Treatment of Premenstrual Dysphoric Disorder

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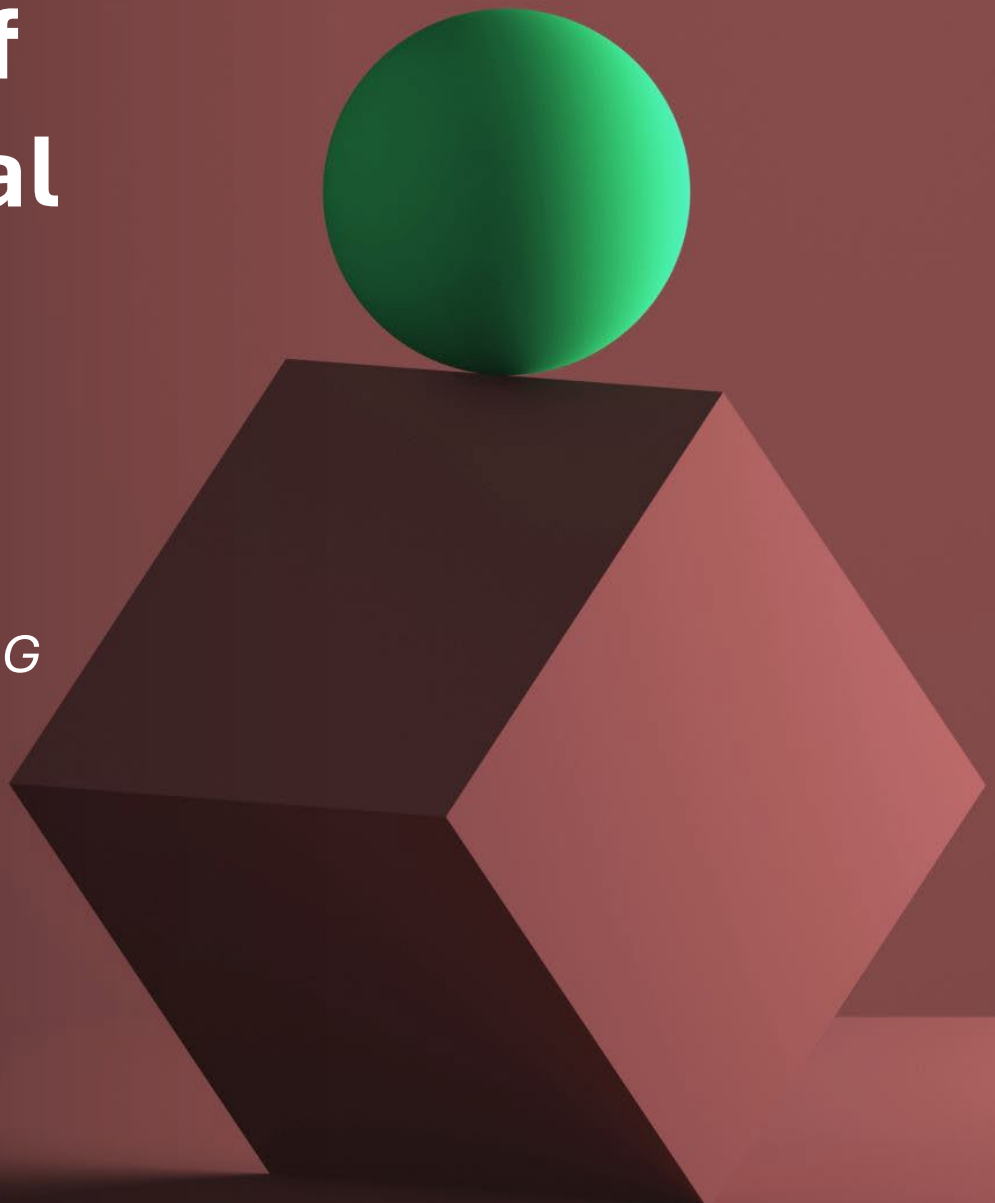
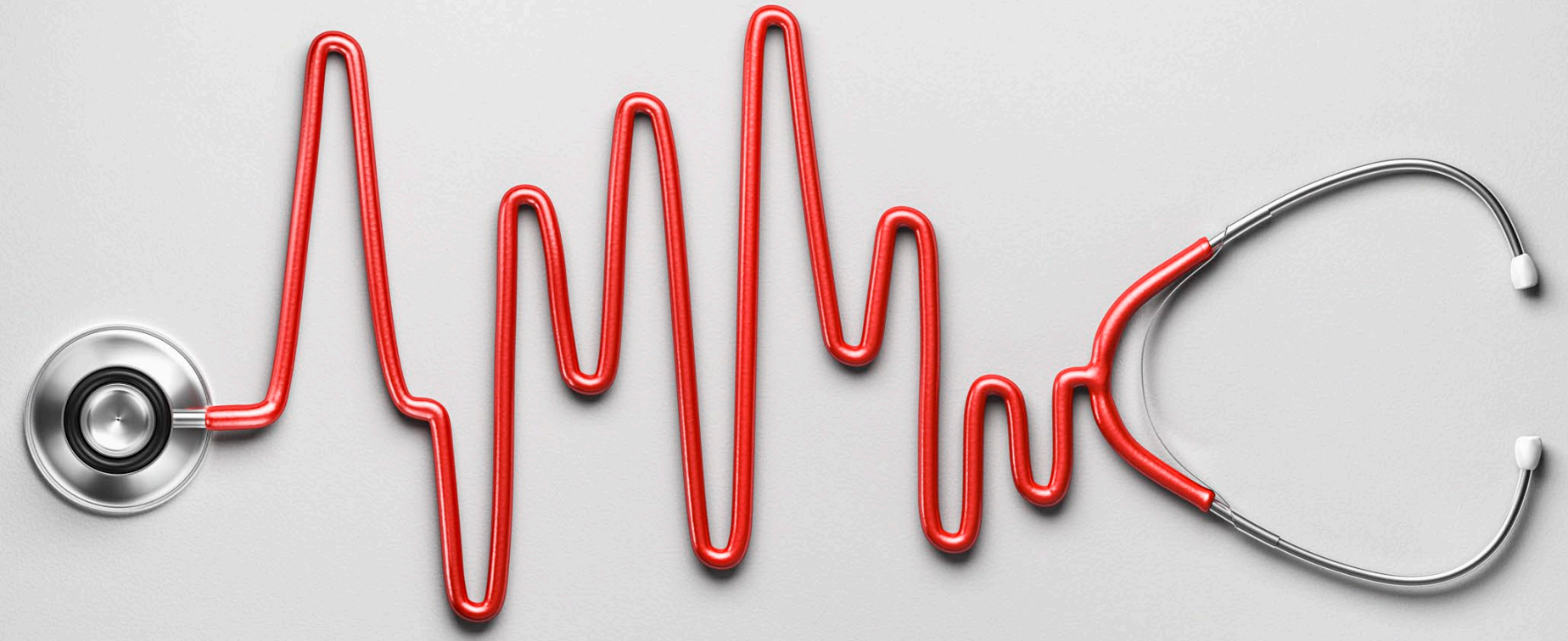
MUSC:

