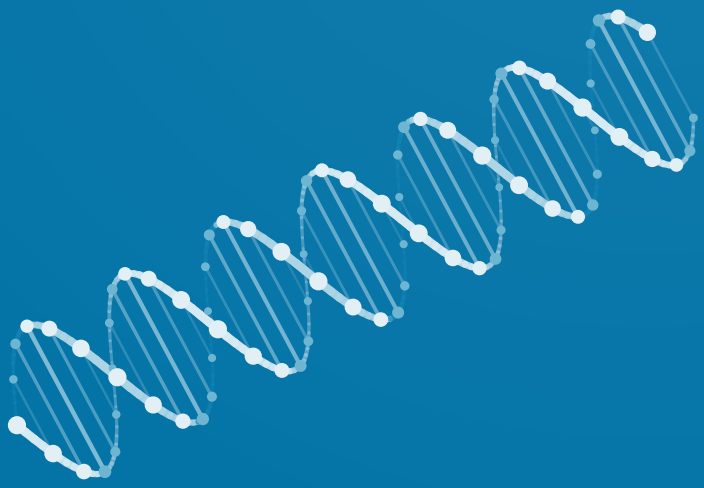
A CLINICAL GUIDE FROM BELLE

PEPTIDES FOR **PERIMENOPAUSE**

A Clinical Guide to Hormone, Metabolic, and Cellular Support



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ABOUT THE AUTHOR

Dr. Patrick **Taylor, MD**

I'm a board-certified family medicine physician and the Chief Medical Officer of Belle, where I lead protocol development for women's hormone and metabolic care nationally.

I trained at the University of North Carolina at Chapel Hill and completed my family medicine residency at the University of Utah, and I'm a Menopause Society Certified Practitioner. I've practiced full-scope family medicine, and my work now centers on hormone optimization, peptide therapy, metabolic health, and longevity.

My interest in this work isn't only clinical. I had cancer as a child, a year of chemotherapy followed by Cushing syndrome from the corticosteroids used to treat it. I was close to 300 pounds starting medical school, and lost 100 pounds through diet and training. That personal history is a large part of why I practice the way I do: I don't believe in shortcuts, and I don't believe in dismissing a patient's symptoms because the labs look normal.

That second part is the reason this guide exists. Perimenopause is one of the most under-recognized transitions in medicine. Women are routinely told their symptoms are stress, aging, or in their head, when there is a clear physiologic explanation and increasingly, evidence-based tools to address it.

Everything in this guide reflects how I actually practice: evidence first, individualized second, no hype.

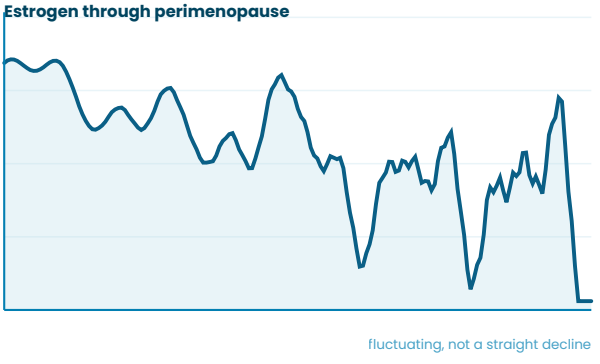
INTRODUCTION

What Perimenopause **Actually Is**

Most women hear "menopause" and think of one moment: the last period. But menopause itself is just a single date, retroactively defined as twelve consecutive months without a period. Everything leading up to it, which is where almost all of the symptoms live, is called perimenopause.

Perimenopause is the period before your last period, and it can last anywhere from seven to ten years.[1] What most women don't know is that it doesn't just mean rapidly fluctuating estrogen and progesterone, it changes your metabolic health right along with it. For most women, it begins in their early-to-mid 40s, but it can start as early as 35.

This matters because perimenopause is frequently missed. Labs can look unremarkable on a single draw, because the hormonal picture is moving, not static, estrogen and progesterone are fluctuating rather than declining in a straight line. A woman can feel the hormonal chaos years before a lab value confirms anything is different.



Estrogen fluctuates rather than declining in a straight line.

