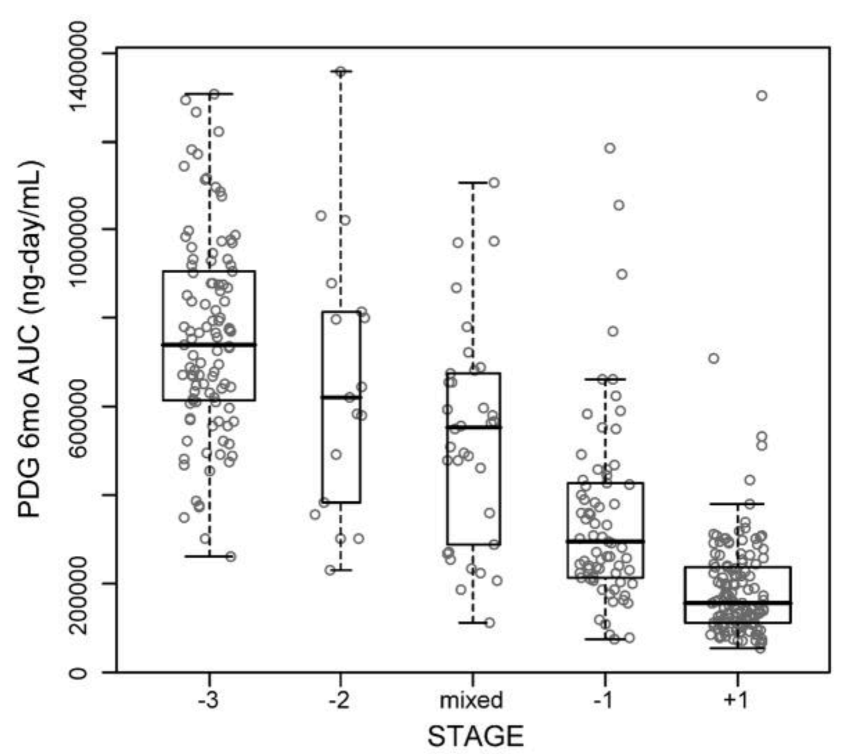
Identifying Hormone Patterns: Progesterone Decline During Menopausal Transition

Introduction:

The menopausal transition is a complex process that significantly impacts a woman's hormonal balance, particularly in relation to progesterone. As women age and approach menopause, progesterone levels naturally decline. This reduction in progesterone is primarily due to decreased luteal secretion and a decline in ovulation frequency. Understanding the physiological changes related to progesterone decline and the effects of unopposed estrogen can provide insights into the symptoms that affect women during this transition.

Progesterone levels in the luteal phase decline as women age (1, 7), and progress through menopause (8, 10). This decrease is attributed to two primary factors:



O'Connor KA, Ferrell R, Brindle E, Trumble B, Shofer J, Holman DJ, Weinstein M. Progesterone and ovulation across stages of the transition to menopause. Menopause. 2009 Nov-Dec;16(6):1178-87. doi: 10.1097/gme.0b013e3181aa192d. PMID: 19568209; PMCID: PMC2783957.

Factors Contributing to Progesterone Decline

Factor 1:

Reduced Luteal Secretion: The corpus luteum, a temporary gland formed after ovulation, becomes less efficient at producing progesterone (6, 12, 13).

Chart example #1 (50 female):

