association[3]

Screen all pregnant women for depression

Dr. Mittal recommends routine screening of all perinatal women.

"The data are not entirely clear about the intervals at which these women should be screened," she says, "but the recommendation would be screening at least once during pregnancy and then again postpartum. Some clinicians screen for depression during each trimester of pregnancy."

At Dr. Mittal's institution, such screening usually takes place at the patient's first prenatal visit.

The screening tools with the most high-quality data backing them include the:

- **Edinburgh Postnatal Depression Scale** (EPDS). "Despite its name, this tool has been validated for use during pregnancy and for use in the nonperinatal woman as well," Dr. Mittal notes. It also is in the public domain (http://www.fresno.ucsf.edu/pediatrics/downloads/edinburghscale.pdf). "It's particularly useful during pregnancy because it assesses the woman for symptoms of depression at the same time that it separates those symptoms from the physical symptoms of pregnancy—there can be some overlap." The EPDS is self-administered, brief (10 questions), and easily assessed by the clinician, with a score of 10 or above indicating a likelihood of depression.[6] It has been validated in more than a dozen languages, as well.
- **Patient Health Questionnaire** (PHQ-9).[7] This is another public-domain tool validated for use during pregnancy (http://www.cqaimh.org/pdf/tool_phq9.pdf). It is utilized widely in primary care and closely associated with depression criteria

CONTINUED ON PAGE 56

CONTINUED FROM PAGE 54

listed in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*. Like the EPDS, it is self-administered, brief (9 questions), and easy to score. In general, PHQ-9 scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression, respectively.[8]

Neither of these tools should override clinical judgment. Even with a positive score, clinical assessment is recommended. Nor are these tools designed to detect anxiety, personality disorders, and phobias.

Try to address the issue before conception

The best time to address perinatal depression, of course, with a conversation about prevention, is during the preconception period. Having time before pregnancy to determine the best perinatal management approach is especially valuable.

"What's important for an ObGyn to consider when counseling someone who is contemplating pregnancy and who has a history of depression is the need to weigh the risks of treatment during pregnancy against the risks of nontreatment," says Dr. Mittal. Two ways to do that are to assess the severity of her depressive symptoms—both currently and historically—and explore her response to treatment.

"Obviously, suicidality and psychosis suggest very severe illness, whether they are currently present or occurred in the past, and so does a history of psychiatric hospitalization," says Dr. Mittal. "In such cases, the untreated illness itself carries significant risk, and when it is weighed against the perhaps smaller risk of antidepressant medication during pregnancy, the risk-benefit analysis likely is very different than it might be for someone with mild to moderate depression. I would definitely agree that addressing severity from the beginning is important."

An understanding of the patient's response to treatment also is beneficial. Has any treatment been helpful? If so, that information can guide the choice of treatment during pregnancy, says Dr. Mittal. Even knowing whether a woman has responded to nonpharmacologic therapy such as psychotherapy can help shape the treatment plan.

"It might mean that there's a way to limit the risk of exposure to a variety of psychotropic medications," Dr. Mittal says. "Or if the patient has had a good response to a particular medication, it might make sense to try that agent again—or, if she's currently taking it, to stick with it."

Even if preconception counseling is difficult to achieve, ObGyns see a large number of women of reproductive age during the course of routine gynecologic care.

"I do think it's worth having a discussion about reproductive planning, especially in the context of their psychiatric illness or history, even if they aren't currently planning a pregnancy," says Dr. Mittal.

When to refer the patient to a psychiatrist

Again, the severity of symptoms comes into play.

"In severe mental illness—bipolar disorder, psychotic disorders, or a history of severe illness requiring psychiatric hospitalization—it is important to have a psychiatrist involved," says Dr. Mittal.

"Even if the woman is stable during pregnancy, the postpartum risk—especially in bipolar disorder—is extremely high. The postpartum period is a vulnerable time, anyway, because obstetric care is coming to its end, and there's a lot changing irrespective of mental illness. So a patient who's at high risk for postpartum illness should have a psychiatrist on board as early as possible."

Consultation with a psychiatrist is another option when managing women with severe depression, a significant psychiatric history, or refractory illness.

