



MASSACHUSETTS
GENERAL HOSPITAL

55 Fruit Street
Boston, MA 02114
617.726.2000

MGH Center for Women's Mental Health

Reproductive Psychiatry Resource and Information Center

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Dear Readers,

We are pleased to bring you our third newsletter from the Center for Women's Mental Health. Previous issues are available on our website at www.womensmentalhealth.org.

This summer issue describes important new studies in the field of women's mental health and addresses how findings from these investigations may inform clinical decisions. The field of reproductive psychiatry continues to grow as more data become available across a range of areas. As new studies are being continuously conducted in this field, the clinical implications of such work are often ambiguous, leaving patients and care providers with questions regarding the most appropriate course of treatment.

Our newsletter tries to bridge the gap between data emerging from new investigation and the clinical implications of such studies. The mission of the Center is to provide critical current information for patients and care providers in the rapidly changing field of women's mental health.

Sincerely,

Lee S. Cohen, MD

New Research from the CWMH: Findings Presented at the 2005 APA Annual Meeting

Can Women Taking Lithium Breastfeed Their Infants?

It is clear that women with bipolar disorder are at high risk for relapse during the immediate postpartum period (Viguera et al., 2000). There is evidence that the resumption of lithium prior to or within 24-48 hours of delivery can significantly reduce the risk of postpartum illness (Cohen et al., 1995). While this intervention is the current standard of care for this high risk population, women have historically been instructed to avoid breastfeeding while taking lithium based on early reports suggesting high levels of lithium in the breast milk and several cases of lithium toxicity in nursing infants (Schou and Amdisen, 1973). While the American Academy of Pediatrics guidelines are less restrictive in their current recommendation, they do urge caution. However, systematic studies regarding the levels of exposure to lithium in nursing infants and the potential risks of this exposure have been lacking.

In a recent study from Dr. Adele Viguera at the Center for Women's Mental Health, 10 women taking lithium and their nursing infants were evaluated. Lithium levels in milk, as well as infant and maternal serum levels of lithium, were measured at approximately 6 weeks postpartum. Infant thyroid and renal function were also assessed. In this group of women, lithium carbonate dose averaged 841 mg/day (range 600-1200 mg/day). The average lithium concentration in breast milk was 0.36 ± 0.11 mmol/L (range $<0.1 - 0.51$) or 51% (range 17%-73%) of the maternal serum levels (average of 0.72 ± 0.22 mmol/L, range 0.41 - 1.16). Corresponding infant serum levels averaged 0.15 ± 0.07 mmol/L (range 0.09-0.30). Eight of the 10 infants had levels below 0.2 mmol/L. There were no adverse events reported in 9 of the 10 infants; one infant had slightly elevated TSH (thyroid stimulating hormone) that soon normalized once lithium was discontinued.

Although the sample size in this study was relatively small, it is thus far the largest systematic study quantifying exposure to lithium in children nursed by mothers taking lithium. While early reports raised concerns regarding exposure to high levels of lithium in nursing infants, this study suggests that lithium levels in infants are relatively low and were about 25% of maternal levels. Furthermore, the incidence of serious adverse events in babies exposed to lithium through breast milk was low.

Clinical Relevance: Given the many benefits of breastfeeding, some women taking lithium may opt to nurse their infants. While we have little data regarding the long-term effects of exposure to lithium contained within the breast milk, it appears that the risk of serious adverse events in the nursing infant is relatively low. Nonetheless, infants are vulnerable to the same side effects as adults, including changes in thyroid and renal functioning; thus, close clinical monitoring of infants exposed to lithium through breast milk is recommended. This monitoring should include measurement of lithium levels, TSH, BUN and creatinine every 6-8 weeks while the child is nursing.