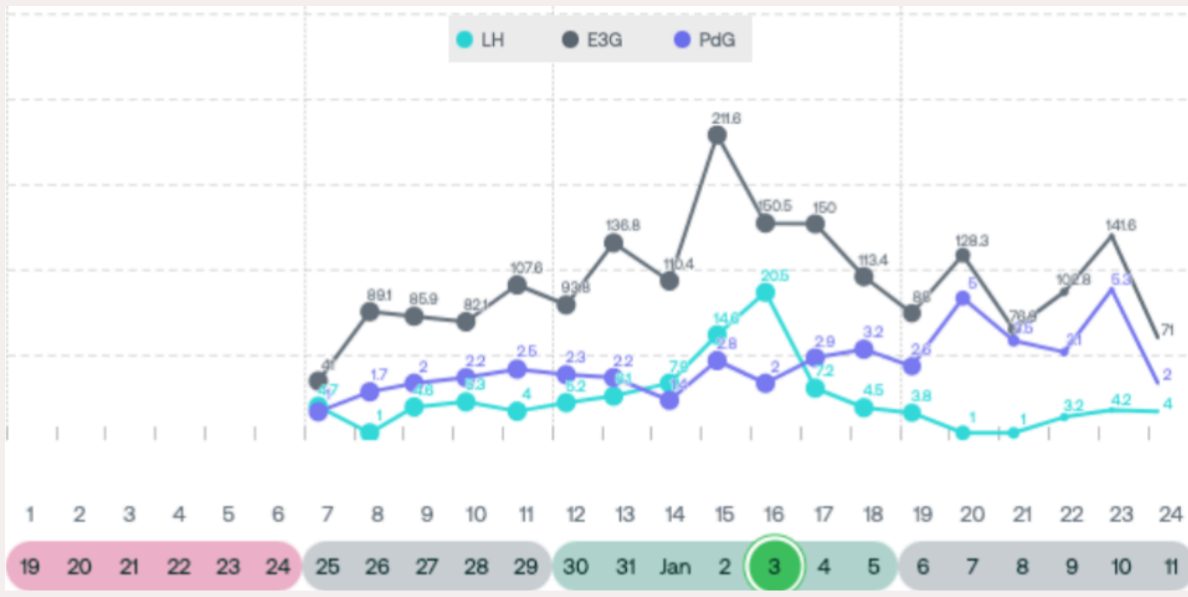


Chart example #1 (50 female)
Mira data discovered:
Low levels of PdG throughout the luteal phase with the highest value being 5.3
Short luteal phase

Chart example #2:

Chart example #2
Mira data discovered:
Low levels of PdG throughout the luteal phase with the highest value being 8.

Chart example #3 (39 female):

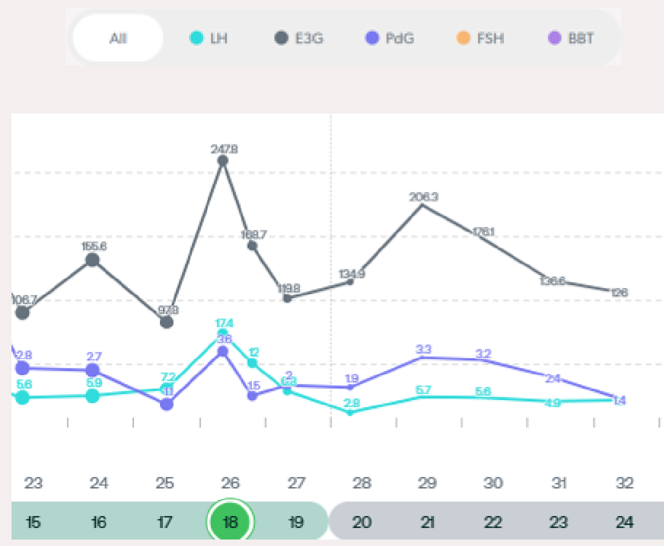


Chart example #3 (39 female)
Mira data discovered: Low levels of PdG

Chart example #4 (32 female)

