

The Relationship Between Estradiol and FSH During the Perimenopausal Transition

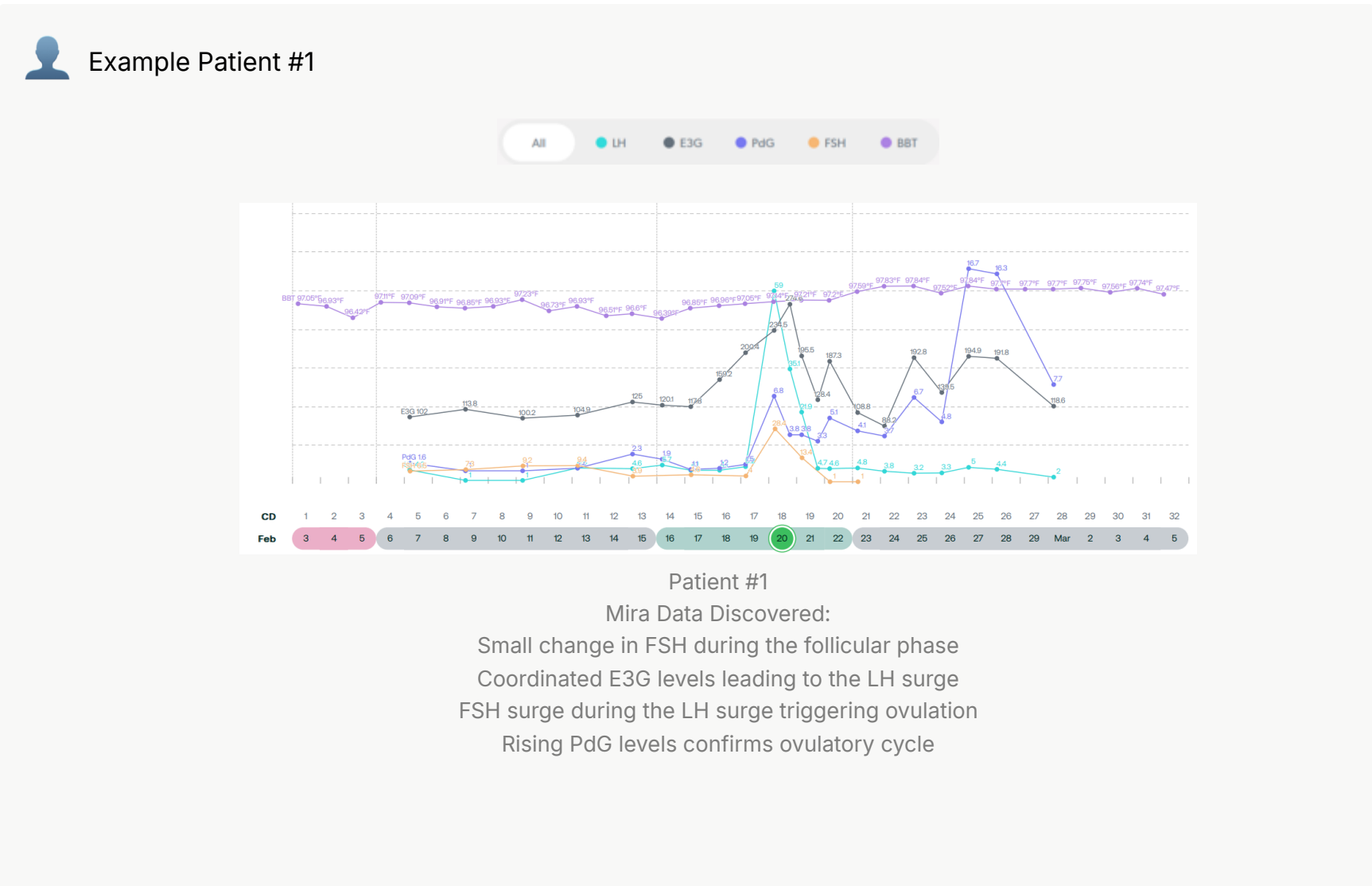
Assessing hormonal levels during perimenopause using a single measurement of FSH and estradiol can be unreliable due to the natural variability of these hormones and their complex interactions. The normal physiological feedback between estradiol and FSH involves FSH stimulating ovarian follicle development and estradiol production, while elevated estradiol levels exert negative feedback on FSH secretion. FSH levels are expected to rise as ovarian function declines. Menstrual cycles during this transition can vary significantly, being either ovulatory or anovulatory, with each exhibiting variable hormonal patterns, including very short or very long cycles. These fluctuations make interpreting hormonal data challenging, as the hormonal profile varies depending on the type of cycle. Hormonal data should always be reviewed within the clinical context, considering the patient's background, medical history, available diagnostics, and presenting symptoms to ensure accurate interpretation and appropriate management.

The following key factors highlight the key hormonal changes and their impact on accurate assessment during this transition.

1. Hormonal Changes in Different Cycle Types

During perimenopause, menstrual cycles can vary widely and may be either ovulatory or anovulatory. These variations complicate the interpretation of hormonal data, as both cycle types present different hormonal patterns. Below is an overview of hormonal changes in each cycle type.

- Ovulatory Cycles:** In ovulatory cycles, FSH levels typically show minimal fluctuations (1). There is a slight increase in FSH at the beginning of the cycle, at the end of the previous cycle, and a surge that coincides with the LH surge. These patterns are relatively stable and consistent. Individuals with elevated or variable FSH levels may still experience an ovulatory cycle; however, the egg may not be compatible with fertilization and conception.





