

Sex Therapy in Psychiatric Treatment Has a New Partner: Reproductive Hormones

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Issue: *Reproductive hormones have profound behavioral effects. Actions of estrogen, progesterone, and testosterone may be useful adjuncts to psychotropic medication.*

The remarkable benefits of estrogen replacement therapy in preventing cardiovascular illness and osteoporosis in postmenopausal women are well known. However, hormone replacement therapy is not just for the women's health physician to prescribe. Recent advances in neurobiology have demonstrated that estrogen exerts dramatic effects on the central nervous system (CNS).^{1,2} Psychiatrists are beginning to exploit this fact to benefit women with psychiatric disorders, especially depression.

By targeting key receptors in the CNS, reproductive hormones modulate diverse behaviors such as mood, cognition, and libido.² Thus, sex hormones are neuromodulators. It is not surprising, therefore, that these be-

haviors can change as reproductive hormones change across the normal life cycle. Premenstrual irritability, postpartum "blues," and perimenopausal mood swings may all represent behavioral fluctuations linked to shifts in reproductive hormone levels.²

Additionally, shifts in reproductive hormones can herald the onset of psychiatric disorders.² This shift is exemplified by the impressive link between

episodes of affective disorder and the normal female life cycle.³ Women have about the same rate of new onset of major depressive disorder as men both before puberty and after menopause. The rate skyrockets, however, for women of childbearing potential, with slight decreases during pregnancy and peak increases postpartum and in the 5- to 7-year perimenopausal period prior to the complete cessation of menses.^{2,3}

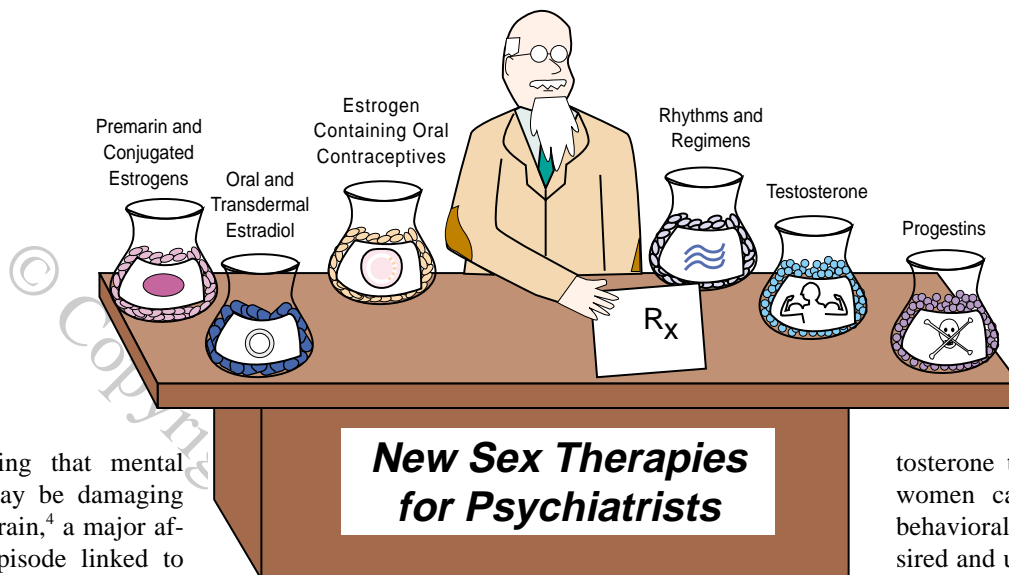
Take-Home Points

- ◆ Endogenous production of estrogen, progesterone, and testosterone affects mood, cognition, and libido
- ◆ Changes in reproductive hormones across the life cycle can affect the onset and recurrence of episodes of affective illness and other psychiatric disorders
- ◆ Antidepressants can be augmented by clever use of reproductive hormones such as administration of estrogen as oral contraceptives or estrogen replacement therapy, by avoidance of progesterone, by careful use of testosterone, and through altering the rhythm of hormone administration

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Recalling that mental illness may be damaging to your brain,⁴ a major affective episode linked to any shift in reproductive hormones greatly increases the risk of recurrence during a subsequent shift in reproductive hormones, a phenomenon known as kindling.⁵ Also, estrogen replacement therapy may significantly reduce a postmenopausal woman's risk for developing Alzheimer's disease.^{2,6} Thus, preventing episodes of mental illness by anticipating them in high risk periods of the life cycle is becoming a psychiatrist's duty.

The use of reproductive hormones to augment psychotropic drugs is in its infancy, with an embarrassing lack of controlled clinical trials. Until these are available, use of reproductive hormones as partners to antidepressants will proceed by art and anecdote perhaps more than by science. Although estrogen replacement therapy is not profoundly antidepressant, it convincingly diminishes mood fluctuations in perimenopause, especially when accompanied by vasomotor instability.^{2,6} Estrogen replacement therapy can, on occasion, successfully augment antidepressants in women who have treatment-resistant depression, but it is impossible to predict in which perimenopausal treatment-resistant women this treatment will work.⁶ Clinicians have the

sense, however, that estrogen replacement therapy produces a quicker antidepressive response (i.e., days) than do antidepressants alone (i.e., weeks). Efficacious hormone therapy includes both estrogen-containing oral contraceptives for early perimenopausal women and estrogen replacement therapy for late perimenopausal women.^{2,6}

Progestins can be a psychiatrist's enemy.^{2,6} Not only can they be associated with menstrual magnification and profound mood swings in women routinely taking progestins for contraception or for hormone replacement therapy, they can even precipitate a new affective episode in the vulnerable. Thus, one psychiatric intervention is to avoid or withdraw progestins in such patients when possible. Another alternative is to give estrogen/progestin combinations (either oral contraceptives or hormone replacement therapy) without interruption rather than use the traditional cyclical regimen, where the serum hormone levels fluctuate. Constant delivery of hormone replacement therapy may smooth out behaviors and provide a stable platform onto which to superimpose antidepressants.^{2,6} Finally, administration of tes-

tosterone to both men and women can have striking behavioral effects, both desired and undesired. Guidelines for psychiatric use of androgens are sorely needed.

This is indeed an exciting era as psychiatry expands its frontiers into the use of reproductive hormones to prevent and treat mood disorders and even Alzheimer's disease. Sex hormones have become attractive partners for the modern psychiatrist. ♦

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