

The Hormonal Cascade

A Wellness Education Guide

Prepared by Dana Lerma, Nurse Practitioner | Lerma Longevity

Hi,

Thank you for being here. If you have been following the series you already know that what you are experiencing is not random and it is not your fault. What you are feeling has a name, a mechanism, and a research base that explains it precisely.

I am a Nurse Practitioner. I am also personally navigating perimenopause. I started teaching this content because I was frustrated by how little useful information was available to me as a clinician going through this myself. The gap between what the research shows and what women are actually told is significant. This guide is my attempt to close that gap for you.

What follows is the research on the hormonal cascade of perimenopause. Five interconnected biological shifts happening simultaneously. Each one real. Each one supported by evidence. And each one pointing toward the same conclusion: your body is not broken. It is responding exactly as biology predicts to a significant hormonal transition.

Let's walk through it together.

Warmly,

Dana Lerma, Nurse Practitioner

Lerma Longevity

What Is Actually Happening in Your Body

At the ASCO 2026 annual meeting and in the research literature that followed, a pattern became clear that I have been watching for years. The same metabolic and inflammatory systems at the center of the GLP-1 and cancer research conversation are the exact systems shifting in your body during perimenopause. That connection is why I put this guide together.

This is not one study. It is a converging body of research pointing toward the same underlying biology: the relationship between estrogen, insulin resistance, chronic inflammation, and long-term health. Understanding that biology is what makes the difference between feeling confused by your symptoms and knowing exactly what is happening.

The Hormonal Cascade

When women move through perimenopause the hormonal landscape shifts in ways that affect nearly every system in the body simultaneously. One shift triggers the next. Here is what the research shows is happening.

The Estrogen Signal

Estrogen is insulin-sensitizing. As it declines during perimenopause insulin sensitivity tends to decline with it. Your body requires more insulin to process the same amount of carbohydrates it handled easily before. More insulin means more fat storage signaling. Research from the Study of Women's Health Across the Nation found women gain approximately 1.5 kilograms per year during the perimenopause transition, not because they are eating more, but because their hormonal environment changed how their body processes what they eat.

Estrogen also directs where fat is stored. Before perimenopause it preferentially directs fat to hips and thighs, subcutaneous fat that is metabolically less active. As estrogen falls that signal weakens and fat increasingly stores in the abdomen as visceral fat, which is metabolically active in ways that compound the cascade.

The Cortisol Connection

Estrogen normally moderates cortisol. When estrogen declines that moderating effect weakens. The natural early morning cortisol rise happens earlier and more sharply, which is why so many women in perimenopause wake between 2 and 4 AM feeling alert and anxious without an obvious reason. Research shows 40 to 60 percent of perimenopausal women report significant sleep disruption.

Disrupted sleep raises cortisol further. Elevated cortisol drives visceral fat storage. Visceral fat worsens insulin resistance. Insulin resistance disrupts sleep. The cascade feeds itself.

The Insulin Resistance Loop

As estrogen falls and cortisol rises insulin resistance compounds. The body stops responding to food and exercise the way it used to. This is not a willpower failure. This is a hormonal environment that has changed the rules of how your body processes energy. The same strategies that worked before perimenopause produce different results because the metabolic context is different.

The Muscle Equation

Estrogen directly supports muscle protein synthesis. Research on the menopausal transition shows women lose approximately 2.5 percent of lean muscle mass across perimenopause, and they lose it faster than age-matched men. Muscle is your metabolic floor: every pound of lean muscle raises your resting metabolic rate. When muscle declines, you burn fewer calories at rest even if your activity level has not changed.

The evidence-supported response is clear: protein intake of approximately 1.0 to 1.2 grams per kilogram of body weight per day combined with progressive resistance training 2 to 3 times per week is the most researched intervention for lean mass preservation during this transition.

The Cellular Energy Piece

Estrogen plays a direct role in mitochondrial function, the cellular structures that convert food into usable energy. As estrogen declines mitochondrial efficiency tends to decline with it. This is why the exhaustion of perimenopause is different from ordinary tiredness. It is cellular energy production running at a lower baseline. Sleep alone does not fix it because the issue is not sleep debt.

What This Research Does Not Say

The research described here is observational, which means it identifies patterns, not causes. None of it is a randomized controlled trial. It describes associations seen in groups of people and does not tell any individual what will happen for them.

Nothing in this guide is intended to diagnose, treat, or prevent any disease. This guide is wellness education only.