Example Patient #2 (43F) Ovulatory cycle with Normal FSH Levels



Patient #2 (43F)

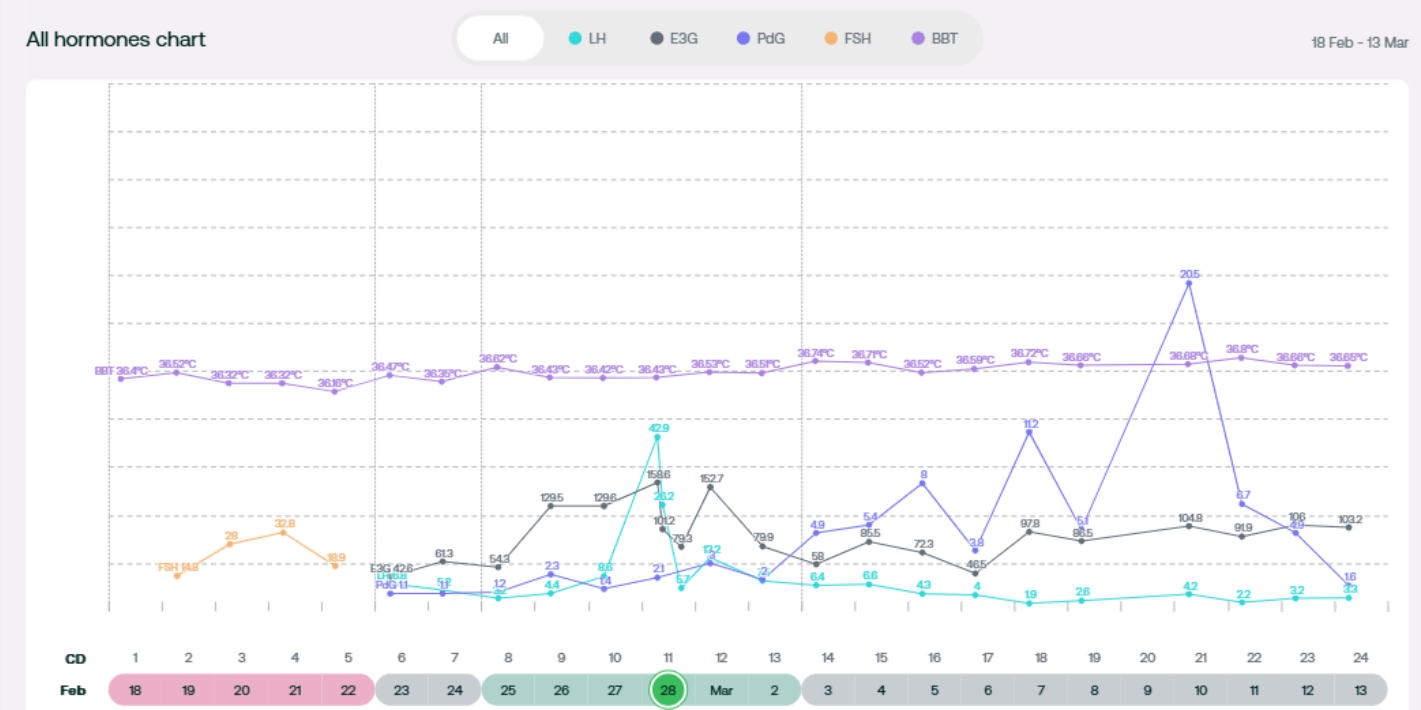
Mira Data Discovered:

Small FSH change on CD 4

Coordinated E3G levels leading to the LH surge on CD 10

Rising PdG levels confirms ovulatory cycle

Same Patient #2 (43F) Continued Ovulatory Cycle with Elevated FSH Levels



Same patient #2 (43F)

Mira Data Discovered:

Higher FSH on CD 2-5

Coordinated but lower E3G levels leading to the LH surge on CD 11

Rising PdG levels confirm ovulatory cycle

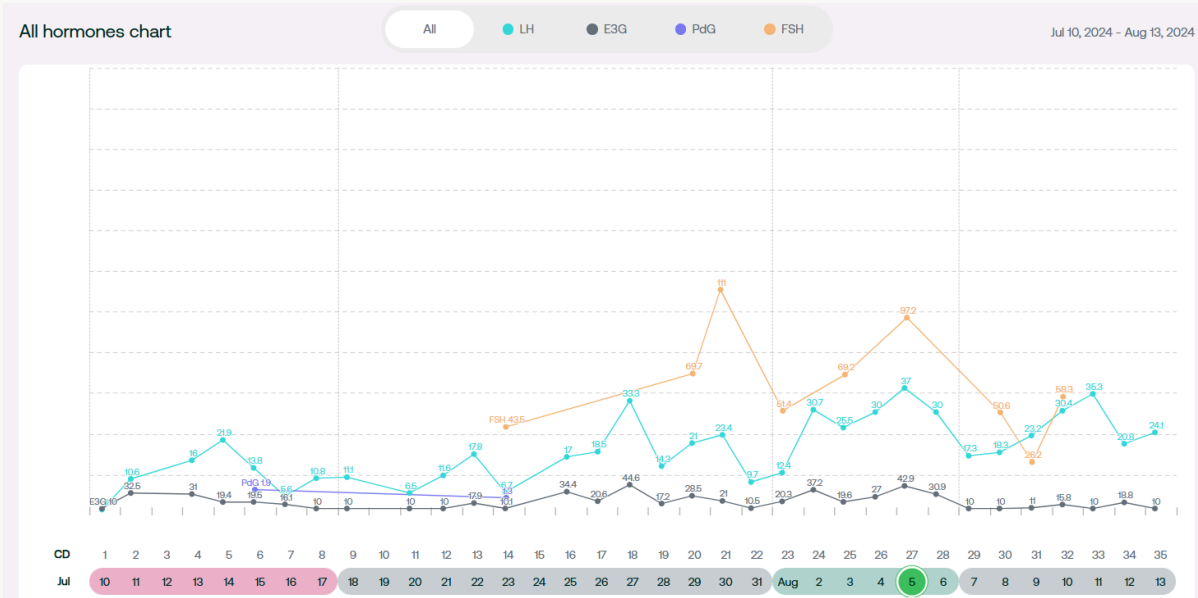
May represent a more suboptimal ovulation than previous cycle

- Anovulatory Cycles:** Anovulatory cycles, which become more prevalent in the 30 months preceding menopause (1), add complexity to hormonal assessments. Some studies have associated anovulatory cycles with low inhibin B, elevated FSH, and decreased estradiol (E2) levels (1). However, other research suggests that while circulating estrogen is generally low during anovulatory cycles, it is possible for a woman to experience cycles that are ovulatory, anovulatory with relatively high estrogen, or anovulatory with low

estrogen (5). Elevated estradiol can also suppress FSH levels (2), further contributing to the fluctuation of FSH from cycle to cycle.



