

Premenstrual Dysphoric Disorder

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Case

- Priya is a 26-year-old G0P0 presents to your office for evaluation after her primary care doctor referred her for help with “irritability and frequent arguments with her partner.”
- As she starts talking to you about the stress of the arguments with her partner she is tearful and says “oh I’m so sorry, I always lose control of my emotions when I’m on my period.”

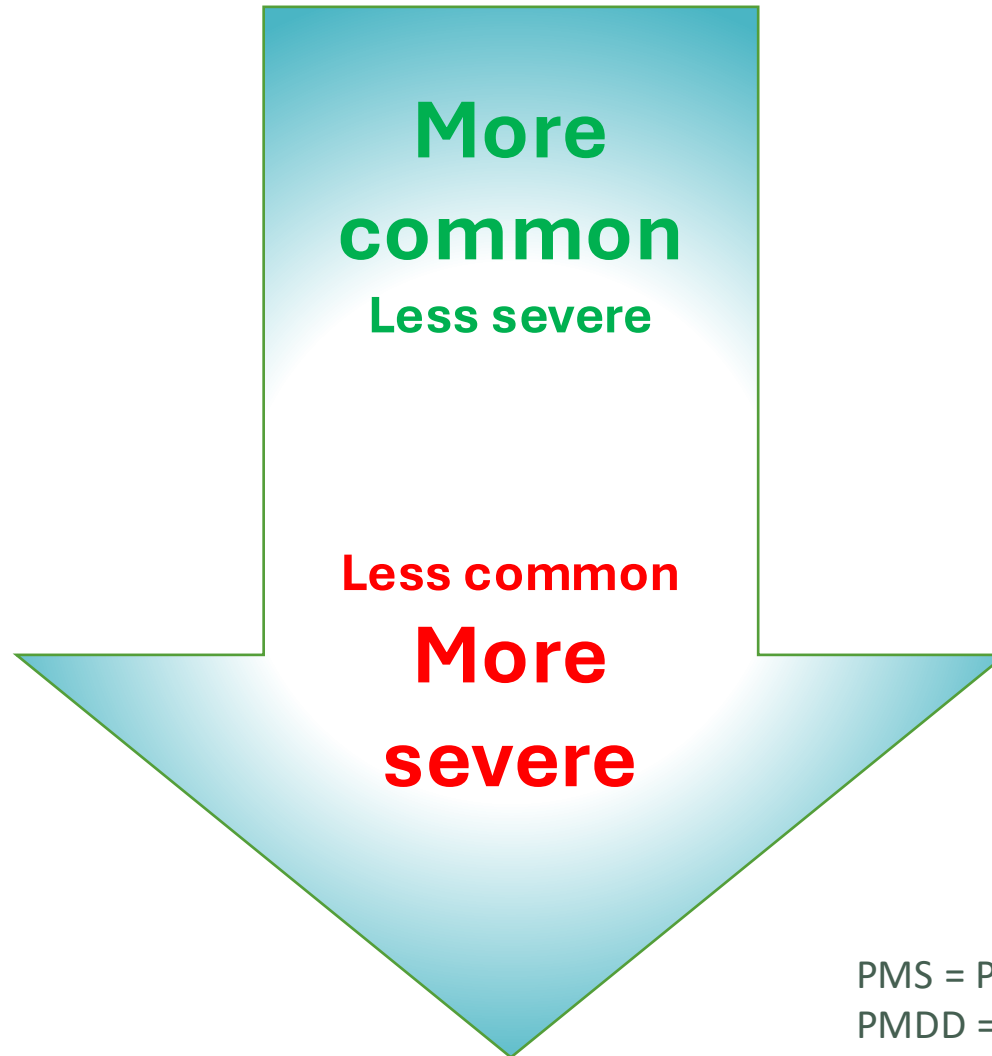
Case

- You ask her more about her mood and she says that she typically feels fine but every few weeks she feels tearful and angry, which causes her and her partner to argue.
- During this time she feels badly about the arguing, has trouble sleeping, feels fatigued, and often gets headaches.
- When you ask her if these weeks of difficulty align with times she has her period she says, “I don’t know. I never kept track but it can’t just be because of that. This is so much worse than PMS.”

