Recognizing and Treating Premenstrual Dysphoric Disorder (PMDD)

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Disclosure

I have no financial interests or relationships to disclose.

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Objectives

- Distinguish between PMS and PMDD
- Understand the incidence of PMDD
- Discuss the pathophysiology of PMDD
- Identify appropriate treatment options of PMDD

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Which of the Following Is Required to Confirm the Diagnosis of PMDD?

A. Serum progesterone levels during the luteal phase
B. Pelvic ultrasound
C. Prospective daily symptom charting for at least two menstrual cycles
D. Elevated prolactin level
E. Psychological evaluation

Which of the Following Neurotransmitter Systems Is Most Strongly Implicated in the Pathophysiology of PMDD?

A. Dopamine
B. Acetylcholine
C. GABA
D. Serotonin
E. Norepinephrine

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A 27-year-old woman presents with mood symptoms before menses. She reports irritability, sadness, and fatigue during the week prior to her period. However, She also has similar symptoms throughout the month.

Which of the Following Diagnoses Is Most Likely?

A. Premenstrual dysphoric disorder
B. Major depressive disorder with premenstrual exacerbation
C. Bipolar disorder
D. Premenstrual syndrome
E. Generalized anxiety disorder

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What Questions Do We Ask?

- Duration of symptoms?
- Associated symptoms?
- Severity of symptoms?
- What has she tried for treatment thus far?
- What are her contraceptive needs?
- What intervention is she willing to try?

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Hormone Fluctuation

- Evidence of worsening of mood disorders during times of hormonal fluctuation
  - Related to menses
  - Related to pregnancy or postpartum
  - Related to menopausal transition
- Abrupt changes in hormone levels may alter the equilibrium of neurotransmitters found in the brain thus increasing risk of mood disorders
  - Estrogen
    - affects serotonin and dopamine signaling
  - Progesterone metabolite allopregnanolone
    - modulates GABA-A receptors, influencing mood regulation

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PMS VS PMDD

What Is the Difference?

- Both PMS and PMDD occur in a **cyclic** pattern
  - Symptoms appear in the late luteal phase and resolve with the onset of menstruation
- PMDD is distinguished from PMS by:
  - Severity of symptoms
  - Predominance of mood symptoms
  - Functional impairment

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Epidemiology

- PMS
  - Affects 20-30% of menstruating women
- PMDD
  - Affects 2-5% of menstruating women

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Case

- A 35-year-old woman reports that 3–4 days before each menstrual period she develops bloating, breast tenderness, headaches, and increased irritability. Her symptoms resolve within the first day of menses. She reports the symptoms are annoying but do not interfere with her ability to work or care for her family.

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PMS

Premenstrual Syndrome Is Characterized by:

- Recurrent Physical, Emotional, or Behavioral Symptoms
- Occurring During the Luteal Phase of the Menstrual Cycle
- Resolving Shortly After Onset of Menses
- Absent During the Follicular Phase

Symptoms Must Be Cyclic and Reproducible Across Cycles

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Common Symptoms of PMS

Emotional / Behavioral

- Irritability
- Mood swings
- Anxiety
- Fatigue
- Difficulty concentrating
- Sleep disturbances

Physical

- Breast tenderness
- Bloating
- Headache
- Joint or muscle pain
- Weight gain
- Food cravings

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Case

- A 30-year-old woman presents with severe irritability, mood swings, and anxiety that occur during the week before her menstrual period. Symptoms resolve within a few days after menses begins. She reports that during this time she argues with her partner and has difficulty functioning at work but feels completely normal the rest of the month.

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Symptoms of PMDD

Common Physical Symptoms

- **Abdominal bloating**
- Breast tenderness
- Headache

Common Affective Symptoms

- Irritability
- **Mood swings**

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Evaluation of PMDD

- Detailed history
  - Menstrual diary
    - Symptoms begin late luteal phase- approximately 5 days prior to onset of menses
    - Symptoms resolve within 3 days of onset of menses
  - Rule out medical or pharmacologic causes of symptoms
    - Thyroid disorder
    - Worsening of mood with combined contraception (estrogen/progesterone)

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Box 1. Diagnostic Criteria for Premenstrual Dysphoric Disorder

A. In the majority of menstrual cycles, at least five symptoms must be present in the final week before the onset of menses, start to *improve* within a few days after the onset of menses, and become *minimal* or absent in the week postmenses.

B. One (or more) of the following symptoms must be present:
   1. Marked affective lability (eg, mood swings; feeling suddenly sad or tearful, or increased sensitivity to rejection).
   2. Marked irritability or anger or increased interpersonal conflicts.
   3. Marked depressed mood, feelings of hopelessness, or self-deprecating thoughts.
   4. Marked anxiety, tension, and/or feelings of being keyed up or on edge.

C. One (or more) of the following symptoms must additionally be present, to reach a total of *five* symptoms when combined with symptoms from Criterion B above.
   1. Decreased interest in usual activities (eg, work, school, friends, hobbies).
   2. Subjective difficulty in concentration.
   3. Lethargy, easy fatigability, or marked lack of energy.
   4. Marked change in appetite; overeating; or specific food cravings.
   5. Hypersomnia or insomnia.
   6. A sense of being overwhelmed or out of control.
   7. Physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of "bloating," or weight gain.