38th Annual Update in Psychiatry





I have no disclosures.

Learning Objectives

Describe	• Describe the hormonal changes related to the menstrual cycle and possible effects on mood.
List	• List the diagnostic criteria for PMDD.
Explain	• Explain current treatment options for individuals diagnosed with PMDD.

Premenstrual Disorders or Menstrual Related Mood Disorders (MRMD)

- Premenstrual Syndrome (PMS)
- Premenstrual Dysphoric Disorder (PMDD)
- Premenstrual Exacerbation (PME)

Epidemiology

90%	One symptom
23-30%	Criteria for PMS
2-5%	Criteria for PMDD
75%	Untreated

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Pathophysiology

- Multifactorial
- Hormone levels not altered
- Theories:
  - Increased sensitivity to normal hormonal fluctuations
  - Dysfunction of the serotonin symptom
    - Declining estrogen -> triggers/exacerbates dysregulation of serotonin system (serotonin transport)
    - Support: Serotonin role in other mood disorders, SSRIs help, Low tryptophan (precursor for serotonin) can increase symptoms
  - Dysfunction of the gamma aminobutyric acid (GABA) neurotransmitter system
    - Progesterone -> allopregnanolone (neuroactive steroid) -> acts on GABA-A -> calming
    - Support: experimental agents, SSRI effects on allopregnanolone

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Which hormone(s) decline(s) at the end of the luteal phase?