Differential

- Premenstrual Syndrome (PMS)
- Premenstrual Dysphoric Disorder (PMDD)
- Premenstrual Exacerbation of another mood disorder
- Other mood disorder (MDD, Bipolar Disorder, etc.)

Premenstrual Symptoms ≠ An illness



**Premenstrual
Molimina**
(normal, non-problematic)

PMS
(bothersome)

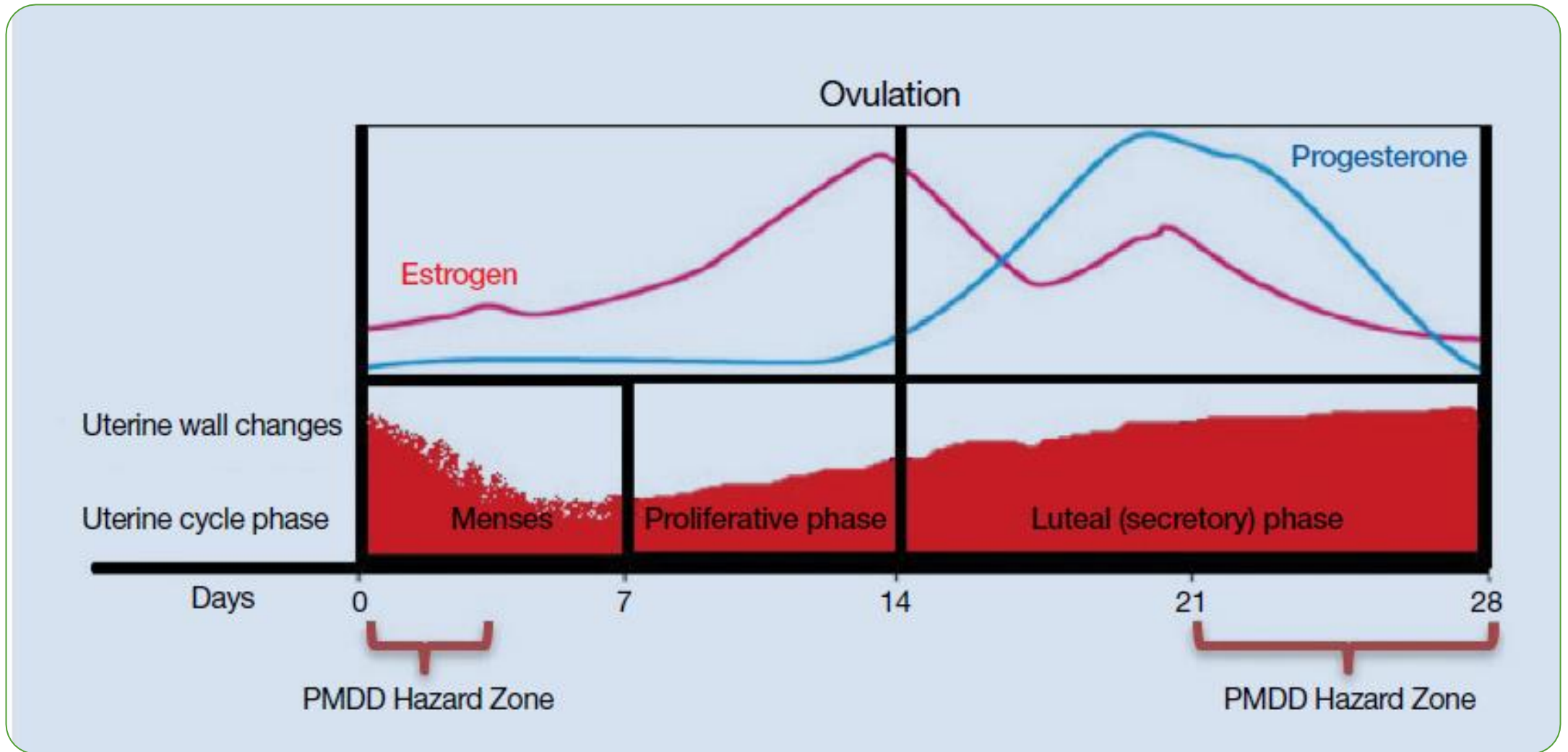
PMDD
(significant impairment)

PMS = Premenstrual syndrome
PMDD = Premenstrual dysphoric disorder

How common are premenstrual disorders?