The symptoms everyone expects:

- ☐ Hot flashes
- ☐ Night sweats
- ☐ Sleep disturbances
- ☐ Vaginal dryness

The symptoms most often missed, or misattributed to something else:

- ☐ Brain fog and word-finding difficulty
- ☐ New or worsening anxiety
- ☐ Irritability
- ☐ Low libido
- ☐ Joint pain
- ☐ Increased belly fat, specifically visceral fat, not just weight gain
- ☐ Elevated cortisol
- ☐ New or worsening insulin resistance

These "missed" symptoms are the ones that send women to a psychiatrist, a rheumatologist, or a primary care visit focused on cholesterol, rather than to anyone thinking about hormones.[2,5] Many patients spend years being treated for anxiety, or told to diet and exercise more, before anyone connects the dots to perimenopause.

7–10 years perimenopause can span before a woman's final period, and it changes her metabolic health right along with her hormones.

Once we understand that perimenopause is a shift in underlying biology, not just "hormones going down," most of what patients experience sorts into four clinical buckets, numbered here in the order they're covered:

01

Insulin resistance

02

Inflammation

03

Hormone imbalance

04

Cellular and mitochondrial dysfunction

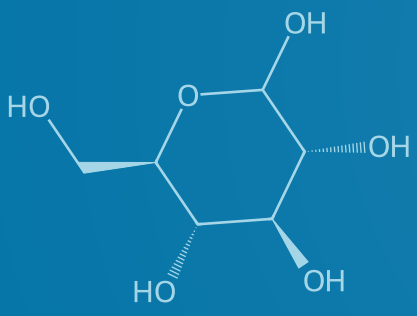
Most patients fit predominantly into one or two buckets, though there's real overlap between all four. There's also a fifth, bonus category: skin and longevity, which draws on tools from the other four buckets but deserves its own space.

01

CLINICAL BUCKET

INSULIN **RESISTANCE**

There are only two times in a woman's life when her body shifts into a state of inherent insulin resistance, largely independent of diet, activity level, or fitness. The first is pregnancy. The second is perimenopause.



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BUCKET ONE: INSULIN RESISTANCE

Insulin **Resistance**

WHERE THIS BUCKET SHOWS UP

You may be in this bucket if you're noticing: new or worsening belly fat despite no change in diet or training, rising cholesterol or A1c on routine labs, new sugar cravings or energy crashes, or a family history of type 2 diabetes that seems to be catching up with you.

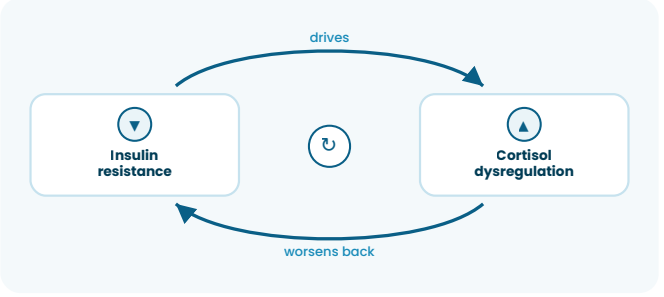
This isn't a metaphor. It's a direct physiologic effect of the rapid, erratic decline in estrogen and progesterone that defines this transition. Estrogen has a real, measurable role in insulin sensitivity and fat distribution.[2] As estrogen fluctuates and then declines, insulin sensitivity drops with it, even in women who haven't changed a single habit.

This is why a lot of women in their 40s see their labs shift and assume they've done something wrong. Often, they haven't. What's changed is the hormonal environment their metabolism is operating in.

What shows up on labs:

- Rising fasting insulin, usually the first thing to move
- Rising A1c, even within the "normal" range, one of the last things to move
- Changing cholesterol panel, often LDL and triglycerides trending up
- Rising hs-CRP, which isn't just a general inflammation marker here, it reflects real damage to the endothelial layer lining your blood vessels, and that's what drives the added cardiovascular risk
- Elevated cortisol, which compounds the insulin resistance further

These trends are documented in longitudinal cohort data tracking women through the menopause transition.[3,4] And the causality runs both ways: chronically elevated cortisol drives insulin resistance, and insulin resistance drives cortisol dysregulation right back. It's genuinely a chicken-and-egg problem, and untangling which came first matters less than treating both.