A. Estrogen

B. Progesterone

C. Both Estrogen and Progesterone

D. Neither Estrogen or Progesterone

E. How am I in a lecture asking me about estrogen and progesterone?!?

The Menstrual Cycle

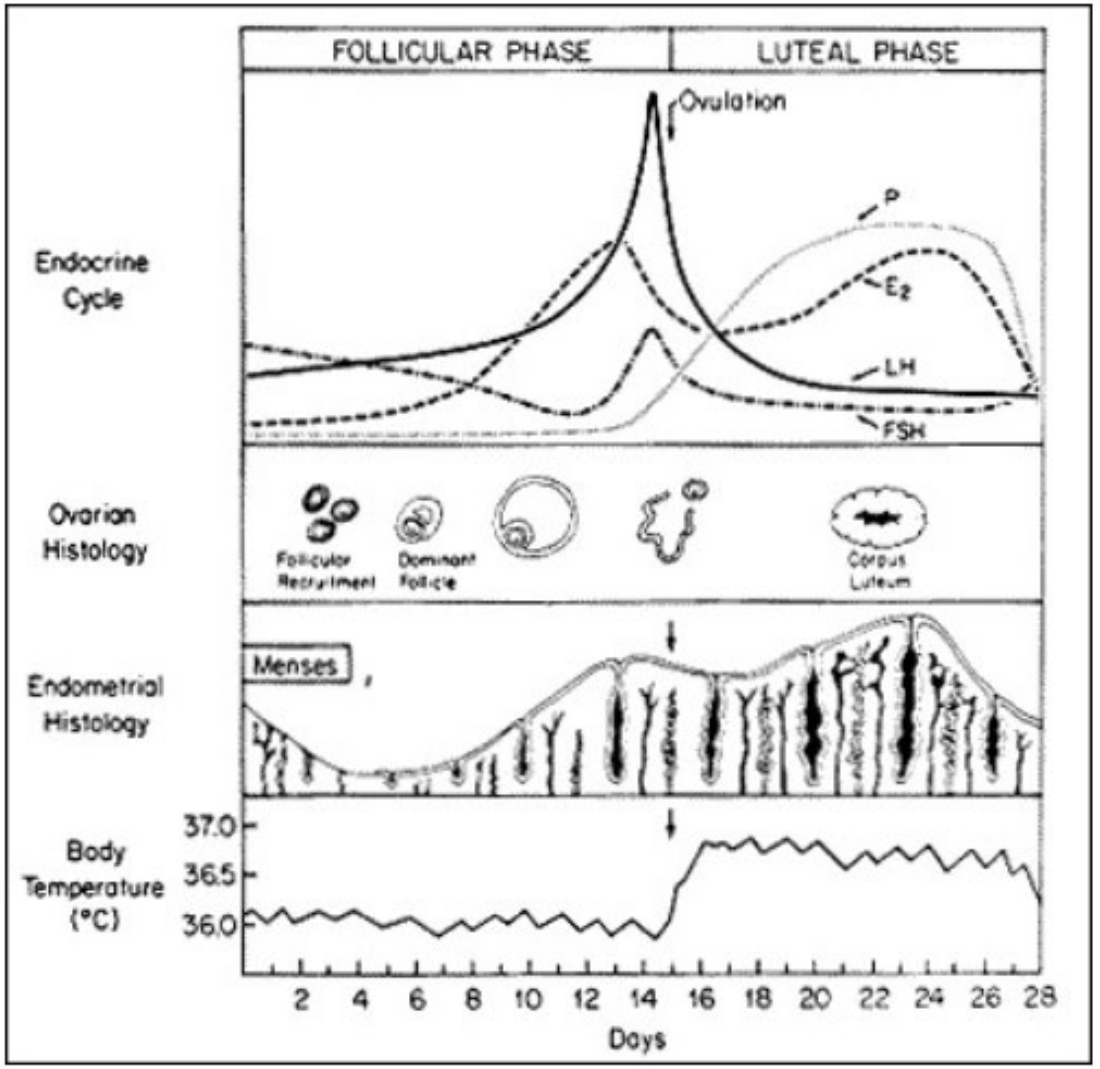

Figure 1.