Should you prescribe antidepressant medication?

Dr. Mittal believes that ObGyns should feel fairly comfortable prescribing antidepressant medication to patients who have mild or moderate depression, provided that the initiation of such medication is the patient's informed choice.

FAST TRACK

Suicidality and psychosis suggest very severe illness, whether they are currently present or occurred in the past

Once severe disease (including bipolar disorder and a history of suicidality or psychosis or psychiatric hospitalization) has been ruled out and a history indicates that the patient has mild to moderate symptoms and has responded to treatment, an ObGyn is well qualified to treat perinatal depression, says Dr. Mittal.

Typically, SSRIs are the first-line treatment for perinatal depression and generally have similar amounts of data about their risk in pregnancy. Paroxetine (Paxil) is the exception, as we have more data about the risk for cardiac defects in neonates exposed to it in utero, Dr. Mittal says.

SSRIs generally are found in low amounts in breast milk, although sertraline (Zoloft) generally is found in the smallest quantity, making it the most commonly used SSRI in pregnancy. Sertraline is followed by citalopram (Celexa), escitalopram (Lexapro), and fluoxetine (Prozac) in the respective amount of medication passed into breast milk.

The literature around the teratogenic risks of psychiatric medications is extremely diverse, she says. The "sum total" of the data suggests that SSRIs have relatively few teratogenic risks. "The overall story around SSRIs does not appear to suggest that they carry a risk of major malformations."

Dr. Mittal also recommends keeping in mind the possibility that psychotherapy alone is sometimes sufficient for a woman with mild to moderate depression.

"If she has a history of responding to psychotherapy alone and also has mild to moderate symptoms, I think a reasonable approach would be to try it again."

"This is where preconception planning is especially useful," she says. "If somebody with mild to moderate symptoms has never had a good trial of psychotherapy, the preconception period is a good time to determine whether it might be effective, to shape the optimal treatment plan."

Two forms of psychotherapy have solid evidence of efficacy in perinatal depression:

- **cognitive behavioral therapy** (CBT)—an action-oriented approach that treats maladaptive thinking as the cause of pathologic behavior and "negative" emotions
- **interpersonal psychotherapy** (IPT)—a treatment in which the patient is educated about depression and its symptoms and her relation to the environment, especially social functioning. Unlike some other forms of therapy, IPT does not focus on underlying personality structures.

There are other forms of psychotherapy, but CBT and IPT have a large evidence base and are generally time-limited, rather than open-ended. They also are manualized and problem-focused, says Dr. Mittal.

How to prescribe an SSRI

SSRIs generally are initiated at a low dose and gradually titrated up (if necessary). A typical starting dose of sertraline, for example, would be 25 to 50 mg. The patient should be counseled about potential side effects, which include increased perspiration, somnolence or insomnia, nausea, diarrhea, headache, dizziness, and restlessness. These effects generally begin to subside the first week or two after initiation.

Sexual side effects such as reduced desire and difficulties with orgasm also may occur and generally do not diminish over time.

The patient also should be advised not to discontinue the SSRI abruptly, if at all possible, because of the risk that she might develop mild discontinuation syndrome. Although this syndrome is short-lived, self-limited, and non-life-threatening, it is uncomfortable. Symptoms include changes in mood or anxiety, shakiness, tremor, or gastrointestinal disturbance. If the patient elects to discontinue an SSRI, tapering over 4 to 7 days is preferable. However, in the event that the patient exhibits an adverse reaction or intolerance to antidepressant medication, immediate discontinuation may be appropriate, says Dr. Mittal.

After initiating SSRI therapy, follow-up in 2 weeks is appropriate, after which time oversight can be transferred to the patient's primary care provider. In the United States, primary care physicians prescribe the bulk of SSRI medications.

FAST TRACK

Psychotherapy alone sometimes is sufficient for a woman with mild to moderate depression

CONTINUED ON PAGE 58

CONTINUED FROM PAGE 57

It may take 6 to 8 weeks for the medication to begin to reduce depressive symptoms, although sleep and appetite sometimes improve within 1 or 2 weeks.