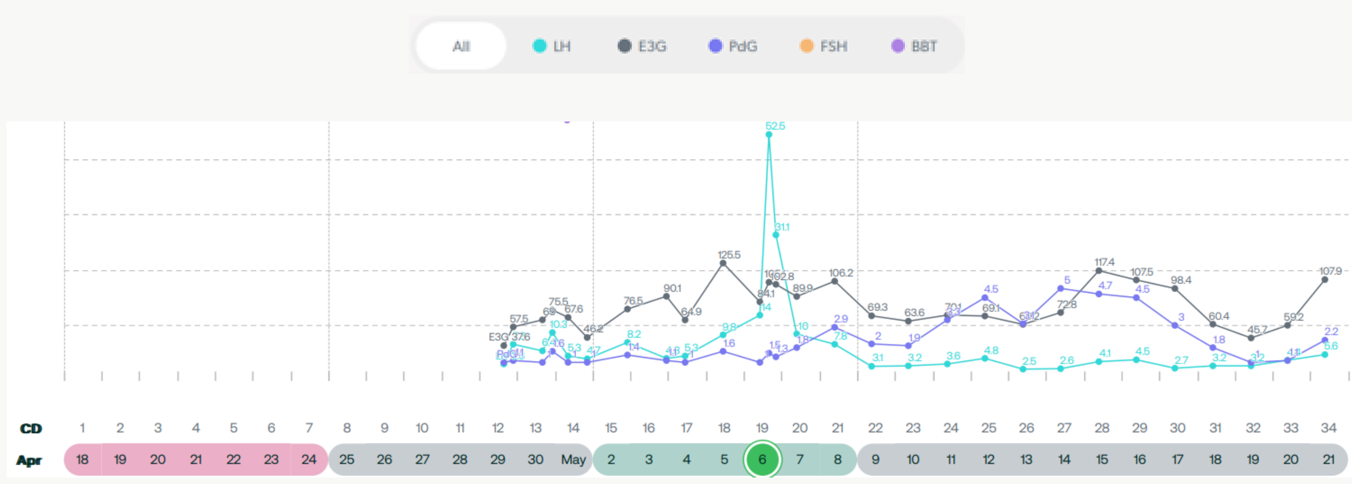


Chart example #4 (32 female)
Mira data discovered:
Low levels of PdG throughout the luteal phase with the highest value being 5

Chart example #5 (34 female):

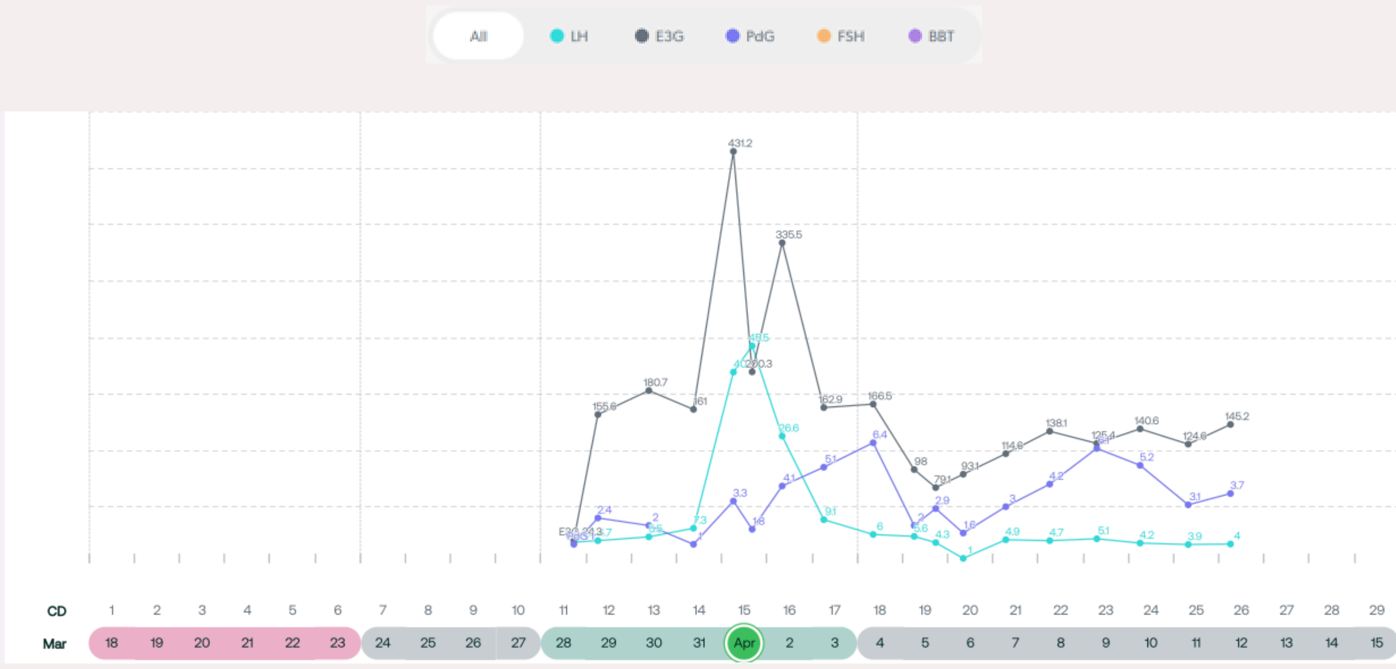
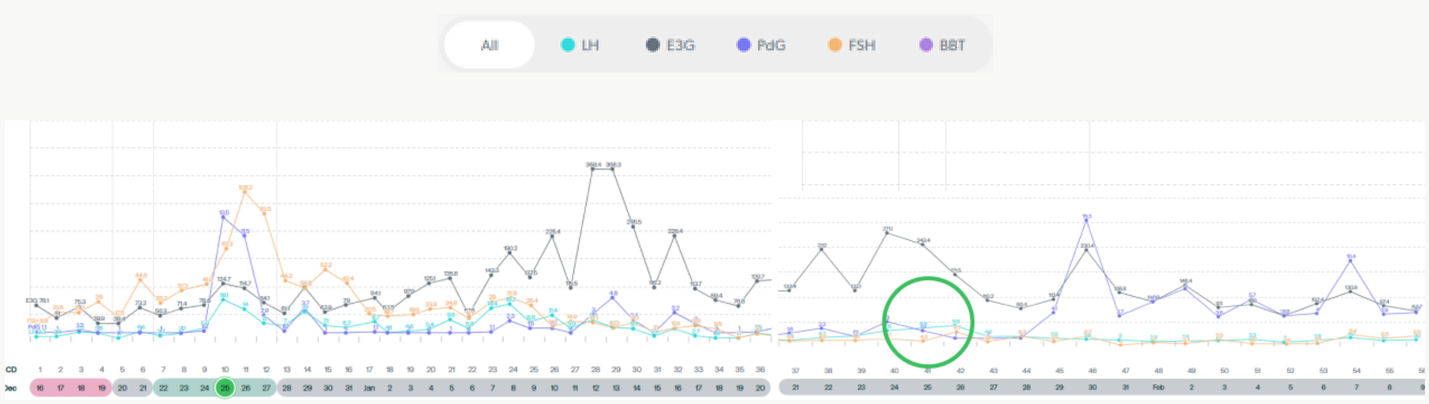