Reed & Carr (2000)

Premenstrual Syndrome (PMS)

Physical or mood-related symptoms

- Bloating, lethargy, breast tenderness
- Anxiety, irritability, feeling of rejection

Cyclic in nature

Onset in luteal phase

Resolve during or shortly after menstruation

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Premenstrual Dysphoric Disorder (PMDD)

- Added to DSM-5 in 2013 (depressive disorder)
- Added to ICD-11 in 2019
- Typically seek treatment in late 20s/early 30s
- Peaks around 30-39 years
- Typically chronic, but can worsen after pregnancy/aging

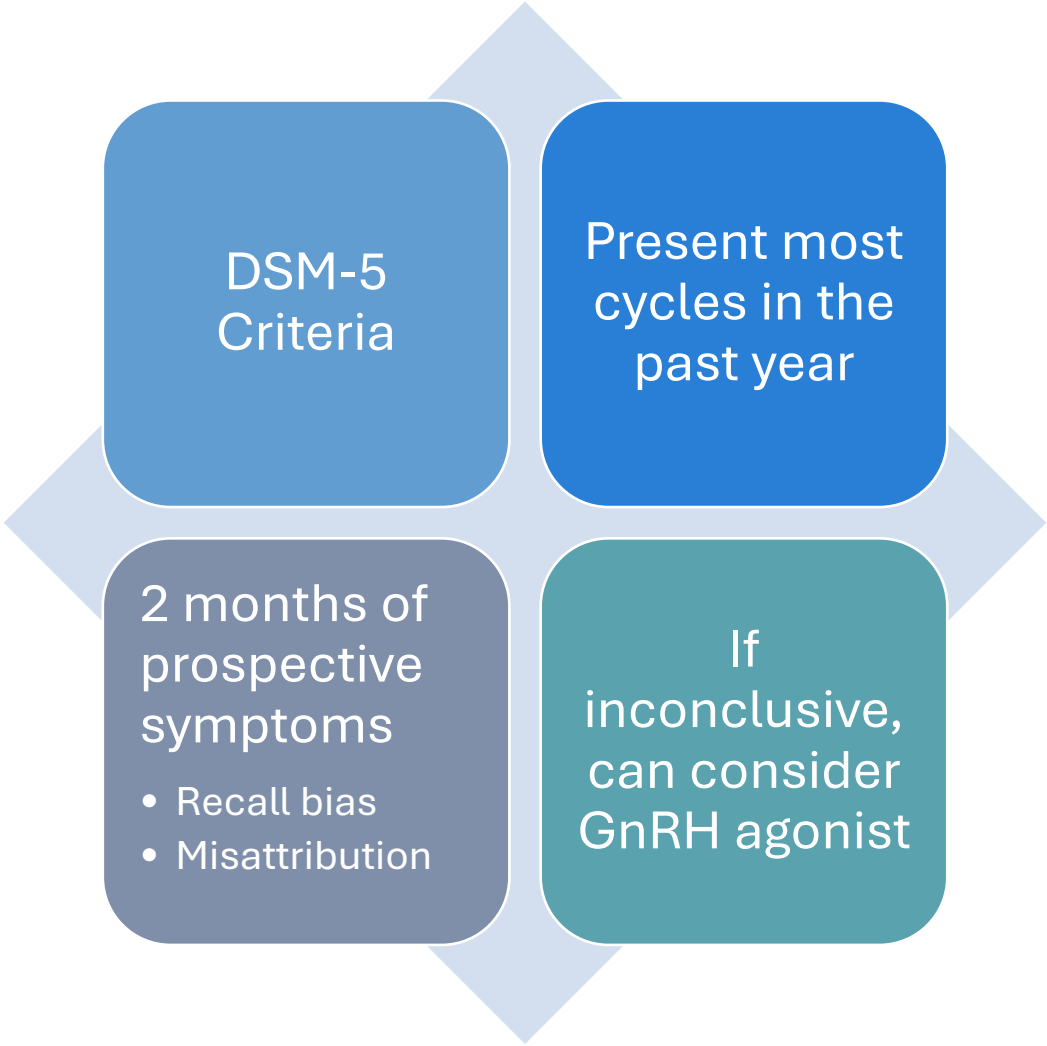
Ismaili et al. (2016), IAPMD Website

Premenstrual Exacerbation (PME)