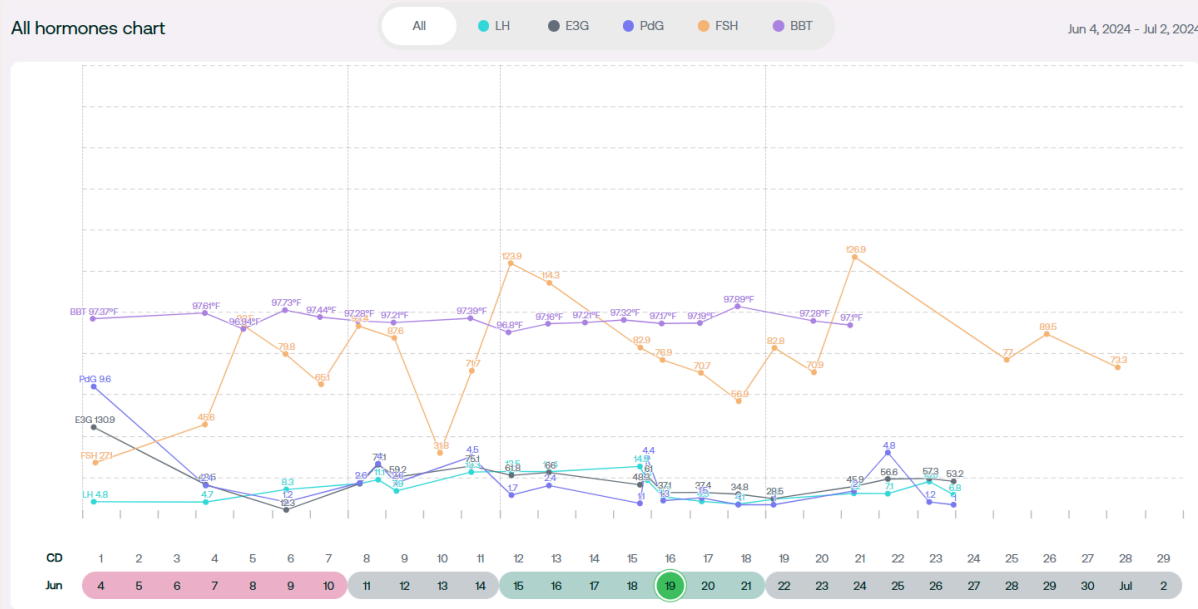
Example Patient #3 (45F): Anovulatory Cycle with Hormonal Imbalance



Patient #3 (45F):
Mira Data Discovered:
Baseline elevated LH
Consistently elevated FSH levels
Low E3G
Anovulatory cycle



Example Patient #4 (43F): Anovulatory Cycle with Elevated FSH and Low E3G



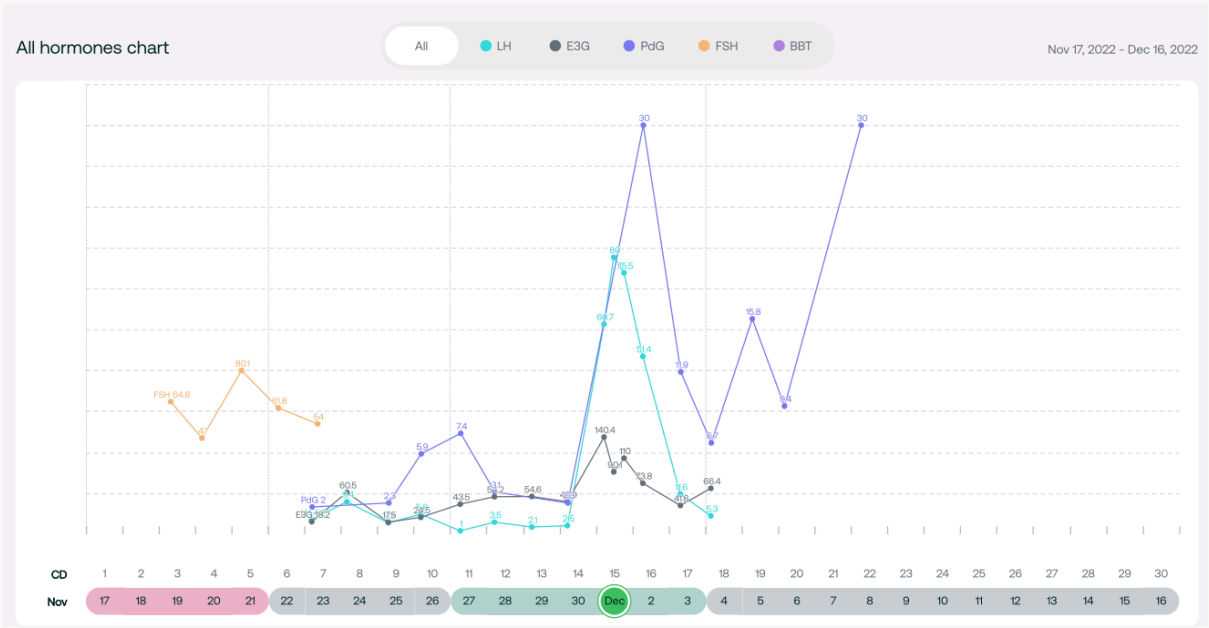
Patient #4 (43F):
Mira Data Discovered:
Consistently elevated FSH
Low E3G levels
Lack of hormone coordinated
Anovulatory cycle

2. FSH Fluctuations

Although FSH levels rise as ovarian function declines, they can vary significantly between cycles in an individual woman. Studies have shown that only 60% of women with initially elevated FSH levels during IVF treatment exhibit persistently elevated levels in subsequent cycles (3). Therefore, a single elevated FSH level should not be solely relied upon to diagnose or treat perimenopause.