Cortisol and insulin resistance drive each other.

Peptides used in this bucket, ranked by priority:

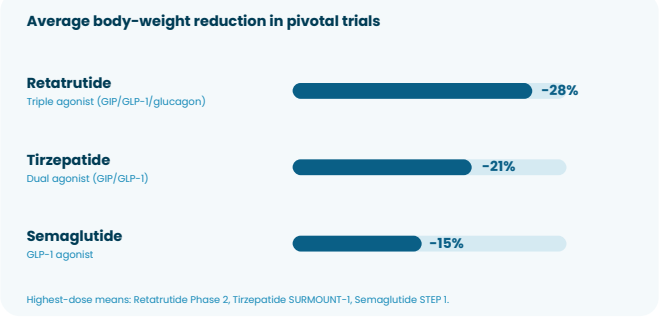
01 **Retatrutide, Tirzepatide, Semaglutide (GLP-1 receptor agonists)**

02 **MOTS-c**

03 **5-Amino-1MQ**

04 **SLU-PP-332**

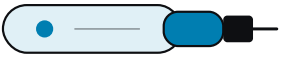
05 **AOD-9604**



GLP-1 class weight-loss results, from the pivotal obesity trials.

GLP-1 Receptor Agonists, Retatrutide, Tirzepatide, Semaglutide

This class works by mimicking incretin hormones your gut releases after eating. Retatrutide goes furthest, a triple agonist adding glucagon receptor activity on top of GIP and GLP-1.[6] Tirzepatide is a dual agonist, GIP and GLP-1.[7] Semaglutide targets the GLP-1 receptor alone.[8] Together, these mechanisms deliver a wide range of benefits:



GLP-1 receptor agonists

Retatrutide, tirzepatide, semaglutide

- ☐ Improved insulin secretion
- ☐ Slower gastric emptying
- ☐ Reduced appetite
- ☐ Directly improved insulin sensitivity
- ☐ Real fat loss and weight loss, independent of that insulin-sensitivity benefit

There are options outside of MHT for insulin resistance, inflammation, high cortisol, and elevated visceral fat, and GLP-1s are one of them. Not all of it is FDA-approved or indicated for perimenopause itself, but it can be adjunctive therapy to MHT, especially if insulin resistance, inflammation, high cortisol, or visceral fat are part of the picture. MHT addresses the hormonal side of the transition; a GLP-1 addresses the metabolic shift happening in parallel.

GLP-1s: More Than Weight Loss

If you've only heard of this class for weight loss and diabetes, there's more to it. Patients are seeing decreased inflammation with autoimmune conditions like psoriasis and rheumatoid arthritis, and a 2025 study showed lower dementia risk in patients treated

with GLP-1s. We don't fully understand the mechanism yet, but the anti-inflammatory effect is real and it's associated with longevity, not just weight loss.

CLINICAL NOTE

Vasomotor symptoms specifically are an emerging area of interest for this class. Mayo Clinic currently has an active clinical trial studying tirzepatide's effect on hot flashes and biological aging in postmenopausal women.[30] In my own practice, I've seen a similar pattern anecdotally, patients on GLP-1s reporting improvement not only in hot flashes but in joint pain as well, though that specific link hasn't been studied directly yet.

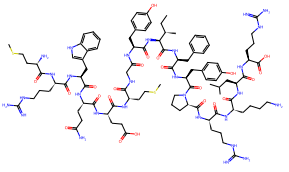
These are used in two very different ways depending on the patient and her goals. At full therapeutic dosing, they're a primary tool for meaningfully reversing insulin resistance and driving significant fat loss. At micro dosing, the goal shifts entirely: this becomes a maintenance and longevity tool rather than a weight-loss protocol. Patients already at a stable, healthy weight often stay on a microdose specifically for the anti-inflammatory effects, ongoing metabolic support, and the emerging benefits around joint pain and vasomotor symptoms covered above, without the appetite suppression or GI side effects that come with a full therapeutic dose.

CLINICAL NOTE

Any meaningful calorie deficit, whether from a GLP-1, a diet change, or anything else, carries a risk of losing lean muscle mass alongside fat. That risk isn't unique to GLP-1s or worse with them. It's managed the same way regardless of what's driving it: adequate protein intake and resistance training.