- Not an official diagnostic specifier in DSM-5-TR
- 40% of women being evaluated for PMDD had PME (2)
- Estimated 60% of females with depression have premenstrual exacerbation (1)

IAPMD Website

Diagnosis PMDD



ACOG (2023), Ismaili et al. (2016), RCOG (2017)

How many of the defined symptoms must be increased to meet the diagnosis of PMDD?

A. 3

B. 4

C. 5

D. 6

Diagnosis: DSM-5

-5 Symptoms
-Luteal phase
-Significant
-Not exacerbation
-Timing

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).

PREMENSTRUAL SYMPTOM TRACKER
(DAILY RECORD OF SEVERITY OF PROBLEMS)

Name:

Month:

INSTRUCTIONS

Print off as many copies as you need to complete a **full two months** worth of tracking. Begin tracking your premenstrual symptoms with this chart today. Fill it out **daily** (preferably at the end of your day). Two full months of menstrual cycle charting will allow for a more accurate assessment.

Each evening note the degree to which you experienced each of the problems listed below. Put an "x" in the box which corresponds to the severity:

1 - not at all **2 - minimal** 3 - mild **4 - moderate** 5 - severe **6 - extreme**

Enter day of the week (e.g. Monday = M)
Note any spotting by entering 'S'
Note menstrual bleeding by entering 'M'
Date (i.e. 1st of the month)

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
SYMPTOMS	1. Felt depressed, sad, "down,", or "blue" or felt hopeless; or felt worthless or guilty	6 5 4 3 2 1																														
	2. Felt anxious, tense, "keyed up" or "on edge"	6 5 4 3 2 1																														
	3. Had mood swings (i.e., suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt	6 5 4 3 2 1																														
	4. Felt angry, or irritable	6 5 4 3 2 1																														
	5. Had less interest in usual activities (work, school, friends, hobbies)	6 5 4 3 2 1																														
	6. Had difficulty concentrating	6 5 4 3 2 1																														
	7. Felt lethargic, tired, or fatigued; or had lack of energy	6 5 4 3 2 1																														
	8. Had increased appetite or overate; or had cravings for specific foods	6 5 4 3 2 1																														
	9. Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep	6 5 4 3 2 1																														
	10. Felt overwhelmed or unable to cope; or felt out of control	6 5 4 3 2 1																														
	11. Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms	6 5 4 3 2 1																														
IMPACT	At work, school, home, or in daily routine, at least one of the problems noted above caused reduction of production of efficiency	6 5 4 3 2 1																														
	At least one of the problems noted above caused avoidance of or less participation in hobbies or social activities	6 5 4 3 2 1																														
	At least one of the problems noted above interfered with relationships with others	6 5 4 3 2 1																														