- Most reproductive age women will experience transient physical and emotional symptoms around the time of menses. Some estimates are as high as 90%
- PMS is fairly common and seen in 30-80% of reproductive age women
- PMDD is estimated to occur in about 3-8% of reproductive age women

Menstrual Cycle



Premenstrual Syndrome

- Identified by ACOG but not in DSM 5
- Symptoms must occur during the luteal phase
- At least 1 affective or somatic symptom
 - Mood lability, irritability, anxiety, feeling depressed, bloating, insomnia, poor concentration, hand/feet swelling, breast tenderness, change in appetite
- Must suffer from identifiable dysfunction in social or economic performance
- Symptoms must be present in the absence of pharmacologic therapy, hormone ingestion, or drug or alcohol use

Premenstrual Dysphoric Disorder Criteria

- ≥ 5 symptoms, at least 1 core symptom
- Occur during last week of luteal phase
- Relieved within a few days of starting menses; does not recur during week following menses
- Interferes with work, school, or usual activities
- Not an exacerbation of another disorder

PMDD Symptoms

≥5 symptoms, including at least 1 core symptom

- Depressed mood
- Moodiness
- Anxiety, edginess, nervousness
- Anger or irritability

Other Symptoms

- Fatigue, lethargy
- Insomnia/hypersomnia
- Difficulty concentrating
- Appetite changes/cravings
- Physical symptoms (headache, breast tenderness and/or swelling, bloating, joint/muscle pain, etc.)
- Decreased interest in usual activities
- Feeling overwhelmed/ out of control

Back to our Case

- You discuss your suspected differential with Priya, in particular your suspicion that these symptoms could be from PMDD. She responds by saying, “How do we find out if that’s what it is?”
- What do you do next?

How do you make a diagnosis?

The Daily Record of Severity of Problems (DRSP).

most commonly used, self-administered rating scale. It will provide a DSM5 diagnosis, should the patient meet criteria)

Calendar of Premenstrual Experiences

Premenstrual Assessment Form

DAILY RECORD OF SEVERITY OF PROBLEMS

Please print and use as many sheets as you need for at least two FULL months of ratings. Name or Initials _____
Month/Year _____

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 (Monday="M", Thursday="R", etc) >																																
Note spotting by entering "S" >																																
Note menses by entering "M" >																																
Begin rating on correct calendar day >																																
		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
1	Felt depressed, sad, "down", or "blue" or felt hopeless; or felt worthless or guilty																															
2	Felt anxious, tense, "keyed up" or "on edge"																															
3	Had mood swings (i.e., suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt																															
4	Felt angry, or irritable																															
5	Had less interest in usual activities (work, school, friends, hobbies)																															
6	Had difficulty concentrating																															
7	Felt lethargic, tired, or fatigued; or had lack of energy																															
8	Had increased appetite or overate; or had cravings for specific foods																															
9	Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep																															
10	Felt overwhelmed or unable to cope; or felt out of control																															
11	Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms																															
At work, school, home, or in daily routine, at least one of the problems noted above caused reduction of productivity or inefficiency																																
At least one of the problems noted above caused avoidance of or less participation in hobbies or social activities																																
At least one of the problems noted above interfered with relationships with others																																

Symptom Tracking Apps

Free App



Me v PMDD™

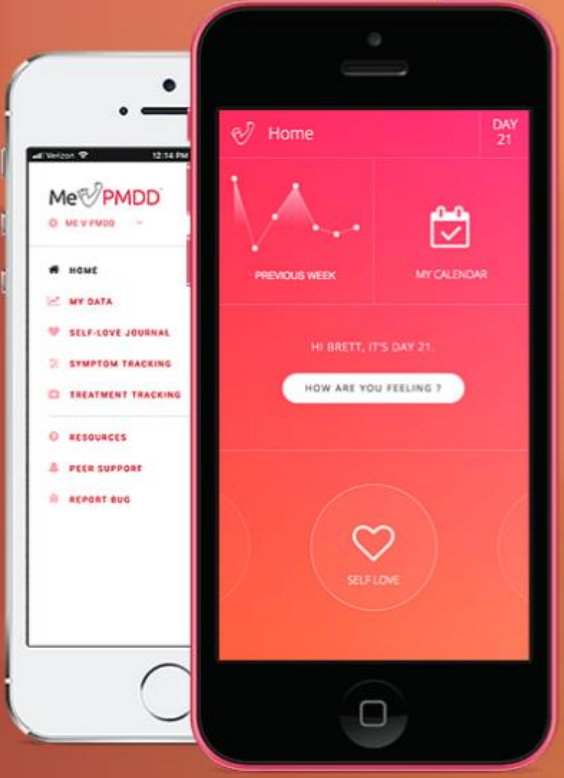
We can do it! We can be victorious, even with **PMDD**!