Ruta Nonacs, MD PhD

These data were presented as a poster at the 2004 Annual Meeting of the American Psychiatric Association. **Click here to view the [poster](#) presented by Dr. Adele Viguera.**

[Viguera AC, Nonacs R, Cohen LS, Tondo L, Murray A, Baldessarini RJ. 2000. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. Am J Psychiatry 157:179-184. | PDF |](#)

[Cohen LS, Sichel DA, Robertson LM, Heckscher E, Rosenbaum JF. 1995. Postpartum prophylaxis for women with bipolar disorder. Am J Psychiatry 152:1641-1645.](#)

[Schou M, Amdisen A. 1973. Lithium and pregnancy III: lithium ingestion by children breastfed by women on lithium treatment. Br Med J 2:138.](#)

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New Research from the CWMH: Findings Presented at the 2005 APA Annual Meeting

Oral Contraceptives for the Treatment of Premenstrual Mood Symptoms in Women with Depression

About 3-5% of women of reproductive age suffer from premenstrual dysphoric disorder (PMDD), where they experience depressive symptoms, anxiety or irritability during the last one to two weeks (the premenstrual phase) of their menstrual cycle. In addition, many women who suffer from depression, including those who have been effectively treated with an antidepressant, report worsening of their depressive symptoms during the premenstrual phase of the menstrual cycle. Although this may be a consequence of sensitivity to fluctuating hormone levels, little is known about the efficacy of hormonal interventions, including oral contraceptives (OCPs), in the treatment of premenstrual worsening of depressive symptoms.

At the 2005 annual meeting of the American Psychiatric Association in Atlanta, Georgia, Dr. Hadine Joffe from the Center for Women's Mental Health presented preliminary data assessing the efficacy of the OCP Yasmin for the treatment of premenstrual worsening of depression. These women were 18-45 years of age and had regular menstrual cycles. All of the women had a depressive disorder (major or minor depression or dysthymia) and had been doing well on an antidepressant for at least 2 months except for premenstrually, when their depression symptoms would re-emerge. During the first month of the study, all participants completed a tracking month to prospectively determine that depressive symptoms were present only during the premenstrual phase (Montgomery-Åsberg Depression Rating Scale [MADRS] > 14) and increased in severity during the premenstrual phase (Daily Record of Severity of Problems Scale [DRSP] increase by > 50% over follicular phase ratings). Subjects with significant mood symptoms during the follicular phase of the cycle (MADRS > 10) were excluded.

Women with premenstrual worsening of depression were randomized to augmentation of their antidepressant (mostly serotonin-based) with Yasmin. Yasmin is an OCP that is a combination of ethinyl estradiol and a unique progesterone, drospirenone. All participants took Yasmin for 2 months. Yasmin was selected because other studies have found that it improves selected PMS symptoms (Freeman EW, 2002).

With 35 participants enrolled, an interim analysis revealed that 89% of the subjects screened had prospectively confirmed premenstrual worsening of depression. For the first 17 subjects who had completed the study at the time of the presentation, premenstrual DRSP scores for all subjects together were reduced from median 54.4 to 35.3 after 2

months of OCP therapy ($p=0.005$), while DRSP scores during the follicular phase remained low and were not affected by OCP treatment. Premenstrual MADRS scores were similarly reduced ($p=0.008$) while follicular phase MADRS scores remained stable and low. Only 2 of 25 (8%) of women who started OCP treatment were unable to tolerate it because their depression got worse on the OCP.

This interim analysis indicated that 2 months of Yasmin treatment improved premenstrual mood symptoms in women whose depression was otherwise well treated with an antidepressant. In addition, almost all women who report premenstrual worsening of depression were confirmed to have premenstrual breakthrough of depressive symptoms when prospectively assessed. Although this study is preliminary, it is the first to demonstrate that adding oral contraceptives to an antidepressant may be useful for women with depressive disorders who experience premenstrual worsening of their mood despite effective antidepressant treatment throughout the rest of their menstrual cycle. Further analysis of the data will determine whether continued use of estradiol during the placebo week may provide additional benefit.

Ruta Nonacs, MD, PhD
Hadine Joffe, MD, MSc

These data were presented as a poster at the 2005 Annual Meeting of the American Psychiatric Association. **Click here to view the [poster](#) presented by Dr. Hadine Joffe.**

[Freeman EW. Evaluation of a unique oral contraceptive \(Yasmin\) in the management of premenstrual dysphoric disorder. Eur J Contracept Reprod Health Care. 2002 Dec;7 Suppl 3:27-34; discussion 42-3.](#)

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Predictors of Postpartum Depression: Who is at Risk?

Many women imagine new motherhood as a time of total fulfillment, days filled with mother-infant bonding and boundless joy. In reality, however, many women experience significant mood changes following childbirth. Between 50 and 85% of new mothers experience a brief postpartum period of tearfulness and anxiety, termed the "maternity blues." But some 10 to 15% of women experience postpartum depression, or PPD, a longer-lasting and more pervasive type of mood disorder.