IAPMD

1. Felt depressed, sad, "down,", or "blue" or felt hopeless; or felt worthless or guilty	6 5 4 3 2 1
2. Felt anxious, tense, "keyed up" or "on edge"	6 5 4 3 2 1
3. Had mood swings (i.e., suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt	6 5 4 3 2 1
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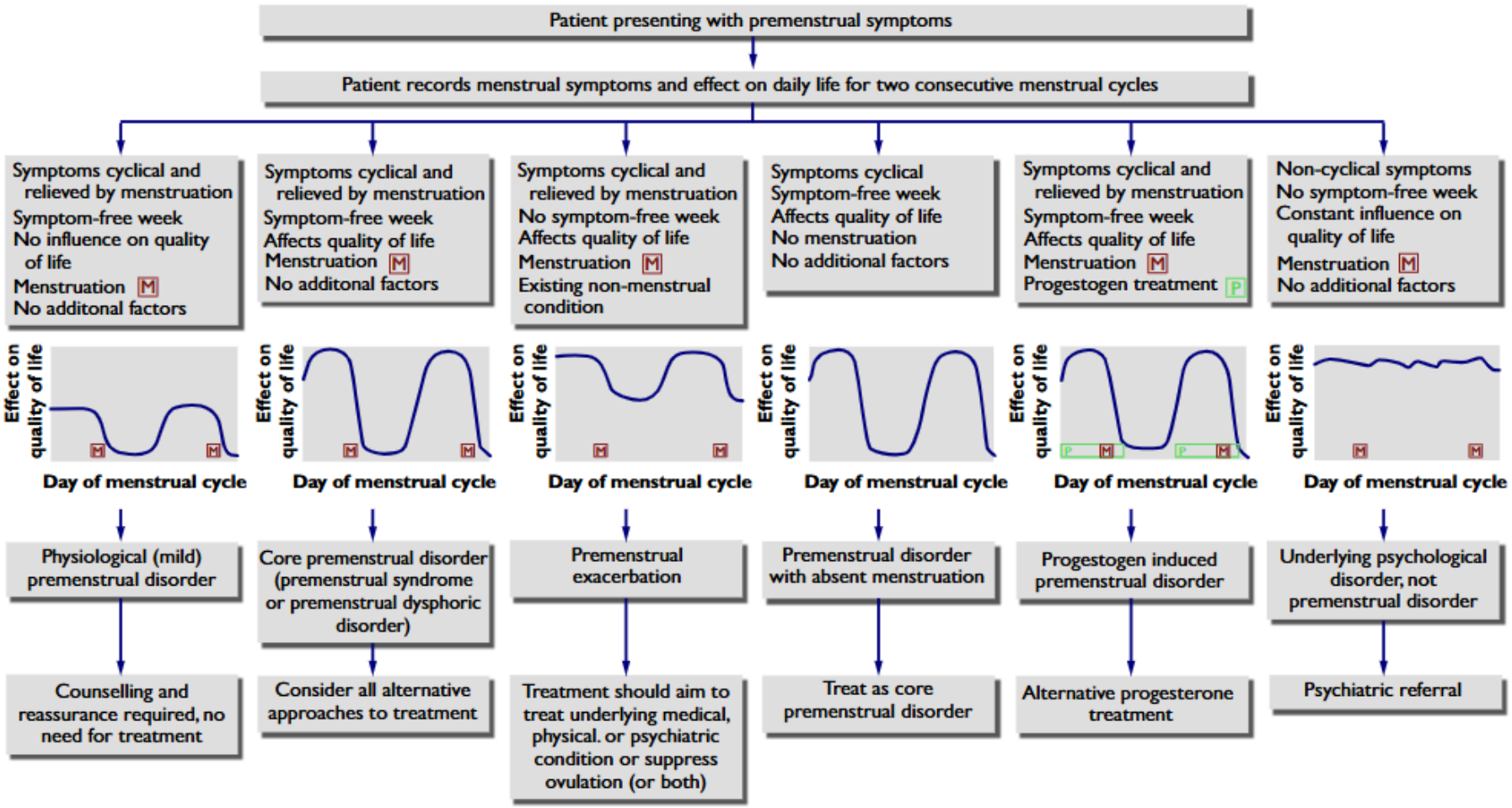
9. Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep	6 5 4 3 2 1
10. Felt overwhelmed or unable to cope; or felt out of control	6 5 4 3 2 1
11. Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms	6 5 4 3 2 1

IAPMD (2021)

Classification of PMS



RCOG (2017)

