

# Premenstrual Syndrome: A Guide for the Clinician

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"A menstrous woman would dull a mirror with a look and the next person to look into it would be bewitched." - Aristotle

In 1931 an American gynecologist named Frank<sup>1</sup> described 15 cases of women who had premenstrual symptoms. Thereafter, many studies on premenstrual syndrome (PMS) followed but most were flawed by serious methodological problems, including poor patient selection, no universal definition of the syndrome, mainly open uncontrolled studies, and retrospective rating of symptoms, which tends to overestimate the prevalence of PMS.<sup>2</sup>

The third edition of the *Diagnostic and Statistical Manual of Mental Disorders* proposed the term Late Luteal Phase Dysphoric Disorder (LLPDD), which refers to the mood disturbance of premenstrual syndrome and excludes women who have symptoms throughout the luteal phase of the cycle. In the latest edition of this manual (DSM IV), this condition was not granted an official category. Instead, it was renamed Premenstrual Dysphoric Disorder (PDD) and relegated to an appendix that contains a number of proposals for new categories and axes provided for further study. Table 1 summarizes the criteria for PDD. In this article, PMS is used interchangeably with PDD.

PMS remains a controversial issue. It is seen by some as a way to reduce the status of women, by linking the normal ovarian cycle to the impairment of women's ability to cope.<sup>3</sup> Others have gone further, labeling psychiatry as an institution that exerts social control over women by influencing and reflecting societal definitions of sex-role-appropriate behavior. By this view, definitions of PMS reflect ideology rather than science.<sup>4</sup>

Yet there are a substantial number of women who experience significant negative changes that vary with the menstrual cycle. It is estimated that up to 90% of women report isolated or minor premenstrual changes.<sup>5</sup> Around 5% of symptomatic women report symptoms severe enough to produce long-term effects on their well-being and family, social and work relationships. Symptoms may be so severe that they lead to completed suicide, suicide attempts, and acts of violence against others.<sup>6</sup> There is also a real possi-

bility that recurrent perimenstrual mood changes of this kind can increase the likelihood of chronic mood disorders in susceptible individuals.<sup>7</sup>

## Etiology

A number of etiological theories for PMS have been suggested that include biological, psychodynamic, family, social, and cognitive components.<sup>8</sup> The current consensus is that normal ovarian function is the cyclical trigger for biochemical or neurotransmitter events within the central nervous system and other target tissues which cause the symptoms. Studies of platelet and whole blood serotonin concentration suggest serotonin deficiency in patients with PMS.<sup>9</sup>

## Evaluation

It is important to have patients with suspected PMS prospectively rate and record their symptoms and the severity on a daily basis. Table 2 lists symptoms that are important to track. Other factors to include in the daily diary are basal body temperatures (to keep track of ovulation), weight, menstruation, and stress factors. Using DSM-IV criteria, the diagnosis is only confirmed by the use of prospective ratings during the course of 2 menstrual cycles. Recording symptoms retrospectively is inaccurate and

Table 1.—DSMIV Research Criteria for Premenstrual Dysphoric Disorder

- A. In most menstrual cycles during the past year, 5 or more of the following symptoms were present for most of the time during the last week of the luteal phase (the period between ovulation and onset of menses), began to remit within a few days after the onset of the follicular phase (the period between onset of menses and ovulation), and were absent in the week post menses, with at least one of the symptoms being either 1, 2, 3 or 4.
  1. Markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts.
  2. Marked anxiety, tension, feelings of being "keyed up" or "on edge."
  3. Marked affective lability, eg, feeling suddenly sad, tearful; increased sensitivity to rejection.
  4. Persistent and marked anger or irritability or increased interpersonal conflicts.
  5. Decreased interest in usual activities, eg, work, school, friends, hobbies.
  6. Subjective sense of difficulty in concentrating.
  7. Lethargy, easily fatigued or marked lack of energy.
  8. Marked change in appetite, overeating, or specific food cravings.
  9. Hypersomnia or insomnia.
  10. A subjective sense of being overwhelmed or out of control.
  11. Other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of bloating, and weight gain.
- B. The disturbance markedly interferes with work or school or with usual social activities and relationships with others.
- C. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as Major Depressive Disorder, Panic Disorder, Dysthymic Disorder, or a Personality Disorder (although it may be superimposed on any of these conditions).
- D. Criteria A, B, and C must be confirmed by prospective daily ratings during at least 2 consecutive symptomatic cycles.