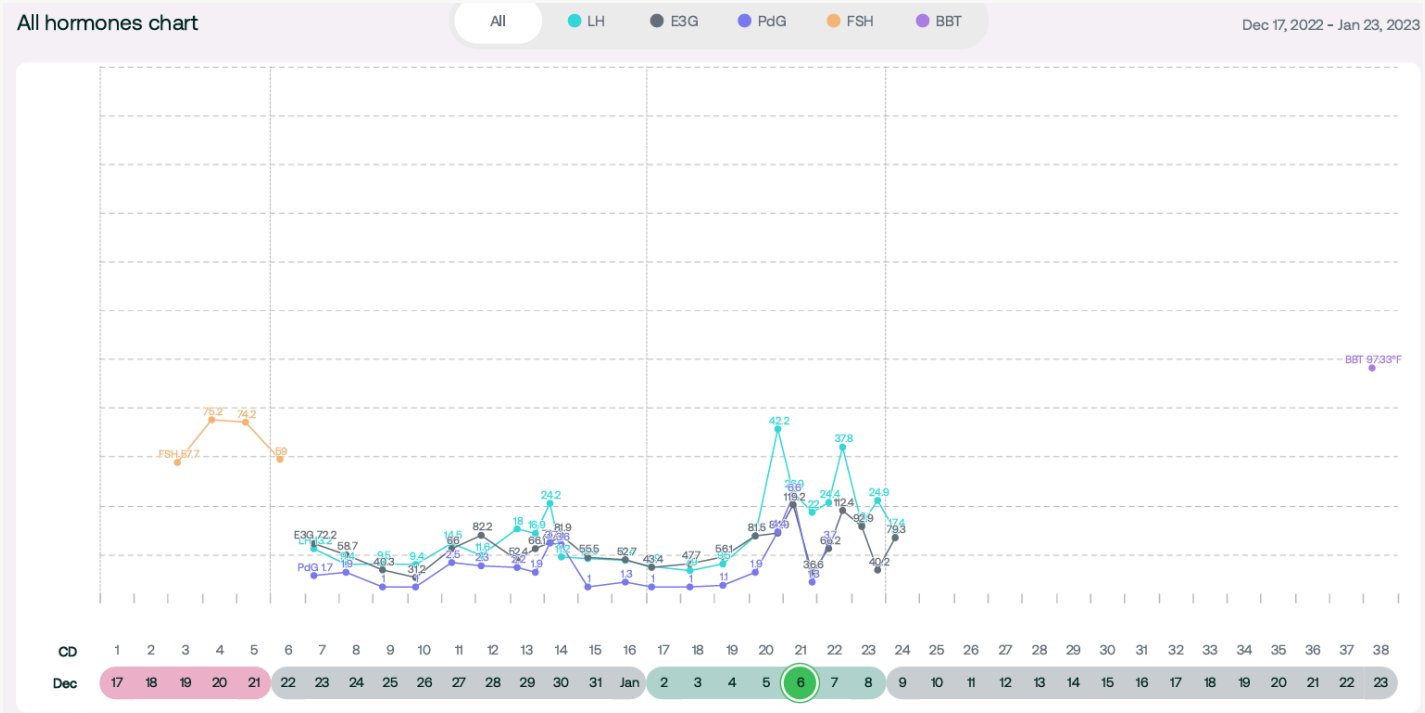


Example Patient #5 (44F): Ovulatory Cycle with Elevated FSH
Nov/Dec 2022



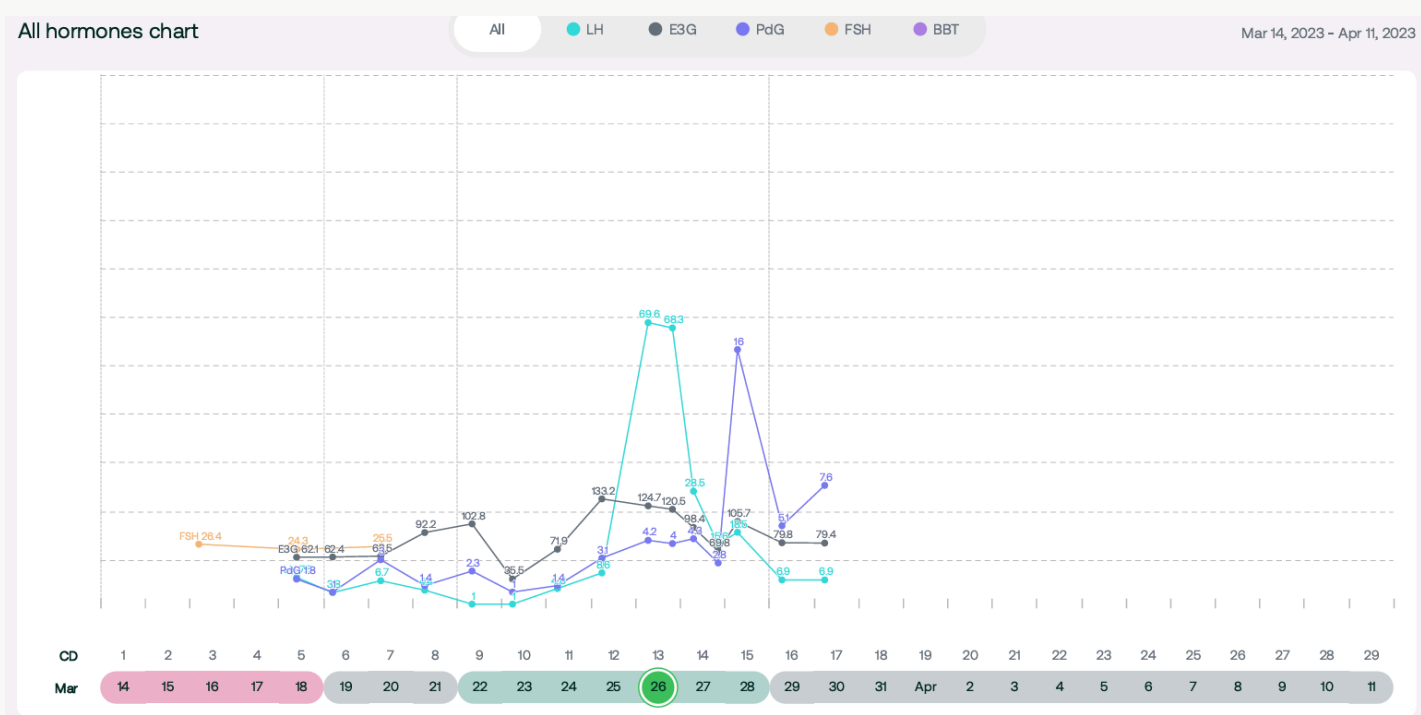
Patient #5 (44F)
Mira Data Discovered:
Elevated FSH levels on CD 3-7
Minimal E3G changes but coordinated with an LH surge
PdG changes after LH surge
Ovulatory cycle

Same patient #5 (44F): Suspected Anovulatory Cycle with Hormone Imbalances
Dec 2022-Jan 2023



Patient #5 (44F)
Mira Data Discovered:
Elevated FSH levels on CD 3-6
Consistently elevated baseline LH with two LH surges
Generally low E3G with some coordination with second rise in LH.
Suspected anovulatory cycle