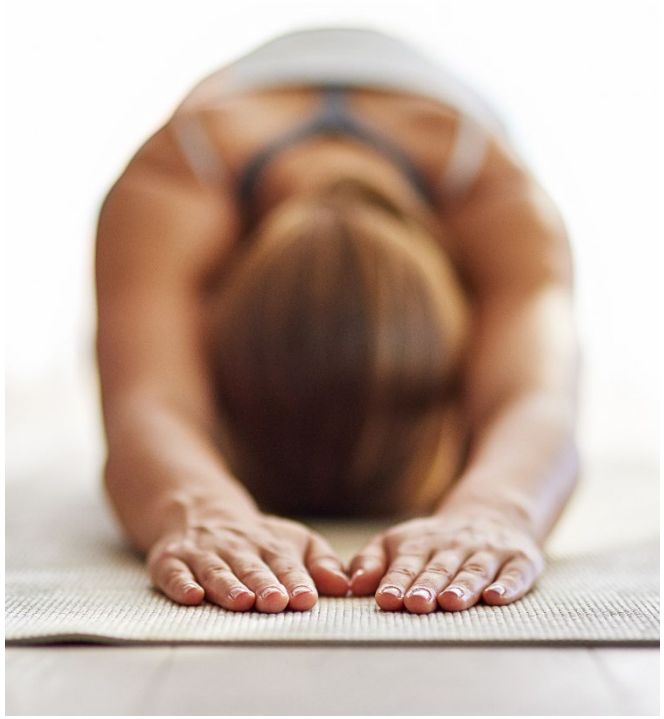
Management Options

LIFESTYLE/BEHAVIORAL

SEROTONIN AGENTS

OVULATION SUPPRESSION

Management: Lifestyle changes



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Exercise: Routine moderate exercise

- 150-300min/week (moderate intensity)
- 75-150min/week (vigorous intensity)

Calcium 1,000-1,200 mg/day

- Theory: symptoms due to dysfunctional Ca metabolism (Estrogen lowers calcium levels)
- IOM (NAM) recommends max of 2,500mg/d

Vitamin B6 (50-100mg daily)

Magnesium (200-460mg daily)

Vitamin E (400 IU daily)

Acupuncture

- RCT suggests improvement (poor study)
- Low risk for harm

Vitex agnus castus (chasteberry)

- Simulates dopamine receptors (suspected, but unclear) -> affects prolactin and progesterone
- RCT with benefit (poor study)
- More research needed

NSAIDS

- Inhibits production of prostaglandins
- Improvement in physical symptoms and some mood symptoms (possibly secondary to pain control)

Management: CBT

Reframes negative and irrational thought patterns

Small-to-moderate improvement in affective symptoms

SSRIs have more rapid response, but efficacy of CBT at 6 months compared with SSRI alone and SSRI + CBT

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Management: SSRIs

First-line pharmacologic treatment

FDA approved:

- Sertraline
- Paroxetine
- Fluoxetine

SNRI: Venlafaxine

2013 Cochrane review (31 RPCT)

- Sertraline, fluoxetine, paroxetine, escitalopram, citalopram
- Significant improvement compared to placebo:
  - Moderate effect: Overall symptoms, psychological symptoms, functional impairment, irritability
  - Small effect: physical symptoms

ACOG (2023), Ismaili et al. (2016)

Management: SSRIs

Continuous dosing

Intermittent dosing

- Luteal phase
- Symptom onset

Luteal phase increase

Comparable efficacy (limited data)

- Intermittent only if:
  - Confirmed diagnosis
  - No additional psychiatric comorbidity
  - Regular menstrual cycles

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A patient reports improvement in PMDD symptoms with SSRI use. How long do you recommend continued use prior to tapering off?

A. I recommend attempt to taper at 6-12 months, as this is the first time she has received treatment for mood symptoms.

B. I would recommend she continue long-term, and we will schedule visits yearly to reevaluate

C. Forever

Management: SSRIs

Chronic condition

- Relapse rate high

Treatment resistance considerations:

- Change from intermittent to continuous
- Increase dose with symptoms
- Try different SSRI
- Refer to specialist