Chart example #5 (34 female)
Mira data discovered: Low levels of PdG

Chart example #6 (49F):



Patient # 6 (49F)
Mira Data Discovered:
Non-ovulatory LH surge on CD 10 and CD 11 (lack of PdG changes afterward)
Extended follicular phase
Small LH surge on CD 41 and 42
Small PdG changes after second LH surge suggests ovulatory event (period followed)

Factor 2:

Decreased Ovulation Frequency: With advancing age, there's a decline in the frequency of ovulation or an increase in anovulatory cycles (2, 3, 6, 8, 12). This contributes to lower progesterone levels as progesterone is primarily produced by the corpus luteum following ovulation.

- Disruptions in the hypothalamic-pituitary-ovarian (HPO) axis, which regulates ovulation, can occur during perimenopause (9) leading to the following situations:
    - Estradiol peaks without a corresponding LH surge (13).

Chart example # 1: Estradiol peaks without a corresponding LH surge

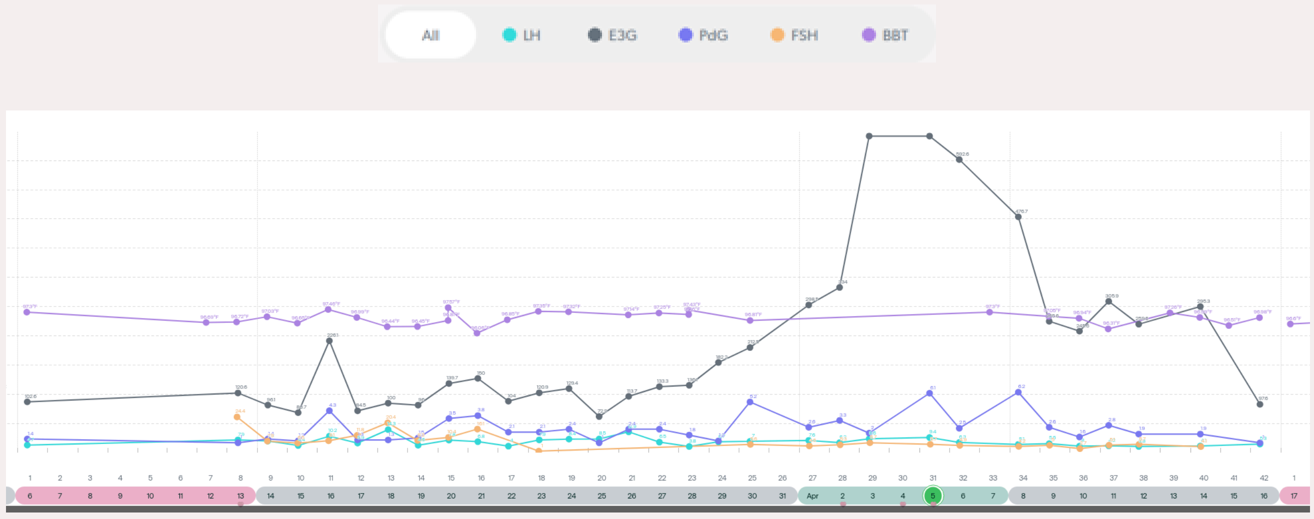


Chart example #1
Mira chart discovered:
Elevated E3G without corresponding LH surge
Lack of PdG changes
Anovulatory cycle

