Commentary on "Menstrually Related Disorders: Points of Consensus, Debate, and Disagreement"

Walter A. Brown, M.D.

The idea that a discussion among a group of experts at the annual American College of Neuropsychopharmacology (ACNP) meeting would result in some clarity about "Menstrually Related Disorders" is so good spirited—as good spirited as the ACNP meeting itself—that fearing I would find more or less what I did, I hesitated to read the resulting report. I hesitate even more to offer my comments; who wants to rain on a picnic? On the other hand, the authors have chosen to publish this and in a format that invites scrutiny. So here goes.

The points of consensus are indeed indisputable, but are they informative? Under "Etiology and Pathophysiology," for example, we are told that "the pathophysiology of MRDs is likely to be multidimensional and multifactorial, involving various physiologic and biochemical systems." I may be missing something, but as far as I can tell this bit of enlightenment applies to all of the disorders that afflict us, gout to gonorrhea, paranoia to pediculosis. Likewise for "vulnerability of affected patients plays a major role in development of specific subtypes and symptoms" and "environmental and psychologic factors probably contribute to the development of symptoms as well as determination of their severity." That this stuff was actually written down, and for other people to read, I attribute to the rosy glow endorsing all ACNP meeting activities.

The proposed name, "Menstrually Related Disorders," may well sound great to some ears. To me, it seems an unfortunate alliance of nonspecific terms, as unhappy a mouthful as late luteal phase dysphoric disorder.

Under "Diagnostic Criteria," the points of consensus are sensible but singularly imprecise, and the points of disagreement are incomprehensible, at least to me. Under "Treatment of MRDs," the points of consensus are indisputable and uninformative in equal measure.

The points of debate under "Etiology and Pathophysiology" and areas of debate under treatment provide a list of pertinent research questions. These are the most useful sections of the document.

To be fair, any group tackling this problem would probably produce as fuzzy a document. What seems most at issue is unstated: Is our nosology enhanced by the addition of "Menstrually Related Disorders?"

Given the profound effects of gonadal steroids on cellular function, it should come as no surprise that the signs and symptoms of a wide range of afflictions fluctuate in relation to the menstrual cycle. But should these afflictions be combined as a diagnostic entity?

The menstrual cycle is not alone as a natural phenomenon that influences the course of disease. The weather influences the expression of many illnesses, so does age. Our understanding of the etiology, pathophysiology, prognosis, and treatment of disease is clearly enhanced by understanding the effect of climate and age on the expression of symptoms. However, I doubt that combining the huge number of conditions influenced by climate and age into diagnostic categories—climate-related disorders and age-related disorders—adds usefully to our nosology.

On the other hand, some conditions are not just influenced or modified by climate or age; they require a specific climate or age for their expression. Seasonal

From the Brown University School of Medicine, and the Department of Veterans Affairs Medical Center, Providence, Rhode Island.
Address correspondence to: Walter A. Brown, M.D., Department of Veterans Affairs Medical Center, 830 Chalkstone Avenue, Providence, Rhode Island 02908.
Received August 20, 1992; accepted January 27, 1993.

Published by Elsevier Science Publishing Co., Inc.
655 Avenue of the Americas, New York, NY 10010
0893-133X/93/$6.00

affective disorder and Alzheimer's disease come to mind.

Likewise, it may be worthwhile to identify conditions the expression of which requires a specific phase of the menstrual cycle and to differentiate these conditions from the innumerable ones for which a phase of the menstrual cycle is a risk or modifying factor.

As far as I know, the only disorder that bears an obligatory relationship to the menstrual cycle is Premenstrual syndrome (PMS). It is estimated that 2% to 10% of menstruating women have disabling PMS (Logue and Moos 1986). The extent to which the clinical and research communities have ignored PMS is all too clear in the contrast between the attention given to PMS and that given to major depression, a condition with a similar prevalence.

Among the reasons for the paucity of attention to PMS may be that despite the reasonable presumption that shifts in gonadal steroids account for this condition, researchers have been frustrated in their attempts to find an endocrine aberration in PMS, and, until recently, treatments directed toward this condition have been largely unsuccessful. I am dismayed at the possibility that attention to ill-defined "Menstrually Related Disorders" which may not exist will drive PMS further into obscurity.

Failure to uncover the role of gonadal steroids in PMS impugns our current technology more than it does a hormonal basis for the condition. Until we have methods for assessing in vivo the effects of hormones at the molecular level, the role of gonadal steroids in PMS is likely to remain elusive.

Treatment may be less elusive. Recent studies have consistently shown that compounds which potently block serotonin uptake are powerfully effective in the treatment of PMS (Stone et al. 1991; Sundblad et al. 1992). Although the studies to date have involved administration of these compounds throughout the menstrual cycle, anecdotal evidence suggests that they may be effective when taken during the premenstrual phase alone (Sundblad et al. 1992). Thus, these compounds appear to alleviate PMS more rapidly and perhaps via a different mechanism than they alleviate depression.

The effectiveness and probable specificity of serotonin uptake inhibitors as a treatment for PMS provide a new probe for assessing the pathophysiology of this condition. The effectiveness of this treatment also raises a number of pertinent and answerable clinical questions: When should these agents be administered and in what dose? Are serotonin uptake inhibitors effective and suitable for mild variants of PMS? Are other agents that enhance serotonin transmission effective in PMS? Do antidepressants that don't affect serotonin alleviate PMS? Are serotonin uptake inhibitors useful in treating other, oh, what the heck, MRDs?

ACKNOWLEDGMENT

The author thanks Andrea Stone, M.D. for her useful comments on the manuscript.

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