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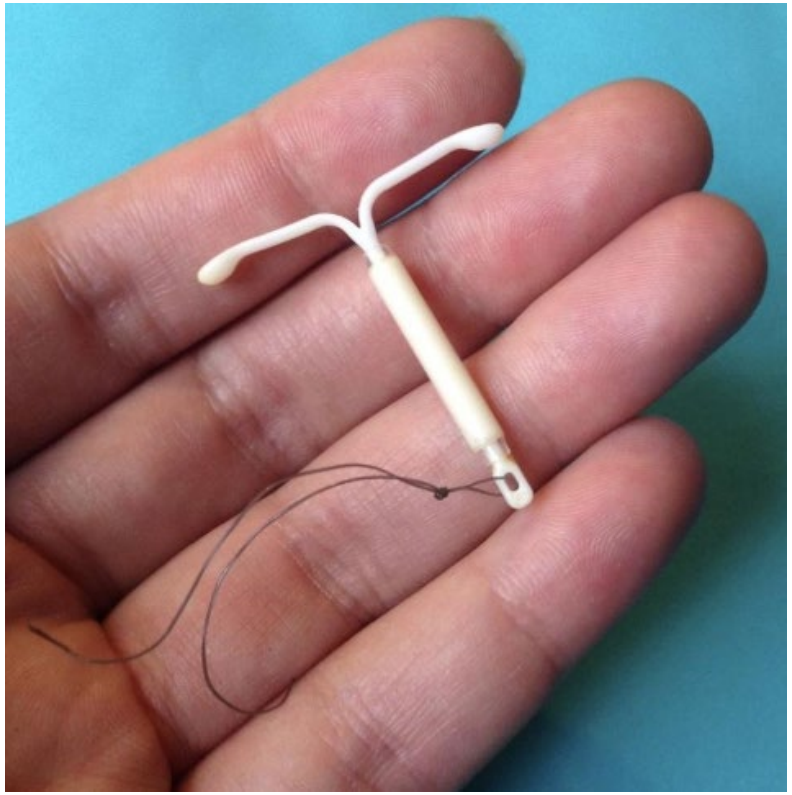
Management: Hormonal Treatments

Combined OCPs:

- Suppress ovulation, resulting in more constant hormone levels
- Might not be as helpful for depressive symptoms
- Most data on drosperinone
  - Only OCP with FDA approval for PMDD
  - Other OCPs have shown improvement as well
- Meta-analysis:
  - Moderate recution in overall symptoms
  - Equal to placebo for depressive symptoms
  - Efficacy did not change by progesterone type or regimen (21, 24, or continuous)

ACOG (2023)



Management: Hormonal Treatments (Continued)

- Current evidence does not support supplemental progesterone/progestin or 52-mg LNG IUD for treatment of PMDD
- Continuous estrogen (implant vs patch) + progesterone might improve symptoms (low quality evidence)
- Research needed to confirm efficacy of contraceptive patch and vaginal ring

ACOG (2023), RCOG (2017)

Management: GnRH Agonists

Leuprolide (Lupron), Nafarelin

Mechanism: Induce anovulation

SE: hypoestrogenic effects (vasomotor symptoms, bone density)

Add back: assists with SE, but precipitate recurrence short-term

Consider if treatment resistant or uncertain of diagnosis

Avoid in adolescents (bone health)

ACOG (2023), RCOG (2016)

Surgical Interventions (Bilateral oophorectomy w/wo hysterectomy)

Only for severe symptoms that have failed other managements

Recommend rial of GnRH agonist first to predict response

ACOG (2023), RCOG (2017)

ACOG Summary of Recommendations

- ACOG recommends SSRIs for the management of affective premenstrual symptoms
- ACOG recommends combined oral contraceptives (COCs) for the management of overall premenstrual symptoms.
- ACOG recommends CBT for the management of affective premenstrual symptoms.
- ACOG suggests gonadotropin-releasing hormone (GnRH) agonists with adjunctive combined hormonal add-back therapy for adults with severe refractory premenstrual symptoms.
- ACOG suggests routine exercise to help manage physical and affective premenstrual symptoms.
- ACOG suggests calcium supplementation of 1,000-1,200 mg per day in adults to help manage physical and affective premenstrual symptoms.
- ACOG suggests adequate calcium intake in adolescents to help manage physical premenstrual symptoms.
- ACOG suggests the use of acupuncture to help manage physical and affective premenstrual symptoms.
- ACOG suggests NSAIDs for the management of premenstrual pain
- ACOG suggests that clinicians provide education about premenstrual symptoms and self-help coping strategies as part of a holistic approach to the management of premenstrual disorders
- Bilateral oophorectomy with/without hysterectomy should be reserved as a treatment option for adults with severe PMS only when medical management has failed and patients have been counseled about the associated risks and irreversibility of the procedure. A trial period of GnRH agonist therapy is advised before surgery to predict a patient's response to surgical management (good practice point)
- Collaboration with or referral to a mental health professional should be considered for patients with premenstrual symptoms if the diagnosis is unclear or underlying mood disorder is suspected.

ACOG (2023)

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Thank You

Questions?