Since postpartum depression can have a devastating impact on the experience of being a new mother and may have significant consequences for the child, it is important to understand which women are at greatest risk for PPD. All women are vulnerable to postpartum depression, regardless of age, marital status, education level, or socioeconomic status. However, there may be certain factors that increase a woman's chance of suffering from postpartum depression. Based on a recent meta-analysis of studies assessing risk factors for postpartum illness, Cheryl Beck has created the Postpartum Depression Predictors Inventory, a list of 13 variables that may be used to identify women at risk for postpartum depression either during pregnancy or soon after delivery (Beck 2001). Ten of those 13 have been shown to be reliable predictors, in many cases, of postpartum depression:

- **Prenatal depression** - Depression during pregnancy may be the strongest predictor for later suffering from PPD.
- **Prenatal anxiety**
- **History of previous depression** - Although not as strong a predictor as a depressive episode during the pregnancy, it appears that women with histories of depression previous to conception are also at a higher risk of PPD than those without.
- **Recent stressful life events**
- **Childcare stress**
- **Inadequate social supports**
- **Poor marital relationship** - One of the most consistent findings is that among women who report marital dissatisfaction and/or inadequate social supports, postpartum depressive illness is more common.
- **Low self-esteem**
- **Difficult infant temperament**
- **Maternity blues** - Especially when severe, the blues may herald the onset of PPD.

In addition, three factors are less definitively predictive, but still arise consistently as factors that increase a woman's risk of PPD, especially in combination with one or more of the factors listed above:

- **Single marital status**
- **Unplanned or unwanted pregnancy**
- **Lower socioeconomic status**

Once the predictors have been identified, how can they be put to use? Before delivery, it may be possible to identify those women at highest risk for postpartum illness. These women would be candidates for more intensive monitoring, as well as certain interventions that may reduce the risk of postpartum illness in this high-risk group (Dennis 2004). For women with histories of depression, some studies have described a beneficial effect of prophylactic antidepressant administered after delivery (Wisner et al 2004). A recent article reviewed 15 studies of non-pharmacologic interventions for the prevention of postpartum depression and concluded that the only effective intervention against PPD may be intensive postpartum support provided by a health professional (Dennis 2005). The efficacy of these interventions was enhanced when women at high risk for PPD were identified. Thus, early interventions and an awareness of risk factors may help protect both the mother and her child from the deleterious effects of postpartum depression.

Juliana Mogielnicki, BA

[Beck CT. Predictors of Postpartum Depression: An Update. Nurs Research. 2001 Sep/Oct;50\(5\):275-285.](#)

[Dennis CL. Psychosocial and psychological interventions for prevention of postnatal depression: systematic review. BMJ. 2005 July 2;331\(7507\).](#)

[Wisner KL, Perel JM, Peindl KS, Hanusa BH, Piontek CM, Findling RL. Prevention of postpartum depression: a pilot randomized clinical trial. Am J Psychiatry. 2004 Jul;161\(7\):1290-2.](#)

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Patient Corner: Should SSRIs Be Discontinued Prior to Delivery?

Q: I am 30 weeks pregnant and have been taking Prozac throughout my pregnancy. My doctor suggested that I stop the Prozac several weeks before my due date. Should I do this? I am worried about getting depressed again.

A: About 10-15% of women suffer from depression during pregnancy. The rates are probably even higher among those women who have histories of depression prior to pregnancy. Thus, many women with recurrent illness make the decision to remain on antidepressant during pregnancy. While there have been many studies supporting the reproductive safety of certain antidepressants, including Prozac and the tricyclic antidepressants, during pregnancy, concerns have emerged as to whether antidepressants, including the selective serotonin reuptake inhibitors (SSRIs), may increase the risk of adverse events in the newborn.