MOTS-c

A mitochondrial-derived peptide, encoded within mitochondrial DNA rather than nuclear DNA. Under metabolic stress, it translocates to the nucleus and activates AMPK, a central cellular energy-sensing pathway.[9,10] That activation is directly tied to fat loss and better weight management, not just a lab-value improvement, since AMPK is one of the primary switches your body uses to burn fat for fuel.



MOTS-c

16-residue mitochondrial-derived peptide

Activating AMPK is closely tied to improved insulin sensitivity and better glucose handling at the cellular level.

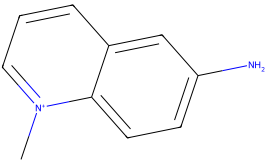
It's one of the more mechanistically elegant tools in this bucket, because it's addressing insulin resistance from inside the mitochondria rather than through the gut-hormone pathway GLP-1s use.

CLINICAL NOTE

Muscle is genuinely one of the organs of longevity. Higher skeletal muscle mass tracks with meaningfully lower all-cause mortality, and low muscle mass is linked to higher risk of osteoporosis, dementia, cardiovascular disease, and type 2 diabetes.[32] MOTS-c connects directly to this: it reduces myostatin, the signaling protein that drives muscle breakdown, by inhibiting the FOXO1 pathway upstream of it.[31] Less myostatin signaling means more preserved muscle, which is exactly why MOTS-c's relevance in this bucket goes well beyond insulin sensitivity alone.

5-Amino-1MQ

Works by inhibiting NNMT (nicotinamide N-methyltransferase), an enzyme highly expressed in fat tissue.[11] Inhibiting NNMT preserves cellular NAD+ and SAM pools, both of which support healthier fat metabolism and mitochondrial function.



5-Amino-1MQ

5-amino-1-methylquinolinium, a small-molecule NNMT inhibitor.

Preclinical studies show this translates into increased insulin sensitivity, increased lipolysis, and measurable fat loss, even without any caloric restriction.[11] That last point matters specifically in perimenopause, where fat redistribution and metabolic slowdown happen regardless of what a patient is doing with her diet.

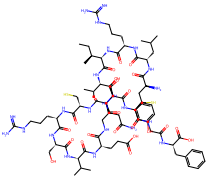
SLU-PP-332

A newer compound, a synthetic agonist of the estrogen-related receptors (ERRs), key regulators of mitochondrial biogenesis and oxidative metabolism. Described as an "exercise mimetic" because activating these receptors produces some of the same downstream metabolic effects as endurance training: more mitochondria, better oxidative capacity, improved glucose handling, and real fat loss.[12] That profile makes it worth watching closely for perimenopausal patients whose insulin resistance isn't fully responding to other tools in this bucket, or who simply can't train as much as they'd like to.

SLU-PP-332

A synthetic pan-agonist of the estrogen-related receptors (ERRα/β/γ).

AOD-9604



AOD-9604

The modified C-terminal fragment (176-191) of human growth hormone.

AOD-9604 is HGH fragment 176-191, the C-terminal end of human growth hormone, and it's used because it's been shown to drive real fat loss, increasing lipolysis, fat breakdown, without increasing IGF-1.[13] That distinction matters. When you stimulate growth hormone release with something like tesamorelin or CJC-1295/ipamorelin, you also stimulate IGF-1 release from the liver. IGF-1 is one of the main anabolic hormones in the body, which is why it builds muscle and modulates growth hormone's effects on cartilage, bone, and visceral fat. But it's not selective, and the potential downside is growth of other organs, liver, spleen, kidneys, heart, and potentially underlying tumor or cancer cell growth. AOD-9604 is being studied specifically to get the metabolic benefit without that tradeoff.

Mechanistically, it has a selective action on fat tissue through beta-3 adrenergic receptors, which:

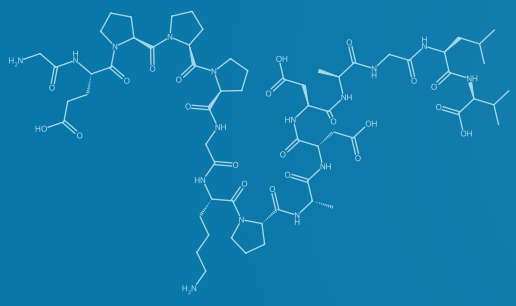
- ☐ Drive lipolysis through the cyclic AMP pathway
- ☐ Increase thermogenesis
- ☐ Stimulate brown fat production

02

CLINICAL BUCKET

SYSTEMIC **INFLAMMATION**

Perimenopause is, underneath almost everything else in this guide, a pro-inflammatory state.