Same patient #5 (44F): Ovulatory Cycle with Elevated FSH
March- April 2023



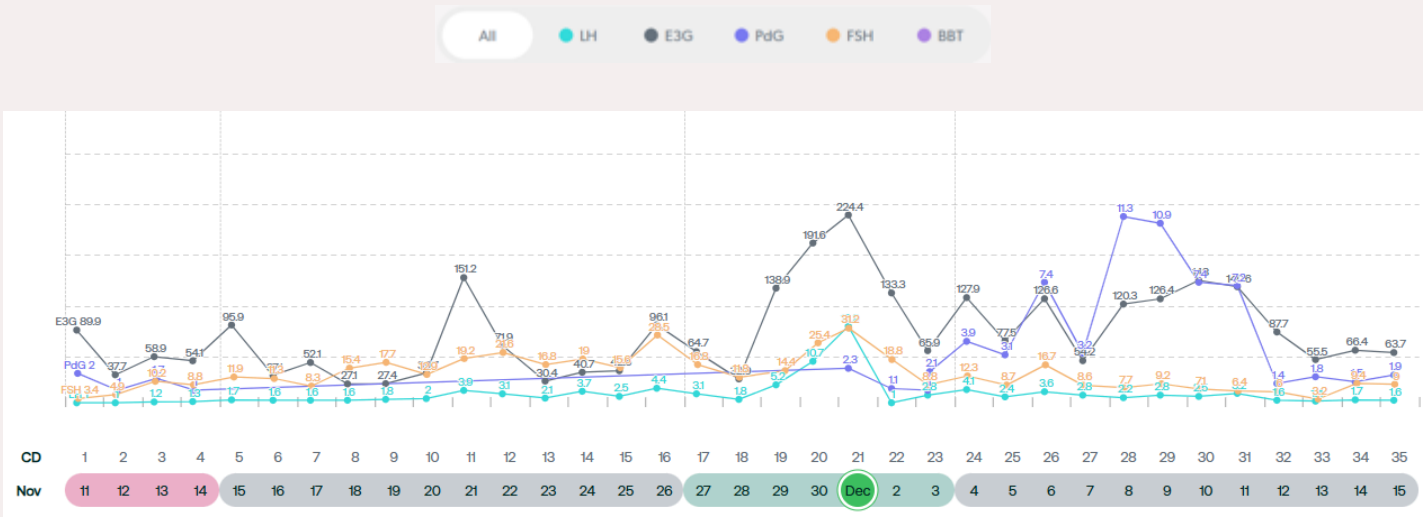
Patient #5 (44F)
Mira Data Discovered:
Elevated FSH on CD 3, CD 5, and CD 7 but lower than Nov and Dec cycles.
Generally low E3G with coordinated changes leading to LH surge
LH surge on CD 13 and CD 14
PdG changes after LH surge
Ovulatory cycle

Cycle summary patient #5 (44F):

Her cycles progressed from ovulatory to anovulatory and back to ovulatory, with varying degrees of elevation in FSH levels.

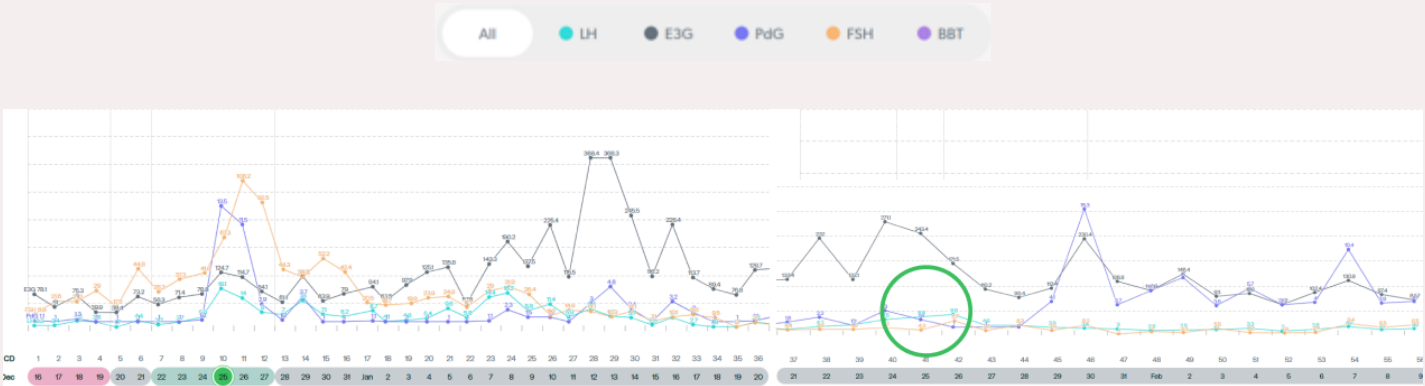


Patient example #6 (49F): Ovulatory Cycle with Mid-Cycle Elevated FSH
Nov/Dec 2024



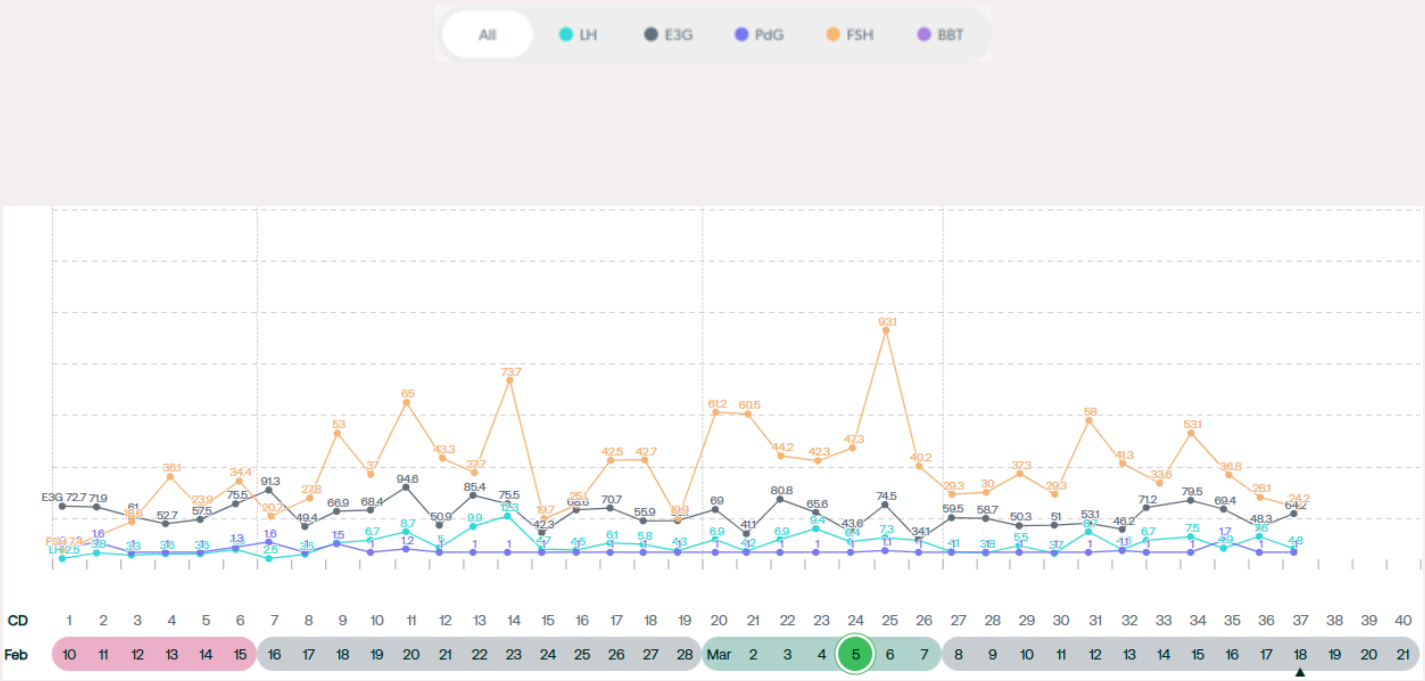
Patient #6 (49F)
Mira Data Discovered:
Mid-cycle elevated FSH levels
Coordinated E3G levels leading to an LH surge
LH surge on CD 20 and CD 21
Rising PdG levels confirm ovulatory cycle