**Table 2.—PMS Symptoms for Prospective Charting**

<b>Physical</b>	
Abdominal distention or bloating	
Maestalgia	
Headache or migraine	
Cramps	
Muscle/joint pains	
<b>Psychological</b>	
Anger/irritability	
Depressed mood	
Crying	
Suicidal thoughts	
Energy levels	
Food cravings, appetite	
Feeling nervous	
Feeling out of control	
Feelings of violence/aggression	
Poor impulse control	

should not be used as a basis for treatment.<sup>10</sup> The process of having a patient keep a daily chart also helps her feel that her symptoms are validated and that she participates in the process of evaluation and treatment.

It is important to rule out other medical, gynecologic, and psychiatric illnesses; endocrine disorders or premenstrual exacerbation of another underlying disorder should be considered. Examples include seizure disorders, thyroid disorders, cancer, systemic lupus erythematosus, anemias, and various infections. These general medical conditions can be distinguished from PMS by history, physical examination, and laboratory testing. Polycystic ovarian disease and endometriosis also should be ruled out. The symptoms of these disorders could present as PMS, but the underlying gynecologic disease should be treated first.

It is important to rule out other psychiatric illness such as an affective disorder. The transient mood changes that many women experience around the time of their period should not be considered a mental disorder; however, when persistent with every cycle and severe enough to markedly interfere with work or school or with usual social activities and relationships, addressing the mood component becomes crucial.

Premenstrual exacerbation of a current mental disorder (eg, mood disorders, anxiety disorders) needs to be ruled out. Fifty percent to 60% of patients presenting to PMS clinics will meet criteria for other psychiatric disorders.<sup>11,12</sup> Treatment of the underlying disorder often leads to satisfying results. It also is important to screen for histories of physical or sexual abuse and substance abuse disorders. A formal psychiatric evaluation may help to clarify the diagnosis in difficult cases.

O'Brien<sup>6</sup> described a gonadotrophin-releasing hormone (GnRH) analogue test that is useful in diagnosing women who have severe symptoms and in whom the diagnosis remains in doubt. Goserelin, a GnRH agonist analogue, is given monthly for 3 months to eliminate cyclical ovarian function completely. Complete elimination of symptoms implies that the symptoms are solely dependent on ovarian activity, and the diagnosis is PMS. If symptoms continue into the third month, an underlying

psychiatric problem could be present.

### Treatment

The etiology of PMS is certainly more complex than the combination of ovarian activity and neurotransmitter changes. Other factors may play a role, including environmental, psychosocial, and personal factors. Stress, interpersonal relationship problems, underlying psychopathology, personality, self-esteem, general health and well-being may all be important. Therefore, nonspecific measures such as counseling, stress management, relaxation techniques, support groups, vitamin therapy, dietary change, and exercise can be helpful. (Table 3)

There is a greater reactivity to stress and a higher level of arousal during the premenstruum.<sup>13</sup> A recent study reported remission of symptoms in 58% of patients participating in a group behavioral treatment, which included instruction on diet, exercise, progressive relaxation, and stress reduction, with another quarter of subjects reporting 50% reduction in symptoms.<sup>14</sup>