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BUCKET TWO: INFLAMMATION

Systemic **Inflammation**

WHERE THIS BUCKET SHOWS UP

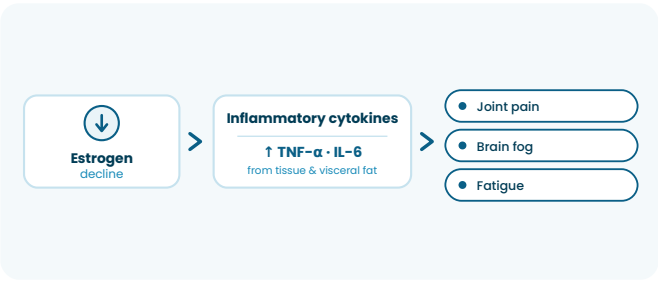
You may be in this bucket if you're noticing: new joint pain or stiffness, new food sensitivities or histamine-type reactions, gut symptoms that weren't there before, or hot flashes and night sweats that feel disproportionate to what other women describe.

Perimenopause is, underneath almost everything else in this guide, a pro-inflammatory state. Estrogen has direct anti-inflammatory effects on joint tissue, the vascular endothelium, and the brain, and its decline removes a protective mechanism that's been running quietly in the background for your entire adult life. That's not generic aging, it's a specific, identifiable hormonal shift, and it shows up everywhere at once: joint pain misattributed to overuse or age, bloating, fatigue that doesn't track with sleep, and brain fog mistaken for cognitive decline instead of what it actually is, estrogen loss acting directly on the nervous system. If several of these show up together, that's not four separate problems. That's one cluster, and it's perimenopause.

A Clear Example

Take frozen shoulder. There's a much higher association between frozen shoulder and women in midlife, driven by loss of estrogen in perimenopause and menopause, and women on MHT are at meaningfully lower risk of developing it.

Estrogen isn't a treatment for frozen shoulder on its own, physical therapy and early intervention still matter, but it's a clean example of a joint problem that gets treated as orthopedic when it's actually hormonal. That's the pattern worth recognizing across this entire bucket.



Estrogen's decline removes a built-in anti-inflammatory brake.

Peptides used in this bucket, ranked by priority:

01 **BPC-157 & TB-500**

02 **GHK-Cu**

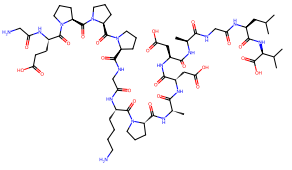
03 **KPV**

04 **GLOW & KLOW blends**

05 **Growth hormone secretagogues (brief mention, full detail in the hormone imbalance bucket)**

BPC-157 and TB-500

These two get talked about as a pair so often that people assume they're interchangeable. They're not, and the difference is exactly why combining them works.



BPC-157

Body Protection Compound 157, the pentadecapeptide fragment of gastric protein.

BPC-157 is a pentadecapeptide from a protective protein in gastric juice, your body already makes a version of it. It upregulates VEGFR2 and activates the Akt-eNOS pathway, driving angiogenesis, new blood vessel formation, at the site of injury.[15] That's tissue scaffolding: rebuilding the vascular supply damaged or inflamed tissue needs to actually repair.

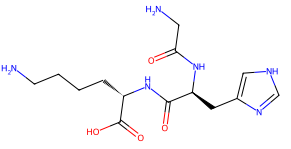
TB-500 is a synthetic fragment of Thymosin Beta-4, your body's own healing peptide, released natively after injury. It works through an entirely different mechanism, actin polymerization, the structural protein that drives cell migration.[16] Where BPC-157 builds the scaffolding, TB-500 gets the repair cells moving into it.

