



# **MONITORING CALCIUM IN WOMEN WITH PREMENSTRUAL DYSPHORIC DISORDER**

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MLSP 6905 Capstone Project Presentation

## What is Premenstrual Dysphoric Disorder?

- Approximately 5 million American Women have PMDD<sup>1</sup>
- Up to 89% of women with PMDD do not receive a diagnosis beyond PMS<sup>1</sup>
- Patients must have at least 5 symptoms, and 1 of these must be a core symptom<sup>1</sup>

### Core Symptoms

- Feelings of sadness or hopelessness, or self-deprecating thoughts.
- Feeling tense, anxious, or “on edge.”
- Marked mood lability.
- Persistent irritability, anger, and increased interpersonal conflicts

### Other Symptoms

- Fatigue.
- Change in sleep or eating patterns.
- Difficulty with concentration.
- Decreased interest in usual activities.
- Feeling overwhelmed or out of control.
- Other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of bloating, and weight gain.

# The Impact of PMDD

- Approximately 3% of American women have PMDD<sup>1</sup>
- Increased risk of miscarriage<sup>4</sup>
- 23% of women who survive a suicide attempt have PMDD,<sup>13</sup>
- Women with PMDD are more susceptible to osteoporosis later in life<sup>3</sup>

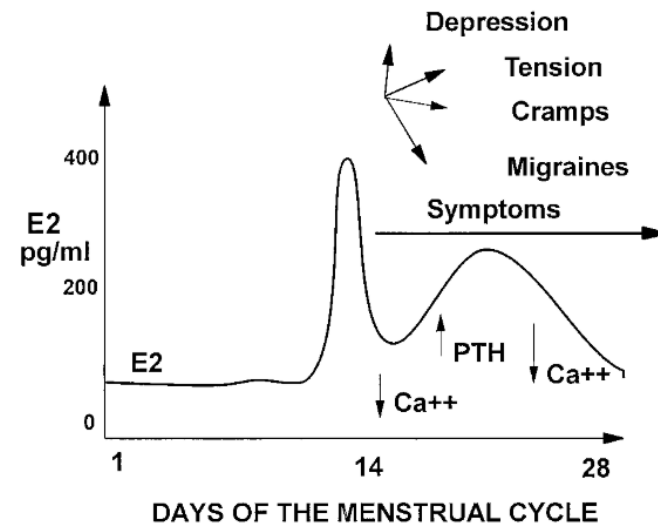
# Calcium and the Menstrual Cycle

Two menstrual cycle phases:

- Follicular days 0-14
- Luteal days 15-28

During the Luteal phase:

- Calcium levels decrease
- Vitamin D levels decrease
- Parathyroid hormone increases



**Fig. 3.** Estradiol influences calcium and vitamin D metabolism across the menstrual cycle inducing fluctuations in calcium concentrations and triggering luteal phase symptoms. E2 represents estradiol; PTH—parathyroid hormone; Ca<sup>++</sup>—ionized calcium.

## Why this project?

- I was diagnosed with PMDD in March of 2021
- Follicular phase calcium from my own tests in December 2019 and March 2020

Calcium	9.2 mg/dL	8.5 - 10.1 mg/dL
Calcium	9.2 mg/dL	8.5 - 10.1 mg/dL

- Luteal phase calcium from my own tests in December 2019 and October 2021

Calcium	8.6 mg/dL	8.5 - 10.1 mg/dL
Calcium	8.7 mg/dL	8.5 - 10.1 mg/dL

## Symptom Comparison<sup>5</sup>

### PMDD

- Depression
  - Sadness
  - Lethargy
  - Social isolation
  - Decreased motivation
- Anxiety
  - Insomnia
  - Paresthesia
- Fatigue
- Irritability
- Labile mood
- Food cravings
- Edema
- Bloating
- Abdominal cramps
- Headache
- Generalized aches and pain

### Hypocalcemia

- Depression
- Anxiety
- Paresthesia
- Fatigue
- Impaired memory
- Impaired intellectual capacity
- Personality disturbances
- Neuromuscular irritability
- Muscle cramps
- Tetany

# Project Research Question

- What tests would be useful for monitoring calcium in women with PMDD?
  - What samples should be used?