Me v PMDD Symptom Tracker is the app every PMDD warrior needs to understand your cycle, your **PMDD**, yourself.

 **IOS**
12.0+ PHONES

 **ANDROID**
11.0+ PHONES

<https://www.mevpmdd.com/>



PreMentrics 12+

PMS O'Brien

Designed for iPhone

★★★★★ 2.5 • 2 Ratings

\$3.99

[View in Mac App Store](#)

Additional resources:

<https://iapmd.org/toolkit>

Scoring the DSRP

- During the week prior to menses, does the patient score at least 4 (moderate) for at least 2 days on one or more of the following: depression, anxiety, mood lability, anger/irritability?
- During the week prior to menses, does the patient score at least 4 (moderate) for at least two days on at least FIVE of the symptoms (1 through 11) listed?
- During the week prior to menses, does the patient have scores of at least 4 (moderate) for at least 2 days on at least one of the 3 areas of functional impairment?
- During the mid-follicular phase (days 6-10 after the onset of menses), does the patient have an average daily symptoms rating score greater than 3 (mild) on any of the symptoms?

Back to our case

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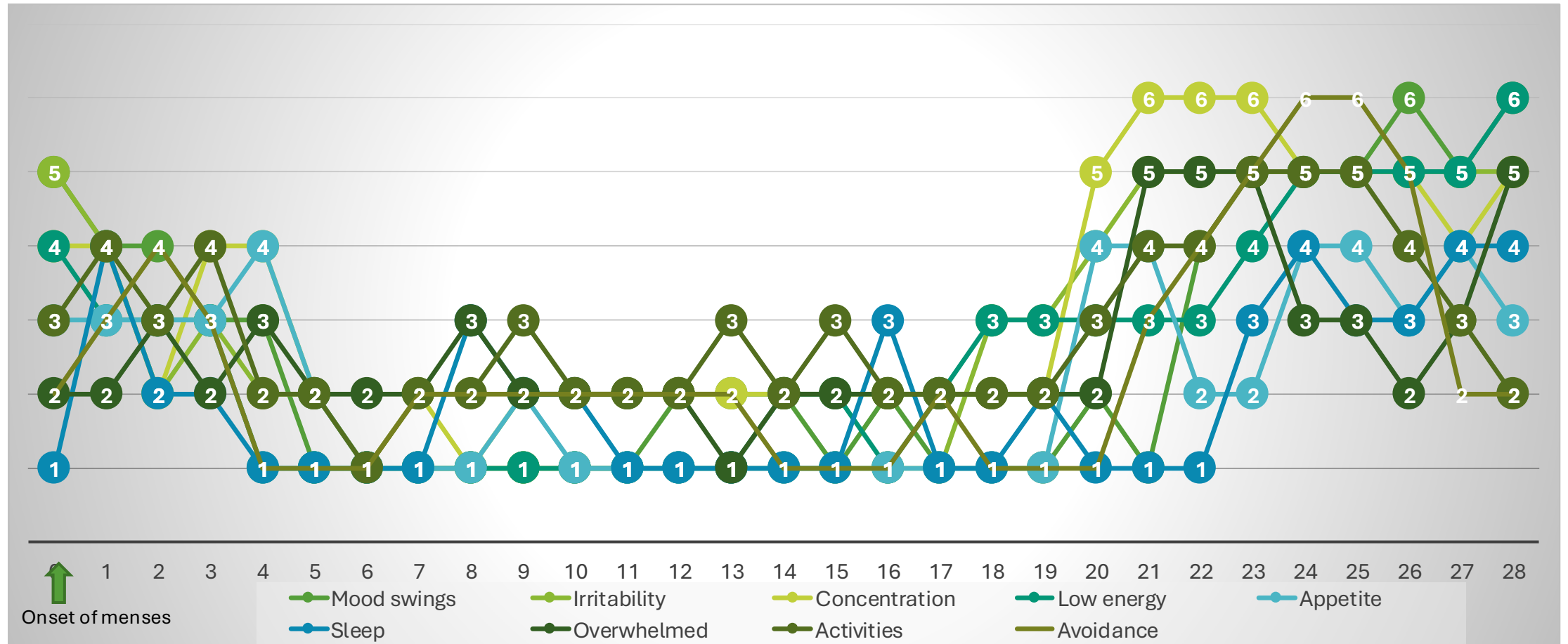
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[illegible]