Dietary change, vitamin therapy and exercise all improve

**Table 3.—Treatment Approaches for PMS/PDD**

Treatment	Dosage
<b>Non-Pharmacological Approaches</b>	
Counseling	
Stress management	
Relaxation techniques	
Support groups	
Exercise	
Dietary and vitamin therapy	
<b>Pharmacological Approaches</b>	
Pyridoxine (B6)	100 mg daily
Progesterone	Pessaries/suppositories 400 mg to 800 mg up to twice daily
Spirinolactone	100 mg daily in 2nd half of cycle
Fluoxetine	20 mg daily (or other SRI at equivalent dose)
Clomipramine	25 mg to 75 mg daily
Bupirone	10 mg to 30 mg daily in 3 divided doses
Alprazolam	2 mg to 4 mg daily in 3 to 4 divided doses
<b>Eliminating the Ovarian Trigger</b>	
Oral contraceptives	
Danazol	100,200,400 mg daily
GnRH analogues	3 to 6 mg sc every 28 days for up to 6 months
Surgery	total hysterectomy with bilateral salpingo-oophorectomy

general health and self-esteem and may increase women's tolerance to premenstrual symptoms. Meals to combat premenstrual hypoglycemia have no justification. Vitamin B<sub>6</sub>, calcium and magnesium may be useful in that they are cofactors in neurotransmitter synthesis (eg, conversion of tryptophan to serotonin).<sup>15</sup> Evening primrose oil (efamol), a prostaglandin synthesis precursor, may be helpful in relieving breast symptoms and depression in some patients.<sup>16,17</sup>

There has been widespread use of progesterone based on studies suggesting that estrogen is high relative to progesterone in patients suffering from PMS. However, randomized, double-blind placebo trials have not supported their efficacy.<sup>18</sup>

Most women who develop premenstrual bloating and abdominal distention in the luteal phase do not show increases in weight,

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total body water, extracellular fluid volume, total exchangeable body sodium, or plasma volume.<sup>6</sup> Diuretics are widely used, however, they might be most helpful in the subgroup of women with premenstrual weight gain.

When dysphoria, irritability, and other psychological symptoms predominate, a trial of a psychotropic may be helpful. Antidepressants that inhibit serotonin (5HT) re-uptake, such as fluoxetine and clomipramine, have been found to be effective in double-blind trials.<sup>19-21</sup> Other antidepressants have been tried with good results in open trials. Buspirone, a 5-HT<sub>1A</sub> partial agonist, also has been shown to be significantly more effective than a placebo for irritability, fatigue, pain and social functioning in 34 patients treated with a mean daily dose of 25 mg 12 days prior to menstruation.<sup>22</sup> Alprazolam, a high potency benzodiazepine, given only during the premenstruum also is effective for mood symptoms and global improvement as compared to placebo.<sup>23,24</sup> Longitudinal intermittent treatment studies with this drug are currently in progress. Other psychotropics that have been tried with less promising results include lithium, fenfluramine, naltrexone, and clonidine.

For severe symptoms that do not respond to less invasive treatments, the next step would be to eliminate the ovarian trigger. This can be done through hormonal treatment or through surgical approaches.

Oral contraceptives can suppress ovulation but hormonal cyclicity remains. This probably accounts for the unpredictable response to such agents. Furthermore, some patients develop side effects to oral contraceptives that are similar to symptoms of PMS.<sup>25</sup>

Danazol is a synthetic androgenic derivative of ethisterone which causes hypothalamic pituitary-gonadotrophin suppression. When given continuously in doses that suppress ovulation and menstruation, the symptoms of PMS are abolished.<sup>26,27</sup> Its usefulness is limited because of its androgenic properties in women of childbearing age.

GNRH agonist analogues act by creating a reversible pseudohypophysectomy and, therefore, a pseudomenopause. Depot goserelin, for instance, has been shown to eradicate premenstrual symptoms.<sup>28</sup> Long-term treatment, however, is not feasible because of risks of osteoporosis and atherosclerotic heart disease. Studies are being conducted in combination with adjuvant conventional hormone replacement therapy.

Surgery may be a last resort for severely affected patients unresponsive to other strategies. Total hysterectomy with bilateral salpingo-oophorectomy can eliminate the symptoms of PMS.<sup>29</sup>

Although the etiology of PMS remains unclear there are strategies a clinician can utilize to alleviate symptoms. The problem is an important one and deserves our continued clinical attention and study.

The author acknowledges the excellent library support provided by Tami Rosado, Librarian, VAMROC, Honolulu.

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