Same patient #6 (49F): Suspected Ovulatory Cycle with Hormone Imbalances
Dec/Jan/Feb 2025



Patient # 6 (49F)
Mira Data Discovered:
Elevated FSH levels
Non-ovulatory LH surge coordinated with significantly elevated FSH on CD 10 and CD 11
Extended follicular phase
FSH levels lower as E3G rises
Small LH surge on CD 41 and 42
PdG changes after second LH surge suggests ovulatory event (period followed)

Same patient #6 (49F): Anovulatory Pattern with Elevated FSH
Feb/March 2025



Patient #6 (49F)
Mira Data Discovered:
Significantly elevated FSH compared to two previous cycles
Minimal E3G changes
Lack of PdG changes
Anovulatory pattern

Cycle summary patient #6 (49F):

Cycle 1 (Nov/Dec): ovulatory cycle with some FSH changes, coordinated E3G with an LH surge, followed by PdG changes.

Cycle 2 (Dec/Jan/Feb): ovulatory cycle with non-ovulatory event at the beginning of the cycle, extended follicular phase, PdG changes after small LH surge suggest an ovulatory event.

Cycle 3 (Feb/March): Significant FSH changes, minimal E3G, and lack of hormone coordination, currently anovulatory.

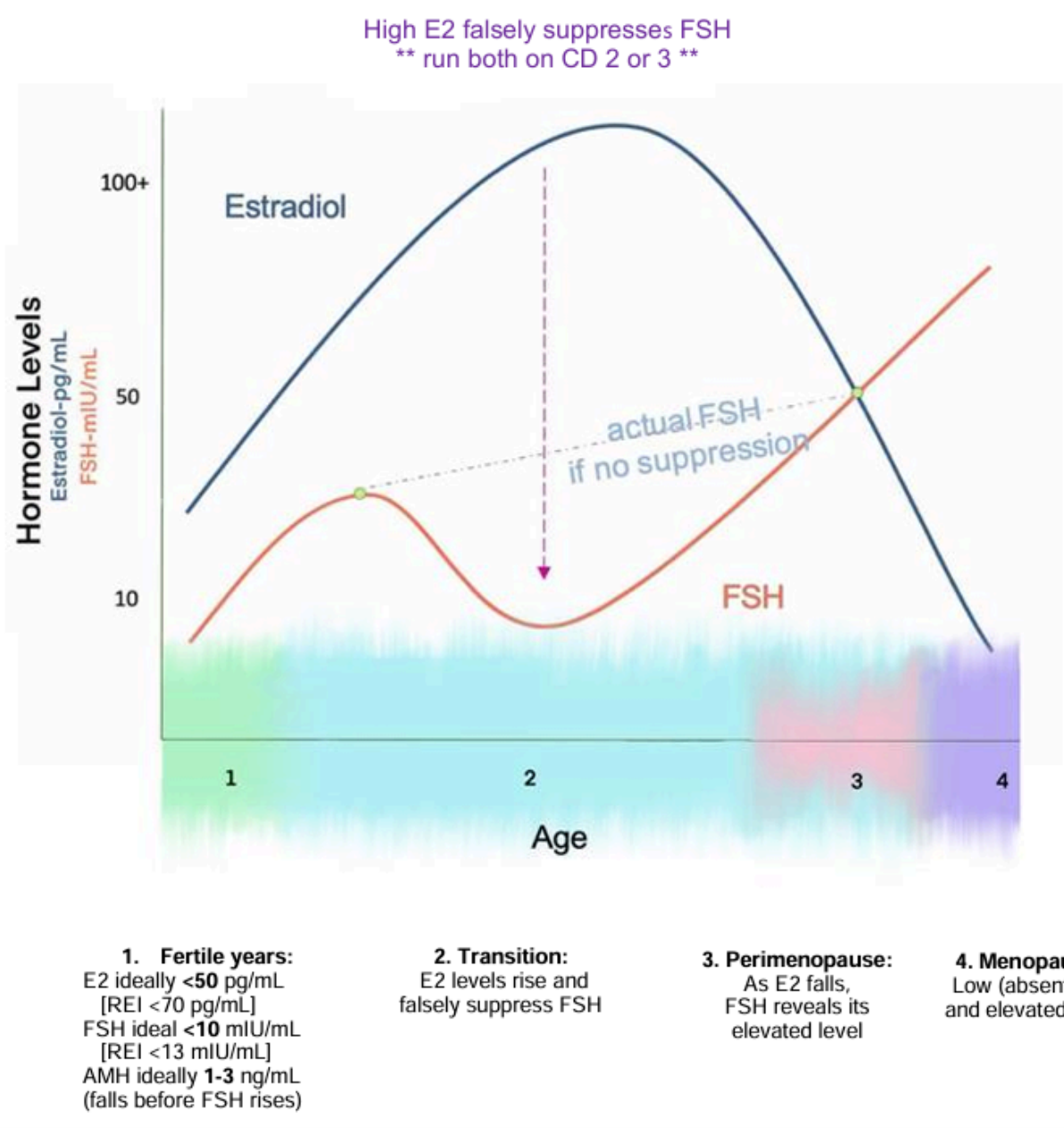
In summary, her cycles demonstrate a progression from an ovulatory cycle with hormonal coordination (Cycle 1), to an extended follicular phase with a non-ovulatory event (Cycle 2), and finally to a current anovulatory cycle with significant FSH changes and minimal hormone coordination (Cycle 3).