Chart example #2 (49 female): Estradiol peaks without a corresponding LH surge

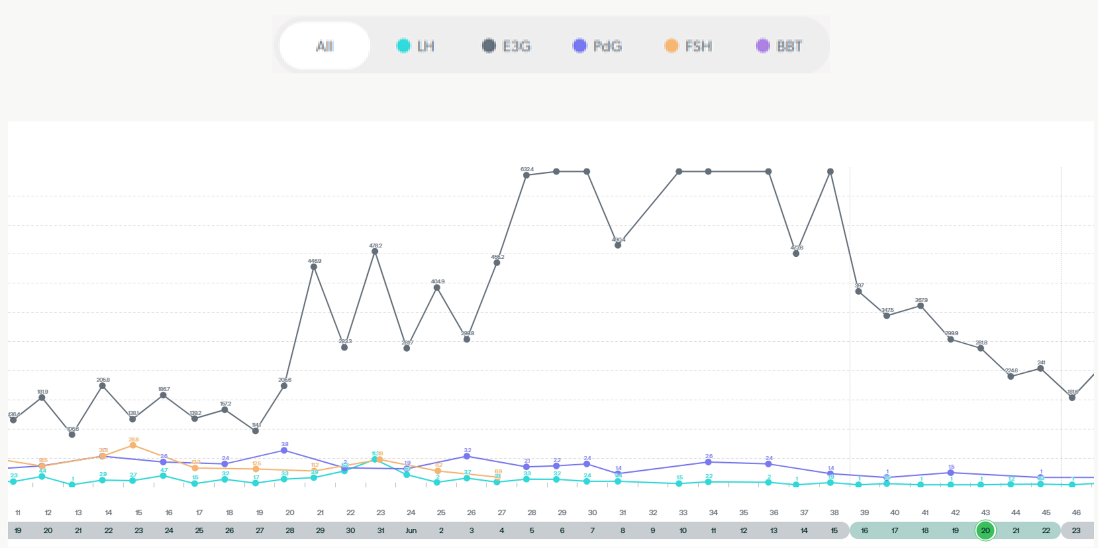


Chart example #2 (49 female) Mira data discovered:
Elevated E3G without corresponding LH surge
Lack of PdG changes
Anovulatory cycle

