

943 Treatment of Depression and Menopause-Related Symptoms With the Serotonin-Norepinephrine Reuptake Inhibitor Duloxetine.

951 Acute Worsening of Chronic Depression During a Double-Blind, Randomized Clinical Trial of Antidepressant Efficacy: Differences by Sex and Menopausal Status.

959 Androgen Deficiency: Association With Increased Anxiety and Depression Symptom Severity in Anorexia Nervosa.

Sex Hormones and the Female Brain: The Toll of Variability and Deficiency

Increasing evidence shows important relationships between reproductive endocrinology and psychiatry that will have implications for treatment development.

A growing body of literature supports that variability of gonadal hormone levels is problematic for mental health in women. Premenstrual, postpartum, and perimenopausal mood exacerbations have been observed in women with histories of major depressive disorder, and mood exacerbations have been associated with fluctuating levels of sex hormones.¹ New onset of psychiatric disorders during the postpartum and the perimenopause supports a role of sex steroids for expression of psychiatric disorders.²⁻⁴ Absolute levels of estrogen and progesterone have not been clearly and simply implicated in the etiology of mood disorder risk in women.⁵

Estrogen and serotonin appear to interact in a complex manner that is integrally related to psychiatric disorders in women. In this month's "Focus on Women's Mental Health," Joffe et al. contribute to the growing number of studies in which investigators have assessed antidepressants for perimenopausal depression, both for depressive symptoms and often distressing somatic symptoms. At a time when hormone replacement therapy has grown controversial due to potential risks, antidepressants are a class of medications that have become an attractive treatment option for mood symptoms that accompany the menopausal transition. It is fortunate but not surprising that antidepressants with mechanisms of action on serotonin and other neurotransmitters would benefit mood in the perimenopause. It is fascinating that antidepressants would decrease somatic symptoms (such as vasomotor symptoms) that result from variability of gonadal sex hormones.

Harvey et al. analyzed gender differences from a chronic depression treatment study with female participants categorized as premenopausal or postmenopausal. Episodes of mood worsening, sex differences, and menopause status were assessed for the sample, and relationship to baseline premenstrual mood exacerbation was examined in premenopausal women. Premenopausal women were significantly more likely during the study to present with episodes of mood deterioration than postmenopausal women and men. Premenstrual mood exacerbations at baseline were significantly associated with acute mood exacerbations during the study. The authors thoughtfully discuss how such findings complicate clinical methodology in major depressive disorder research.

Eating disorders and sex hormones are a topic of research as examined by Miller et al., who assessed testosterone levels in women with anorexia nervosa. Anorexia nervosa is associated with, and is in part defined by, abnormal reproductive hormones and function, as anovulation and amenorrhea are part of the clinical definition and clinical picture. The authors found that low levels of androgens were related to greater levels of depressive symptoms and anxiety. This work may contribute to a better understanding of the etiology of and treatments for anorexia nervosa. Interestingly, with these findings, the authors build on their previous

work in which they demonstrated improved mood in treatment studies using testosterone in women with hypoandrogenism.

The interface between reproductive endocrinology and psychiatry remains an intriguing arena for future research. These groups of investigators contribute important findings in this area. We welcome your suggestions or comments regarding the "Focus on Women's Mental Health" special section. Please e-mail me at marlenef@email.arizona.edu with your feedback.

Marlene P. Freeman, M.D.
Deputy Editor

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