3. Estradiol's Effect on FSH Readings

Elevated estradiol levels can suppress FSH readings (2) due to the physiological feedback mechanism in which estradiol exerts negative feedback on FSH secretion. This suppression may result in normal FSH levels despite underlying ovarian insufficiency, emphasizing the importance of measuring both FSH and estradiol across multiple cycles. Ideally, testing should be done on cycle day 2 or day 3 in cycling women, with an acceptable testing range from cycle day 1 to day 5. It is essential to consider the patient’s background, medical history, available diagnostics, and presenting symptoms for a comprehensive evaluation.

Relationship between Estradiol and FSH
Across a Hormonal Lifespan

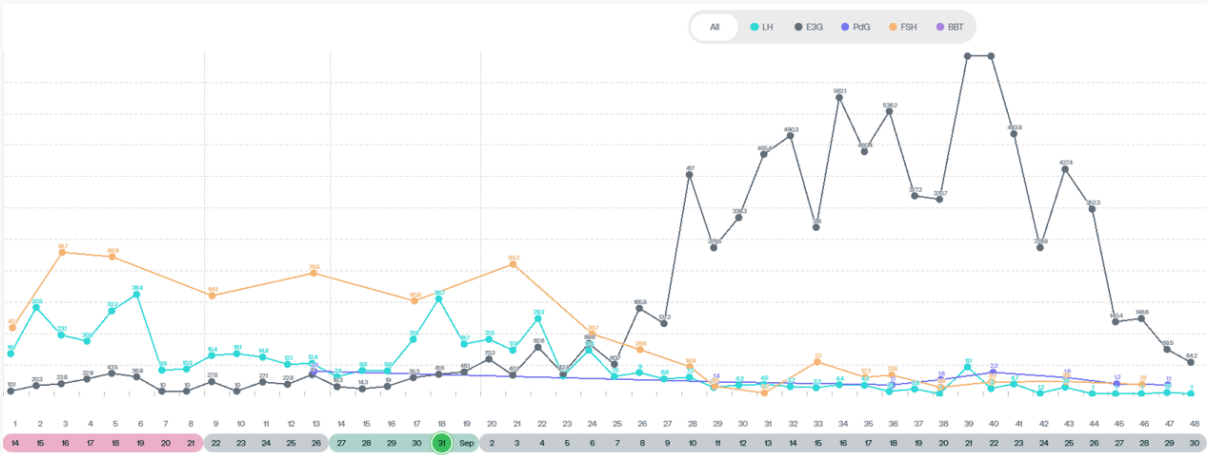
By Stefani K. Hayes, ND, LAc



Relationship Between FSH and Estradiol Across a Hormonal Lifespan
Video explanation with Dr. Stefani Hayes:
[Click here to watch](#)



Example Patient # 7 (45F): Anovulatory Pattern with Hormone Imbalances



Patient # 7 (45F)
Mira Data Discovered:
Initially elevated FSH levels but as E3G rises FSH is suppressed



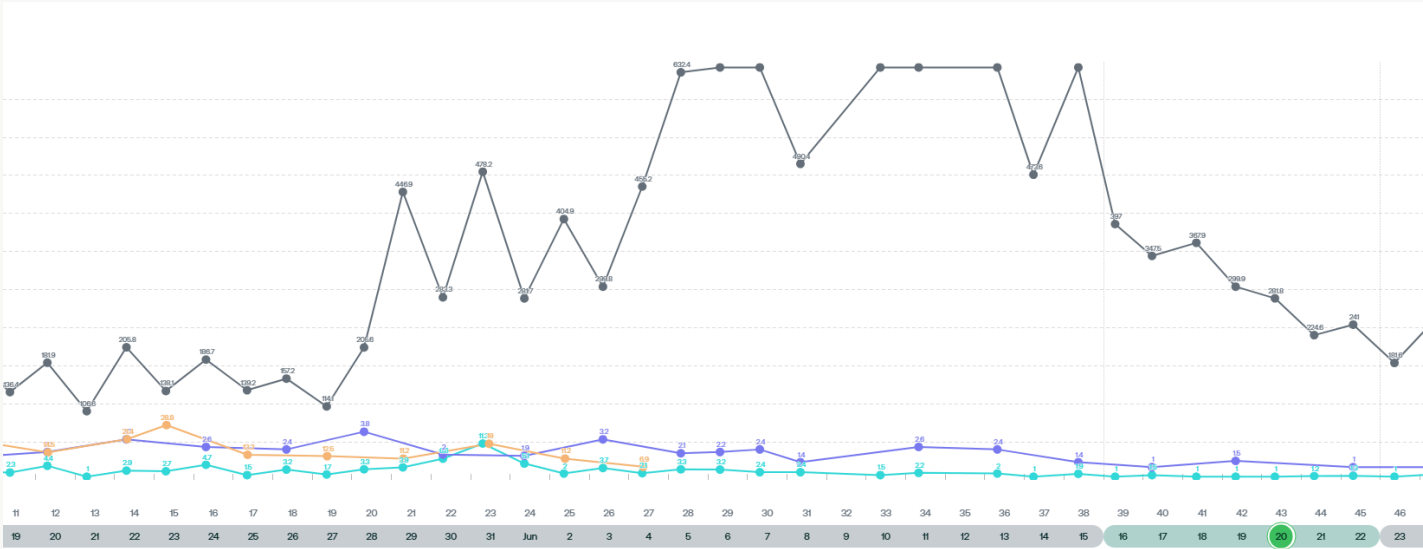
Example Patient #8 (43F): Anovulatory Pattern with Hormone Imbalances



Patient #8 (43F)
Mira Data Discovered:
Initially elevated FSH levels but as E3G rises FSH is suppressed



Example Patient #9 (49F): Anovulatory Pattern with Hormone Imbalances



Patient #9 (49F)
Mira Data Discovered:
Initially elevated FSH levels but as E3G rises FSH is suppressed

4. Impact of Estrogen Treatment on FSH

Estrogen treatment can suppress FSH levels due to the physiological feedback mechanism, leading to misleading results. A 2024 study examined the effects of estrogen pretreatment in patients with diminished ovarian reserve. Researchers found that administering 4 mg/day of 17β-estradiol effectively suppressed premature FSH elevation, improving ovarian response during fertility treatments (4). Therefore, a decrease in FSH levels after starting estradiol therapy can be normal and should be considered when reviewing FSH levels.