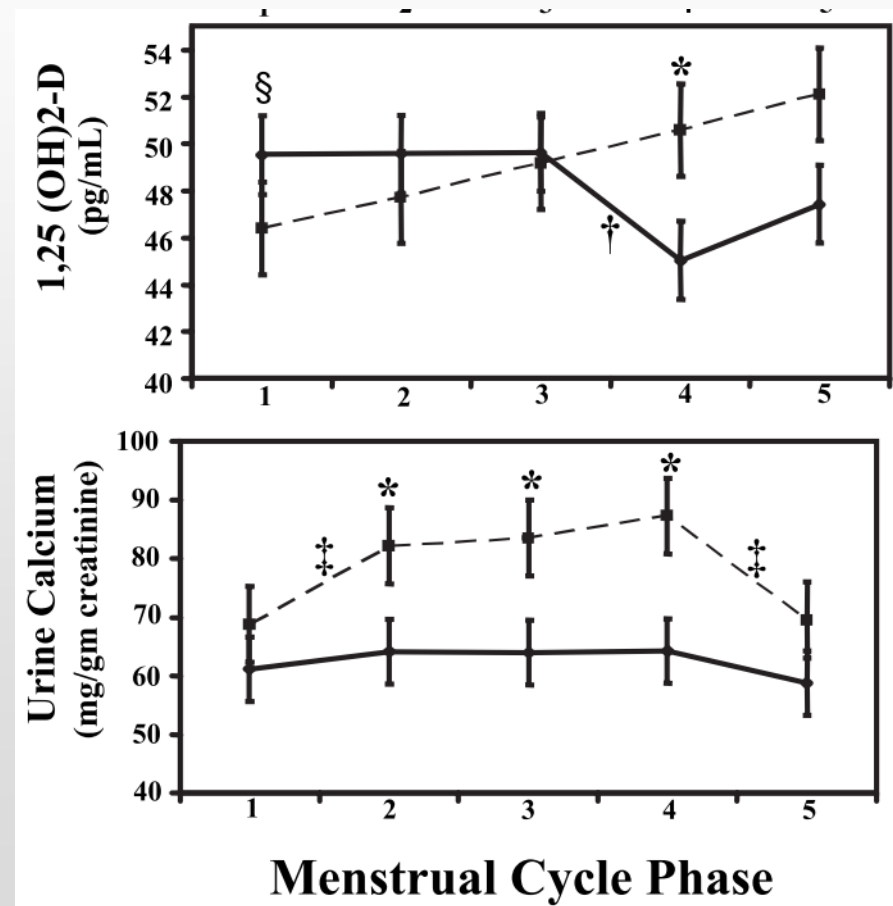
# Calcium in the Human Body

- ~50% of serum calcium is ionized and measurable
- Skeleton is the main repository
- Only loss is in urine
- Vitamin D and parathyroid hormone are the most important regulators



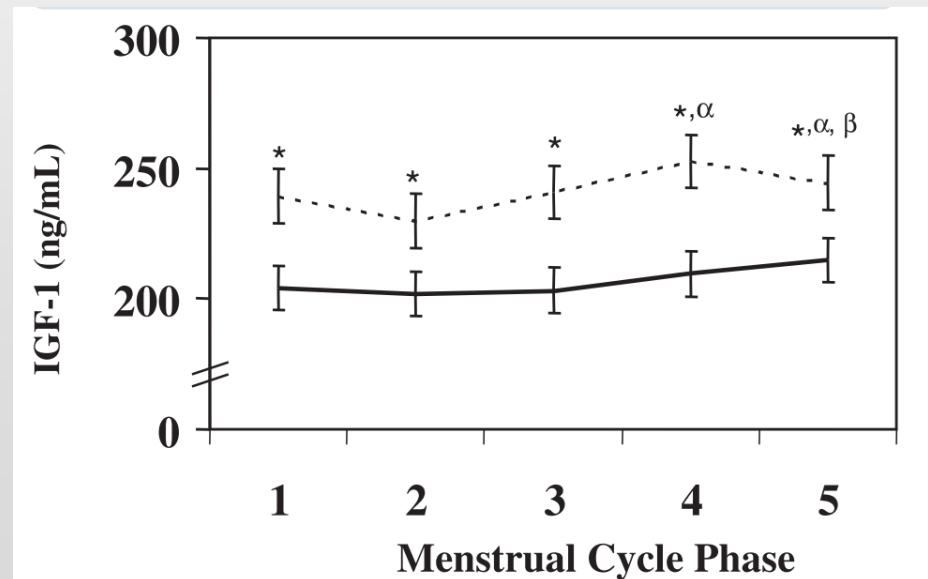
# Calcium and Vitamin D during the Menstrual Cycle

- Dashed line is control group
- Solid line is women with PMDD
- Phases 1 and 2 are follicular, 3 is periovular, 4 and 5 are luteal
- \* indicates significance with a P value < 0.05



# Impaired Ca Retrieval in PMDD

- Estradiol does not enhance  $1\alpha$ -hydroxylation of  $25(\text{OH})$  vitamin  $\text{D}^5$ 
  - Less Ca absorbed
  - less Ca excreted in urine
- Lower IGF-1<sup>3</sup>
  - IGF-1 regulates osteoclastogenesis
  - Impaired bone remodeling



# What we should be measuring in the Lab

- Ideal Sample:
  - 24-hour urine calcium from the luteal phase
  - 1,25-dihydroxy vitamin D from serum
- Acceptable Sample:
  - Random urine calcium from the luteal phase standardized as Ca/Creatinine

# Reference ranges

- 78% of labs verify manufacturer's reference ranges<sup>12</sup>
- Health associated, derived from a population in good health
  - Who is in that population?
- A 2021 study shows that the reference range for 24-hour urine calcium concentration varies by age and race<sup>6</sup>

## Discussion / Conclusion

- There is significant overlap in symptomology between PMDD and hypocalcemia
- Women with PMDD have significantly lower levels of Ca and Vitamin D during the luteal phase
- Testing urine Ca and serum  $1,25(\text{OH})_2 \text{D}$  can help doctors monitor these micronutrients
- Reference ranges may not be appropriate

# Study Limitations / Next Steps

- There are few studies on just PMDD
- Limited sources on reference ranges
- Advocate for doctors to utilize lab testing for PMDD
- More research into reference ranges

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