Questions to Bring to Your Provider

Here are three questions worth bringing to your healthcare provider:

1. What does the research on hormonal shifts and metabolism mean for someone with my health history?

This opens the conversation without putting your provider on the spot. It invites them to apply the research to your specific situation.

2. How does insulin resistance and cortisol dysregulation factor into my long-term wellness picture?

This shifts the conversation from weight specifically to overall metabolic health, which is where the most meaningful discussion usually happens.

3. What would you want to know about my health history before discussing metabolic support options?

This gives your provider the opening to ask the right questions and positions you as an informed, engaged patient.

What This Means for Your Wellness Options

This is education, not medical advice. Every EllieMD protocol requires physician review and approval before anything is prescribed or shipped. What I can do is give you a plain-language look at the compound categories that relate to these metabolic pathways.

Here are some of the options women navigating this transition have discussed with their EllieMD physicians.

Four Compounds to Know About

Metabolic Support

GLP-1/GIP (tirzepatide) injections for meaningful metabolic support: healthy body composition, blood sugar balance, and insulin sensitivity. Also available as GLP-1 (semaglutide) for weight management and metabolic health.

Metabolism and Body Composition

Tesamorelin/KPV injection supporting body composition, visceral fat reduction, and gut anti-inflammatory pathways.

Cellular Energy

NAD+ injection for mitochondrial function, cellular energy production, and healthy aging at the cellular level.

Investigational

MOTS-c injection: a mitochondria-derived peptide with emerging research in insulin sensitivity. Not FDA-approved. Physician evaluation required.

An Important Note

Which compound, which protocol, and whether any product is appropriate at all is a medical decision made only by your EllieMD physician after a full review of your health history. No two protocols are the same.

Have Questions?

Reach out to me directly before you purchase and I will help you think through which option fits your situation. Once you have purchased, your EllieMD physician handles all medical decisions. I also encourage you to share these options with your primary care physician especially if you have existing health conditions or take prescription medications.

How to Get Started with EllieMD

Step 1: Register

Type elliemd.com/lermalongevity into your browser, click GET STARTED, and create your free account in about 2 minutes.

Step 2: Complete Your Health Questionnaire

After registering, complete a medical questionnaire about your health history and goals.

Step 3: Purchase Your Compound

Browse to PRODUCTS and select the compound you want to start with.

Step 4: Physician Protocol Design

A licensed EllieMD physician reviews your health history and approves your personalized protocol.

Step 5: Your Protocol Ships to You

Once approved, your compounds ship directly to your door and your physician is available via messaging for any questions.

TO GET STARTED, TYPE THIS INTO YOUR BROWSER:

elliemd.com/lermalongevity

Questions? Email me directly at dana@lermalongevity.com

A Personal Note

I want to be transparent with you. I am personally navigating perimenopause. I have experienced the fatigue that sleep does not fix, the weight that feels different, the nights where I wake at 3 AM and cannot get back to sleep. I teach this because I live it.

I became a brand partner with EllieMD because I believe in physician-guided wellness support. I believe women deserve access to options that are grounded in research and overseen by licensed physicians who take their health history seriously.

If anything in this guide resonated, if you read it and thought this is me, I want to hear from you. Dana reviews every wellness assessment personally. You are not a number in a system. You are a woman who deserves a thoughtful, personalized response.

Warmly,

Dana Lerma, Nurse Practitioner

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The research referenced is observational and does not establish cause and effect. Nothing here diagnoses, treats, or prevents any disease. All products referenced require physician review and approval through EllieMD. Please discuss any wellness protocol with your physician, especially if you have existing health conditions or take prescription medications.

Dana Lerma is an independent EllieMD Brand Partner. EllieMD links in this guide are affiliate links. Dana may earn a commission on services initiated through these links.

References

1. SWAN Study. Study of Women's Health Across the Nation. Weight gain and body composition changes across the menopausal transition. swanstudy.org
2. McDonald ES, et al. GLP-1 agonists are associated with a significant reduction in breast cancer incidence in women. JCO Oncol Pract. Published online June 2, 2026. ASCO 2026 Abstract 10506. ascopubs.org/doi/10.1200/OP-26-00485
3. ASCO 2026 Abstract 3143. Real-world data on GLP-1 receptor agonists and metastatic progression in obesity-related cancers. Presented at the 2026 ASCO Annual Meeting, Chicago.
4. Dai H, et al. GLP-1 receptor agonist use and cancer risk in adults with overweight or obesity. JAMA Oncol. Published online August 21, 2025. jamanetwork.com/journals/jamaoncology

TAKE THE NEXT STEP

Ready to understand what this looks like for your specific situation?

lermalongevity.com/intake

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