Summary:

FSH and estradiol levels fluctuate significantly during perimenopause, making single measurements unreliable for assessment. The feedback mechanism between estradiol and FSH, along with the potential influence of estrogen therapy on readings and cycle variability, can complicate the interpretation of results. Tracking hormone patterns over time provides a clearer picture, helping to distinguish between ovulatory and anovulatory cycles and guide more accurate treatment decisions.



Key takeaways:

1. Hormonal Changes in Different Cycle Types

- Typically, **ovulatory cycles** show stable FSH patterns with coordinated hormone fluctuations.
- **Anovulatory cycles**, more common before menopause, can present elevated FSH, low estradiol, or high estradiol suppressing FSH.
- These variations complicate hormonal assessments.

2. FSH Fluctuations

- FSH levels vary significantly between cycles.
- A single elevated FSH reading does not reliably indicate perimenopause.

3. FSH and Estradiol Feedback Mechanism:

- Elevated estradiol can suppress FSH, leading to misleadingly normal FSH levels despite ovarian insufficiency.
- Tracking both hormones together, ideally at the beginning of the cycle, provides a clearer and more accurate assessment.

4. Effect of Estrogen Treatment on FSH

- Estrogen therapy can lower FSH levels.
- Research shows that estradiol pretreatment can suppress premature FSH elevation and improve ovarian response, a method typically administered in fertility settings by a fertility specialist.

Tracking hormone patterns over time with Mira, in collaboration with the patient's background, medical history, available diagnostics, and presenting symptoms, provides providers with a more accurate understanding of perimenopausal changes, enabling them to tailor treatments effectively and ensure appropriate management.

References:

1. Burger HG, Hale GE, Dennerstein L, Robertson DM. Cycle and hormone changes during perimenopause: the key role of ovarian function. *Menopause*. 2008 Jul-Aug;15(4 Pt 1):603-12. doi: 10.1097/gme.0b013e318174ea4d. PMID: 18574431.
2. Deadmond, A., Koch, C. A., & Parry, J. P. (2022). *Ovarian reserve testing*. In K. R. Feingold, B. Anawalt, M. R. Blackman, et al. (Eds.), *Endotext*. MDText.com, Inc. <https://www.ncbi.nlm.nih.gov/books/NBK279058/>

3. Frazier, L. M., Grainger, D. A., Schieve, L. A., & Toner, J. P. (2004). Follicle-stimulating hormone and estradiol levels independently predict the success of assisted reproductive technology treatment. *Fertility and Sterility*, 82(4), 834-840. <https://doi.org/10.1016/j.fertnstert.2004.02.144>
4. Lin, L., Chen, G. & Liu, Y. Value of estrogen pretreatment in patients with diminished ovarian reserve and elevated FSH on a long antagonist regimen: a retrospective controlled study. *J Ovarian Res* 17, 114 (2024). <https://doi.org/10.1186/s13048-024-01415-2>
5. Santoro, N. (2016). Perimenopause: From Research to Practice. *Journal of Women's Health*, 25(4), 332. <https://doi.org/10.1089/jwh.2015.5556>

Additional resources provided by Dr. Stefani Hayes:

Related to FSH being falsely suppressed by elevated Estradiol levels.

- Lin, L., Chen, G. & Liu, Y. Value of estrogen pretreatment in patients with diminished ovarian reserve and elevated FSH on a long antagonist regimen: a retrospective controlled study. *J Ovarian Res* 17, 114 (2024). <https://doi.org/10.1186/s13048-024-01415-2>

Related to the fact that estradiol rises before it falls in DOR/perimenopause

- Allshouse A, Pavlovic J, Santoro N. Menstrual Cycle Hormone Changes Associated with Reproductive Aging and How They May Relate to Symptoms. *Obstet Gynecol Clin North Am*. 2018 Dec;45(4):613-628. doi: 10.1016/j.ogc.2018.07.004. Epub 2018 Oct 25. PMID: 30401546; PMCID: PMC6226272.
- Importance of testing FSH and Estradiol together at the beginning of cycle ● ASRM guidelines: https://www.asrm.org/globalassets/_asrm/practice-guidance/practice-guidelines/pdf/best-practices_of_asrm_and_eshre.pdf
- Licciardi, F.L. et al. Day 3 estradiol serum concentrations as prognosticators of ovarian stimulation response and pregnancy outcome in patients undergoing in vitro fertilization. *Fertil Steril*. 1995. 64(5) 991-94.
- Souter, I. et al. The prognostic significance of an elevated Day-3 FSH in young women (<35) undergoing in-vitro fertilization (IVF). *Fertil Steril*. 2012. 97(3). S13.
- Luisi, S et al. 2015. "Premature ovarian insufficiency: from pathogenesis to clinical management". *J Endocrinol Invest*. 38: 597-603.

Related to ideal FSH and Estradiol ranges (FSH <10 [ideal] or 15 [REI]; Estradiol <50 [Ideal] or 70 [REI])

- Toner, J. Modest follicle-stimulating hormone elevations in younger women: warn but don't disqualify. 2004. *Fertil Steril* 81(6). 1493-95.
- Souter, I. et al. The prognostic significance of an elevated Day-3 FSH in young women (<35) undergoing in-vitro fertilization (IVF). *Fertil Steril*. 2012. 97(3). S13.
- ESHRE (Guideline of the European Society of Human Reproduction and Embryology). 2024 "Management of women with premature ovarian insufficiency". POI Guideline Development Group.
- Atasever, M. et al. Diminished ovarian reserve: is it a neglected cause in the assessment of recurrent miscarriage? A cohort study. *Fert and Steril*. January 2016. 105(5):1236-1240
- Licciardi, F.L. et al. Day 3 estradiol serum concentrations as prognosticators of ovarian stimulation response and pregnancy outcome in patients undergoing in vitro fertilization. *Fertil Steril*. 1995. 64(5) 991-94.