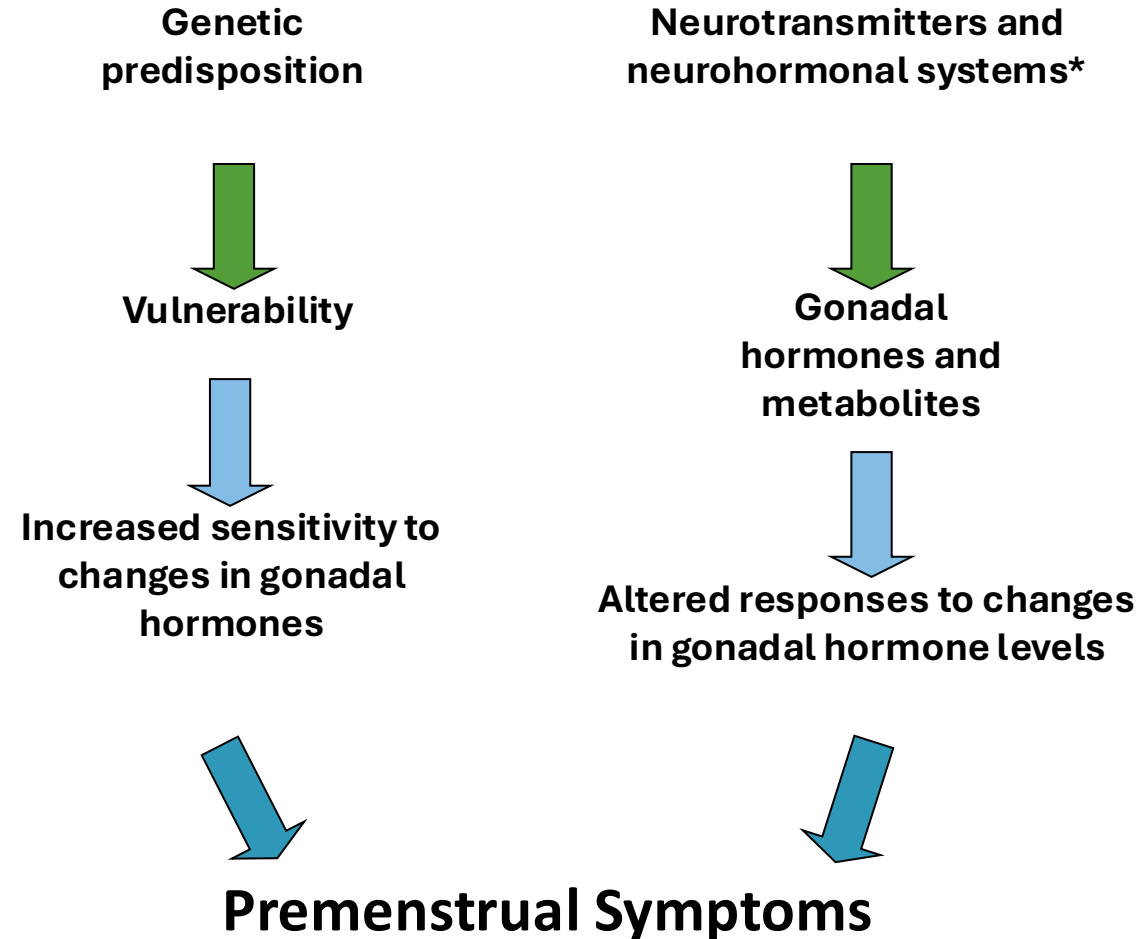
Positive Symptoms from DRSP Across Menstrual Cycle



Back to the case

- You diagnose her with PMDD.
- And she says it is a relief to know there is something to explain this.
- She then thinks and asks, “Wait a minute, why do only some people have PMDD?”