Chart example # 3 (45 female): Estradiol peaks without a corresponding LH surge

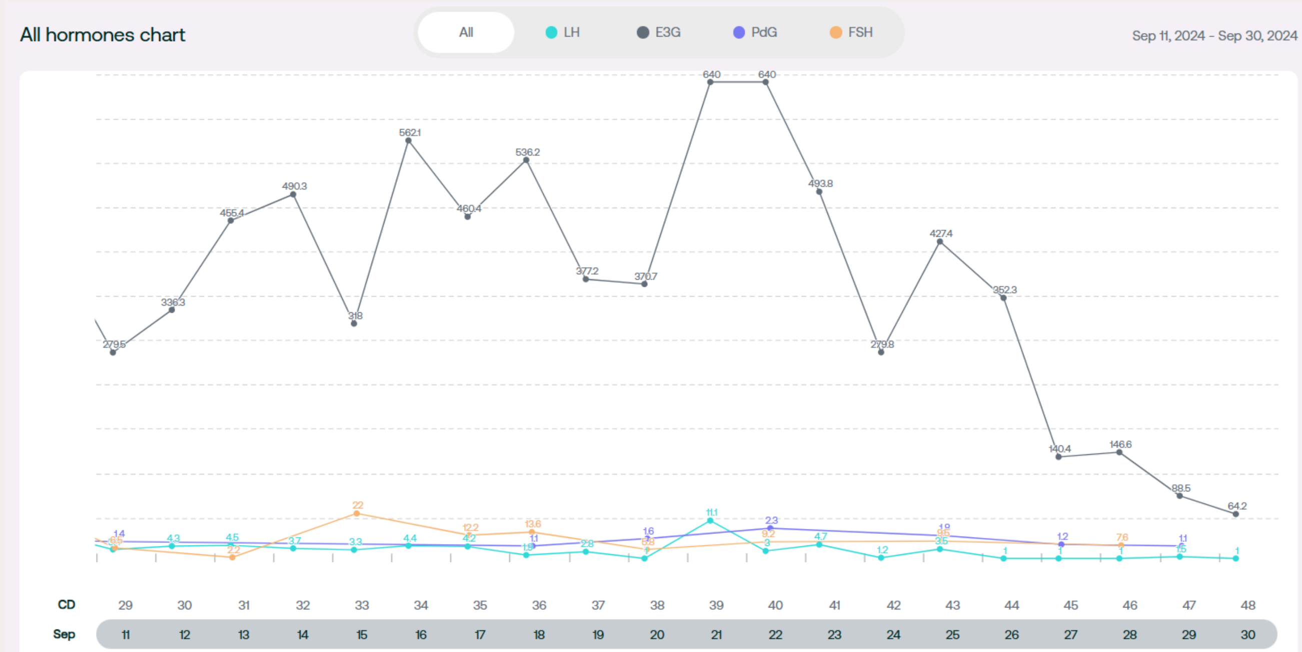


Chart example #3 (45 female) Mira data discovered:
Elevated E3G without corresponding LH surge
Lack of PdG changes
Anovulatory cycle

- Estradiol and LH peak levels without subsequent ovulation (13).

Chart example #1 (35 female): Estradiol and LH peak levels without subsequent ovulation

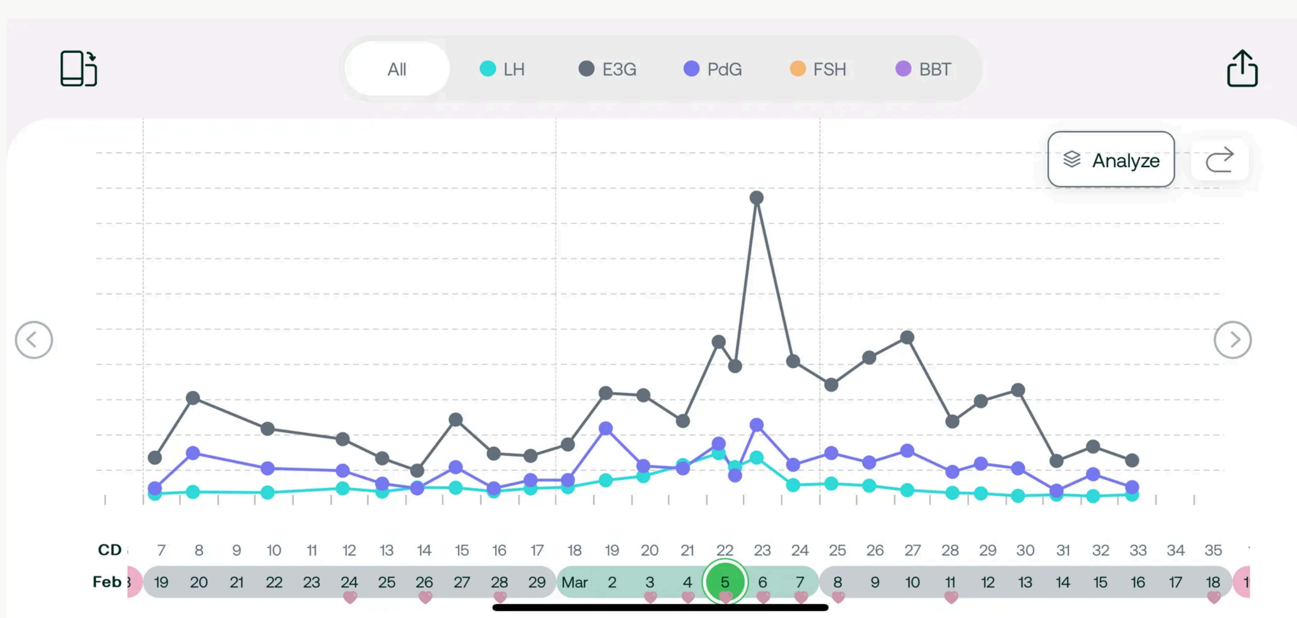


Chart example #1 (35 female)
Mira data discovered:
E3G changes with corresponding LH surge without subsequent ovulation (lack of rising PdG levels and absence of menstruation).