Avoid abrupt drug discontinuation in pregnancy

When asked to recommend one intervention that would have a big impact on reducing the burden of depression in pregnancy, Dr. Mittal zeroed in on the population of women who elect to discontinue antidepressant medication during pregnancy.

"I would suggest that ObGyns discourage these women against abrupt discontinuation," she says. "There is a small body of literature that demonstrates that, in patients with significant illness—severe depression and bipolar disorder, certainly—abrupt discontinuation increases the likelihood of recurrence in the short period of time afterward. If medication is abruptly stopped when a woman discovers she's pregnant, she's likely to need to return to treatment during pregnancy because of recurrent symptoms. What happens in that case is that her pregnancy is exposed to both severe symptoms and the reinitiation of treatment, possibly including additional medications beyond the initial agent," says Dr. Mittal.

Many women assume they should never get pregnant because of their mental health issues, their medications, or both, says Dr. Mittal. Or they believe they must stop their meds if they become pregnant. In fact, some patients report that they have been counseled to avoid medication in pregnancy by their psychiatrist or obstetrician!

"I have spoken to many psychiatrists who say they are not comfortable prescribing to pregnant women, so they either drop the patients or stop their meds!" she says.

When that happens, the patient should find another psychiatrist.

References

1. Nemade R, Reiss NS, Dombeck M. Historical understandings of depression. Mentalhelp.net. http://www.mentalhelp.net/poc/view_doc.php?type=doc&id=12995&cn=5. Published September 19, 2007. Accessed January 13, 2014.
2. Brockington I. A historical perspective on the psychiatry of motherhood. In: Perinatal Stress, Mood, and Anxiety Disorders. Basel, Switzerland: S Karger AG; 2005.
3. Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: A report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. Obstet Gynecol. 2009;114(3):703–713.
4. Pearson RM, Evans J, Kounali D, et al. Maternal depression during pregnancy and the postnatal period. Risks and possible mechanisms for offspring depression at age 18 years [published online ahead of print October 9, 2013]. JAMA Psychiatry. doi:10.1001/jamapsychiatry.2013.2163.
5. Hasser C, Brizendine L, Spielvogel A. SSRI use during pregnancy. Current Psychiatry. 2006;5(4):31–40.
6. Edinburgh Postnatal Depression Scale. http://www.fresno.ucsf.edu/pediatrics/downloads/edinburghscale.pdf. Accessed January 14, 2014.
7. Patient Health Questionnaire (PHQ-9). http://www.cqaimh.org/pdf/tool_phq9.pdf. Accessed January 14, 2014.
8. Kroenke K, Spitzer R, Williams W. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–613.

UPDATE
fertility

CONTINUED FROM PAGE 46

surgery, splenic injuries, and colostomy closure for hemostasis.

References

1. Metwally M, Watson A, Lilford R, Vandekerckhove P. Fluid and pharmacological agents for adhesion prevention after gynaecological surgery. Cochrane Database Syst Rev. 2006;(2):CD001298.
2. Farquhar C, Vandekerckhove P, Watson A, Vail A, Wiseman D. Barrier agents for preventing adhesions after surgery for subfertility. Cochrane Database Syst Rev. 2000;(2):CD000475.
3. The Myomectomy Adhesion Multicenter Study Group. An expanded polytetrafluoroethylene barrier (Gore-Tex Surgical Membrane) reduces post-myomectomy adhesion formation. Fertil Steril. 1995;63(3):491–493.
4. Haney AF, Hesla J, Hurst BS, et al. Expanded polytetrafluoroethylene (Gore-Tex Surgical Membrane) is superior to oxidized regenerated cellulose (Interceed TC7+) in preventing adhesions. Fertil Steril. 1995;63(5):1021–1026.
5. Alejandro G, Flores RM. Surgical management of tumors invading the superior vena cava. Ann Thorac Surg 2008;85(6):2144–2146.
6. Diamond MP; The Sepracoat Adhesion Study Group. Reduction of de novo postsurgical adhesions by intraoperative precoating with Sepracoat (HAL-C) solution: A prospective, randomized blinded, placebo-controlled multicenter study. Fertil Steril. 1998;69(6):1067–1074.