This is an important issue, and we have commented on this topic in greater detail in prior issues of the newsletter ([Vol 1.1](#)) and on the website (in columns from [March 2004](#), and [March 2005](#)). To briefly summarize, several studies have demonstrated symptoms such as jitteriness, irritability, feeding difficulties, and poor neonatal adaptation in infants exposed to SSRIs in utero (Casper 2003, Laine et al. 2003, Simon et al. 2002, Zeskind and Stephens 2004). At this point, it is not known with certainty 1) how common these events are or 2) whether they are secondary to exposure to the medicine. In fact, women who are depressed and are taking no medications are more likely than non-depressed women to give birth to infants that are jittery and more difficult to soothe (Zuckerman et al, 1990). Furthermore, it is important to note that these reports suggest that the symptoms typically require no specific medical intervention and that they resolve spontaneously within 1-4 days, without any lasting effects.

These findings have prompted some physicians to urge their patients to discontinue treatment several weeks prior to delivery. At this point, it is not clear whether or not this type of intervention actually reduces the risk of adverse events in the neonate. What we suspect, however, is that withdrawing treatment as a woman enters into the postpartum period -- a time of heightened vulnerability to depressive illness - places her at increased risk for depression and for the negative effects of this illness on her child. Thus, we do not typically recommend that antidepressants be discontinued prior to delivery.

Ruta Nonacs, MD, PhD

[Zeskind P, Stephens L. 2004. Maternal Selective Serotonin Reuptake Inhibitor Use During Pregnancy and Newborn Neurobehavior. Pediatrics 113: 368-75.](#)

[Casper RC et al. 2003. Follow-up of children of depressed mothers exposed or not exposed to antidepressant drugs during pregnancy. J Pediatrics 142: 402-8.](#)

[Laine K, Heikkinen T, Ekblad U, Kero P. 2003. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. Arch Gen Psychiatry 60: 720-6.](#)

[Nulman I, Rovet J, Stewart DE, Wolpin J, Pace-Asciak P, Shuhaiber S, Koren G. 2002. Child development following exposure to tricyclic antidepressants or fluoxetine throughout fetal life: a prospective, controlled study. Am J Psychiatry 159: 1889-95.](#)

[Nulman I, Rovet J, Stewart D, Wolpin J, Gardner HA, et al. 1997. Neurodevelopment of children exposed in utero to antidepressant drugs. N Engl J Med 336: 258-62.](#)

[Simon GE, Cunningham ML, Davis RL. 2002. Outcomes of prenatal antidepressant exposure. Am J Psychiatry 159: 2055-61.](#)

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Current Research Studies

Bipolar Disorder in Pregnancy

Do you have questions about bipolar disorder and anti-depressants or mood stabilizers during pregnancy? If you are pregnant and diagnosed with bipolar disorder (or manic depression), you may be eligible for this research study. Participants meet with research coordinators and psychiatrists who specialize in bipolar illness during pregnancy. Contact: Marisa Johnson at (617) 726-2912 or mjohnson33@partners.org

Postpartum Depression

Are you a pregnant woman with a history of depression who is less than 36 weeks pregnant? Contact: Kim Kelly at (617) 724-6540 or kkelly11@partners.org

Breastfeeding and Psychiatric Medications

Are you breastfeeding and taking psychiatric medications? Contact: Juliana Mogielnicki at (617) 724-6989 or jmogielnicki@partners.org

Neurobehavioral Outcome of Children Exposed to Psychotropics During Pregnancy

Are you a mother with a history of bipolar disorder who has young children? Contact: Juliana Mogielnicki at (617) 724-6989 or jmogielnicki@partners.org

PMS and Bipolar Disorder

Have you been diagnosed with bipolar disorder and have premenstrual worsening of mood symptoms? Contact: Maya Rydzewski at (617) 643-3078 or mrydzewski@partners.org.

Depression in Post-Menopausal Women

If you are a post-menopausal woman who is feeling depressed or down and has not had a menstrual period in the past year, you may be eligible to participate in a research study evaluating how a non-hormonal medication helps with depression and menopausal symptoms. Contact: Brittny Somley at (617) 724-1181 or bsomley@partners.org.

Menopause and Recent Discontinuation of Hormone Replacement Therapy

Do you have hot flashes? Have you tried Hormone Replacement Therapy and recently stopped it? Are your menopause-related symptoms still bothering you?

Contact: Maya Rydzewski at (617) 643-3078 or mrydzewski@partners.org.

Perimenopause and Insomnia

Are you a perimenopausal woman with irregular periods? Are you having trouble falling asleep at night? Feeling tired?

Contact: Brittany Somley at (617) 724-1181 or bsomley@partners.org.

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