Chart example #2: Estradiol and LH peak levels without subsequent ovulation

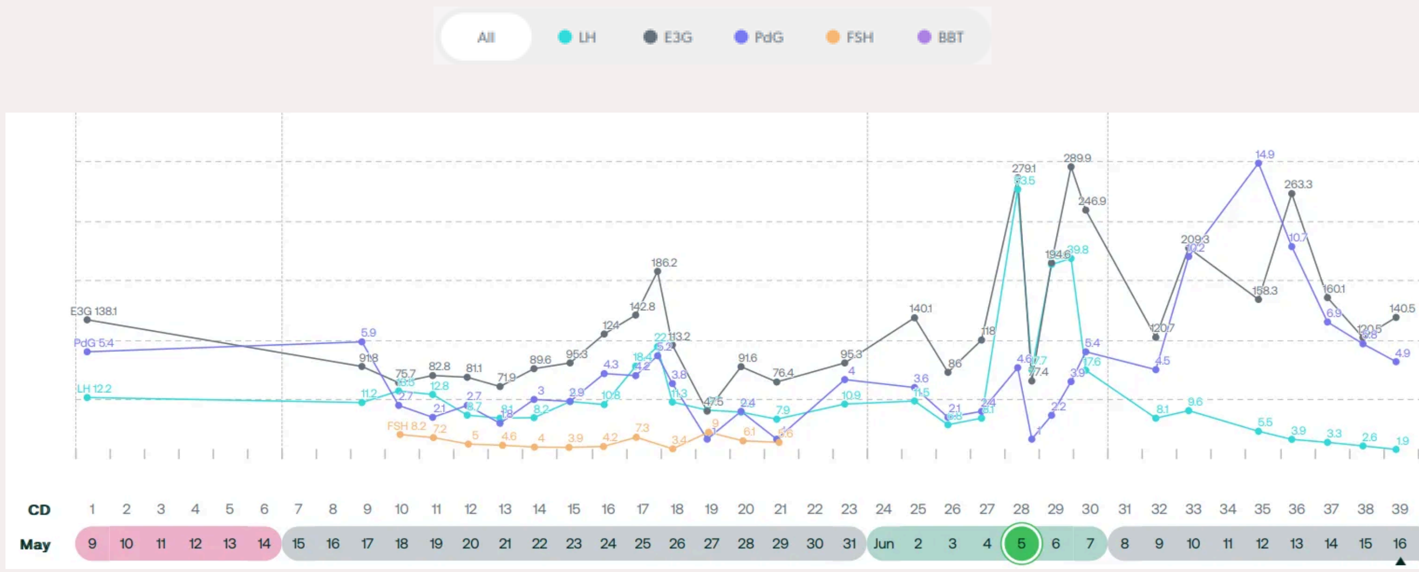


Chart example #2
Mira data discovered:
Coordinated rising E3G with corresponding LH surge on CD 17 without subsequent ovulation (lack of PdG).
Second rise of E3G with corresponding LH surge on CD 28-30 with subsequent ovulation (rising PdG pattern).