Why might this happen?



Genetic predispositions

Possible different sensitivity to normal hormone fluctuations and neuroactive steroids

Possible Etiologies

- Allopregnanolone
 - Metabolite of progesterone that is a positive allosteric modulator of GABA
 - Abrupt withdrawal may play a role in inducing symptoms (Hantsoo & Epperson, 2020)
- Estradiol
 - Enhances effects of serotonin by altering Serotonin transporter expression and decreasing COMT and MAOA
- Stress
 - Studies show a correlation of trauma and abuse with PMDD symptoms. Possibly mediated through GABA and role of allopregnanolone
- BDNF
 - A new area of interest as there are differences in BDNF levels across the cycle - one study showed those with PMDD had higher serum BDNF in the luteal phase (Oral et al., 2015)

How do we treat PMDD?

- Lifestyle Modification
 - Aerobic exercise, stress reduction, dietary modifications
- CBT
- Pharmacotherapy
 - SSRIs
 - Oral Contraceptives
 - GnRH agonists (reserved to stop ovulation in severe cases)

SSRIs

- Sertraline, Paroxetine and Fluoxetine have FDA approval for PMDD
- Can be dosed continuously as you would typically
- Can also be dosed at symptom onset or at onset of luteal phase
 - Efficacy is similar and may be preferable for those who do not want to take medication every day

Medication	Starting Dose	Target Dose
Sertraline	25-50mg	50mg-200mg
Paroxetine	10-20mg	20mg-50mg
Fluoxetine	10-20mg	20mg-60mg

Oral Contraceptives

- Oral contraceptives have mixed to poor evidence for treatment of PMDD symptoms
- Exception is OCP formulated with drospirenone
 - Similar in structure to aldosterone. Binds to aldosterone receptors increasing sodium and water excretion
 - Estradiol with drospirenone showed reduction in symptoms and improvement in functioning compared to placebo in RCT
 - This may be a reasonable option for those with PMDD who are also looking for contraception

Complementary Treatments

- Calcium 500-1000 mg/day: moderate evidence but not as effective as SSRIs
- Exercise: weak evidence but is healthy
- Diet: Moderate positive evidence - small portions of complex carbohydrates, which are high in fiber, and reduce intake of sugar to improve symptom severity
- B-6: evidence that doses of 50 mg-100 mg help primarily physical symptoms
- Vitex Agnus Castus (Chasteberry): herbal supplement strong evidence but not as effective as SSRIs and preparations are not uniform
- St. John's Wort: mixed evidence

Back to our Case

- After discussing the diagnosis with Priya, you gather further information.
- You find out that she was on oral contraceptives in the past (she cannot recall exactly which pill) that she stopped because she felt it made her acne worse.
- She also comments that she had difficulty remembering to take a pill everyday and often missed several doses in each pack.
- You also find out she has never been on an SSRI before, has had no prior mental health treatment, and denies any history of manic or psychotic symptoms.
- After this discussion, she asks if there is any treatment that can help with her PMDD.

How do you decide on treatment?

SSRI	OCP w/drospirenone
Suspect underlying mood disorder	Patient wants contraception in addition to PMDD treatment
Patient does not want to take pills daily	Has not responded to SSRIs
History of side effects on OCPs	History of side effects on SSRIs
Medical contraindication to OCPs	Contraindication to SSRIs (mania)
	Predominance of physical symptoms
Patient Preference	Patient Preference

Summary

- Most reproductive age women experience premenstrual symptoms to varying degrees
- PMS and PMDD cause impairment in functioning and impact quality of life
- Symptoms are likely related to underlying sensitivity to changes in hormones and neuroactive steroids during luteal phase
- Can be diagnosed using prospective symptom scales
- Primary forms of treatment are SSRIs (continuous or symptom onset dosing) and estradiol/drospirenone combined OCP

References

- Good review paper: Hantsoo & Payne (2023). Towards understanding the biology of premenstrual dysphoric disorder: From genes to GABA. Neurosci & Behav Reviews. <https://doi.org/10.1016/j.neubiorev.2023.105168>
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