Note: The symptoms in Criteria A–C must have been met for most menstrual cycles that occurred in the preceding year.

D. The symptoms are associated with clinically significant distress or interference with work, school, usual social activities, or relationships with others (eg, avoidance of social activities; decreased productivity and efficiency at work, school, or home).

E. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, persistent depressive disorder (dysthymia), or a personality disorder (although it may co-occur with any of these disorders).

F. Criteria A should be confirmed by prospective daily ratings during at least two symptomatic cycles. (**Note**: The diagnosis may be made provisionally prior to this confirmation.)

G. The symptoms are not attributable to the physiologic effects of a substance (eg, a drug of abuse, a medication, other treatment) or another medical condition (eg, hyperthyroidism).

ACOG CPG 7
Management of Premenstrual Disorders: ACOG Clinical Practice Guideline No. 7. Obstetrics and Gynecology. 2023

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Risk Factors for Development of PMDD

- History of depression
- History of trauma
- History of anxiety
- Lower SES
- Hormonal predisposition

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Feature	PMS	PMDD
Symptom severity	Mild–moderate	Severe
Functional impairment	Minimal	Significant
Core mood symptoms	Not required	Required
Diagnostic criteria	Clinical	DSM-5
Prevalence	20–30%	3–8%

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Treatment Options

- Lifestyle modifications
- Pharmacologic management

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Lifestyle Modifications

- Exercise
- Stress reduction
  - Cognitive behavioral therapy
- Herbal/Vitamin supplementation (likely not better than placebo)
  - Chasteberry 20-40mg daily
  - B6, Calcium, Magnesium supplementation

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Alternative Medicine

- Acupuncture
  - Shown in some studies to be superior to sham in treatment of PMDD

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Pharmacologic Management Options

- SSRI
  - Increase serotonin transmission
- Combined estrogen-progestin oral contraceptives
  - Work by suppressing H-P-O axis

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SSRI

- Effective treatment of PMDD in up to 70% of patients
- Chose as 1st line **IF** the woman does not also require contraception
- Dosing options
  - Continuous
    - Consider this when concern about: compliance, low grade mood symptoms outside of PMDD
  - Luteal phase only
    - Prescribe day 14-28 of cycle
  - Symptom onset only
    - Start with symptom onset and stop few days after onset of menses
- If no improvement with SSRI can consider alternative types of antidepressants (SNRI, Atypicals)

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Role of Estrogen in Treatment of Mood Disorders

- Modulates serotonin and norepinephrine
- Increases GABA activity
- Decreases activity of MAO (involved in serotonin degradation)
- Increases tryptophan hydroxylase (involved in serotonin synthesis)
- Selectively increases serotonin receptor density in brain
- Promotes NE availability
- Involved in increasing NE hydroxylation from dopamine

(Soares. Menopause. 2014)

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Role of Progestins in Treatment of Mood Disorders

- Increases concentration of MAO causing decrease in serotonin concentration (Steiner et al. J Affective Disorders. 2003)
  - Opposite effect from estrogen

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Combined Hormonal Contraceptives

- Use first line in patients who require contraception
- Choose monophasic combined oral contraceptives (COC)
- Remember some patients may have worsening of mood with COC
  - Try a different progestin component
- Only approved COC for PMDD includes drospirenone
- Can dose monthly or continuous
- If unable to tolerate, consider levonorgestrel IUD

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Pharmacologic Management Options

- For severe symptoms, insufficiently improved with monotherapy
  - Consider combination of SSRI/SNRI/Atypical with COC/LNG-IUD

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A 31-year-old G2P2 presents with mood symptoms that occur during the week before her menstrual period and improve shortly after menses begins. She reports irritability, fatigue, breast tenderness, and mild anxiety. She is still able to work and complete her normal activities, although the symptoms are bothersome. She denies suicidal ideation or severe mood symptoms. Symptoms have occurred monthly for the past year.

Which of the Following Is the Most Likely Diagnosis?

A. Major depressive disorder
B. Premenstrual dysphoric disorder
C. Premenstrual syndrome
D. Bipolar disorder
E. Persistent depressive disorder

A 29-year-old G0 presents with severe mood symptoms that occur monthly. She reports irritability, depressed mood, fatigue, and difficulty concentrating that begin about 5 days before menses and resolve shortly after menstruation starts. These symptoms interfere with her work and relationships. She has no symptoms during the remainder of the cycle.

Which of the Following Is the Most Appropriate Initial Treatment?

A. Continuous combined oral contraceptives
B. Sertraline during the luteal phase
C. Cognitive behavioral therapy alone
D. Continuous GnRH agonist therapy
E. Progesterone supplementation during the luteal phase

A Patient with PMDD Begins Fluoxetine. Which of the Following Is the Most Likely Timeline for Clinical Improvement?

A. Within 24–48 hours
B. Within the first menstrual cycle
C. Within 6–8 weeks
D. Within 3 months
E. Within 6 months

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