Chart example #3: Estradiol and LH peak levels without subsequent ovulation

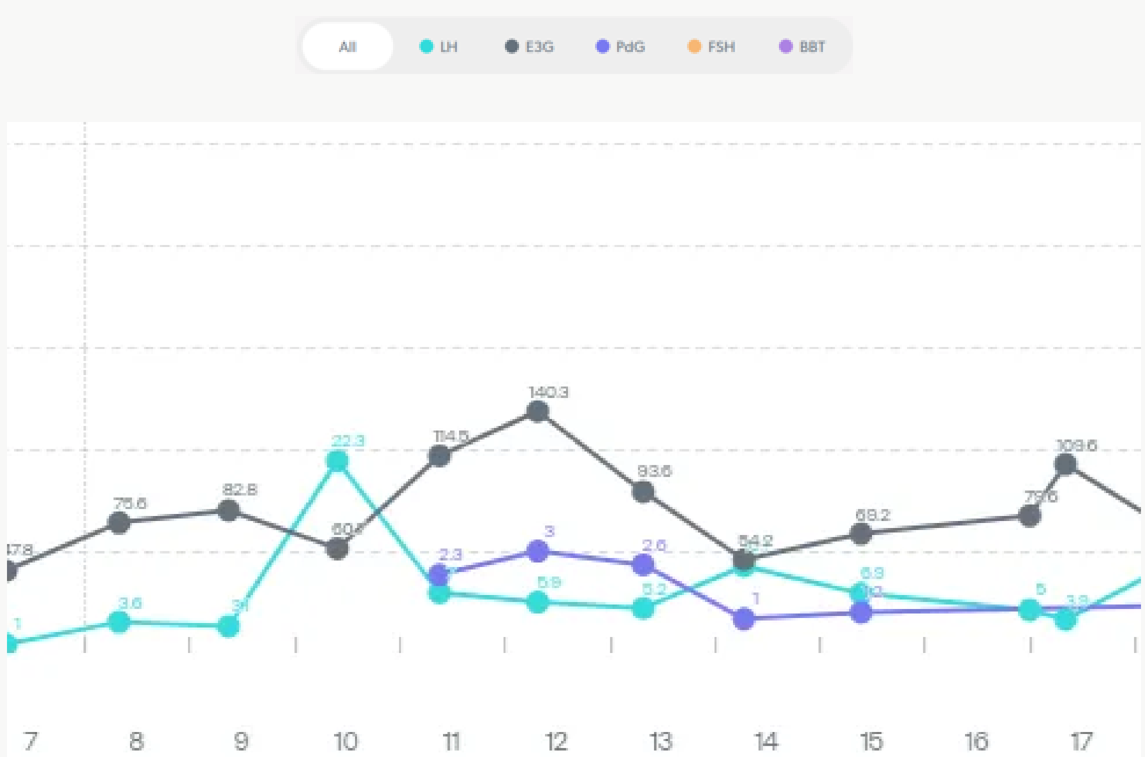


Chart example #3
Mira data discovered:
E3G changes with corresponding LH surge without subsequent ovulation (lack of rising PdG levels and absence of menstruation).

Chart example #4: Estradiol and LH peak levels without subsequent ovulation

Chart example #4
Mira data discovered:
Rising E3G with corresponding LH surge without subsequent ovulation

- LH surges without corresponding changes in estrogen levels or subsequent ovulation.

Chart example #1 (41 female): LH surges without corresponding changes in estrogen levels or subsequent ovulation

Chart example #1
Mira data discovered:
Lack of E3G rise prior to the LH surge.
LH surge on CD 42 without subsequent ovulation
Lack of PdG changes after LH surge and absence of menstruation

Symptoms associated with low progesterone

Low progesterone and/or unopposed estrogen, hormonal imbalances frequently observed during perimenopause with the most symptomatic women exhibiting higher estrogen and lower progesterone levels (9), can contribute to a range of physical and emotional health challenges.

1. **Mood Instability**: Variability in estradiol (E2) levels, especially when paired with low or absent progesterone (P4), is linked to increased depressive symptoms (4). Some studies suggest that women experience more depressive symptoms when estradiol levels are erratic and progesterone is low, which can occur during anovulatory cycles (4, 5). On the other hand, more stable moods tend to be present during ovulatory cycles when progesterone is higher (4).
2. **Heavy Menstrual Flow**: A hormonal imbalance of higher estradiol and lower progesterone levels can cause heavy menstrual bleeding during perimenopause (5). The absence of sufficient progesterone to balance

estradiol contributes to this issue.

3. **Physical Symptoms**: Erratic estradiol levels during perimenopause can lead to symptoms such as bloating and breast tenderness, as well as other common physical discomforts (7).
4. **Lower Resilience and Increased Stress**: Women with lower progesterone levels tend to report higher levels of stress, lower life satisfaction, and more depressive symptoms, regardless of whether they are early or late in perimenopause. Higher progesterone levels seem to confer better mood stability and resilience (11).

Unopposed estrogen with insufficient progesterone can lead to significant mood changes, heavy periods, and other physical symptoms, with progesterone playing a key role in maintaining resilience and minimizing these effects.

Conclusions:

In summary, the decline in progesterone during the menopausal transition, combined with unopposed estrogen, significantly impacts women's health and well-being. Reduced luteal secretion and decreased ovulation frequency lead to hormonal imbalances that contribute to a variety of symptoms, including mood instability, heavy menstrual flow, and physical discomfort. The evidence suggests that women with lower progesterone levels are more likely to experience higher stress levels, lower resilience, and increased depressive symptoms. On the other hand, maintaining more stable progesterone levels, particularly during ovulatory cycles, may help mitigate these effects. Understanding the role of progesterone in perimenopause and menopause is essential for managing symptoms and improving quality of life during this transitional phase.

References

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