CLINICAL NOTE

Wolverine is the two combined, and this is why it outperforms either alone: BPC-157 builds blood supply and scaffolding, cellular turnover. TB-500 drives cell migration into that scaffolding, cell mobilization. Joint pain and systemic inflammation get hit from both angles at once, and that overlap is the whole point.

GHK-Cu

GHK-Cu is a naturally occurring copper-binding peptide found in our own saliva and tissues, and it decreases with age exponentially. It's not a minor player. It regulates over 4,000 genes involved in tissue repair, inflammation, and antioxidant defense. [17] That's the actual scope of what this molecule touches, not an exaggeration.



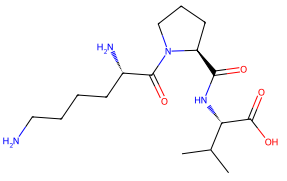
GHK-Cu

Glycyl-L-histidyl-L-lysine copper complex, the tripeptide-copper structure behind its collagen and gene-expression effects.

Mechanistically, it increases fibroblast growth and angiogenesis, and it decreases TNF-alpha and IL-6, the pro-inflammatory cytokines behind most systemic inflammation. In perimenopause specifically, estrogen is running a version of that same anti-inflammatory job everywhere in the body, and as estrogen falls, GHK-Cu is one of the few tools that can pick up part of that workload directly.

KPV

KPV is a small tripeptide fragment of alpha-MSH. Unlike full-length alpha-MSH analogs, it doesn't carry pigmentation effects, but it works by activating the MC1 receptor in the gut wall and inhibiting the NF-kB pathway, [14] giving it strong, targeted anti-inflammatory activity anywhere gut-level inflammation is part of the picture.



KPV

Lysine-Proline-Valine, the alpha-MSH(11-13) fragment responsible for its anti-inflammatory activity without pigmentation effects.

CLINICAL NOTE

This one deserves particular attention. In my own patient population, KPV has been one of the most consistently successful tools I have for two specific perimenopausal problems: histamine-type reactions, which flare for a lot of women during this transition, and vasomotor symptoms, hot flashes and night sweats. I've watched a meaningful number of perimenopausal patients get real, noticeable relief from both. It's one of my favorite tools in this bucket.

GLOW and KLOW

BPC-157, TB-500, and GHK-Cu are frequently combined into a single blend, GLOW, rather than run as three separate injections. The logic is straightforward: BPC-157 and TB-500 handle tissue repair and cell migration, and GHK-Cu adds its own anti-inflammatory and gene-expression effects on top, along with the skin and collagen benefits covered later in this guide. Three complementary mechanisms in one protocol.

KLOW is GLOW with KPV added. I reach for KLOW specifically when gut-level inflammation is part of the picture, IBS-type symptoms, food sensitivities, GI-related bloating, since KPV's MC1 receptor activity in the gut wall gives it a specific advantage there that the other three compounds don't carry on their own.

> **CLINICAL NOTE**
>
> Same logic as everything else in this guide: match the tool to what's actually driving the patient's symptoms. A woman whose main complaint is joint pain and skin changes gets GLOW. A woman whose main complaint includes gut symptoms and food sensitivities gets KLOW. Neither is a default, one-size-fits-all stack.

Growth Hormone Secretagogues, Briefly

Tesamorelin, CJC-1295, ipamorelin, and sermorelin also carry anti-inflammatory effects downstream of restoring more youthful GH pulsatility. Declining GH is part of why inflammation creeps up during this transition, not just a side note to it.

Visceral fat is a major driver of that inflammation, and it's not inert storage. It's metabolically active tissue that secretes TNF-alpha and IL-6, the same pro-inflammatory cytokines driving systemic inflammation elsewhere in this bucket, and it worsens insulin resistance directly. Insulin resistance then drives more visceral fat accumulation, and that visceral fat drives more inflammation in return, a cycle that feeds itself. GH decline accelerates visceral fat gain, which is exactly why restoring more youthful GH pulsatility with these peptides breaks the cycle structurally instead of just managing the inflammation downstream of it.

Worth flagging here: ipamorelin works through the ghrelin receptor pathway, not the GHRH pathway the other three use. The full breakdown of this group, and why that mechanism split actually changes how they're used, lives in the hormone imbalance bucket, since GH decline is fundamentally a hormone story before it's an inflammation story.

03

CLINICAL BUCKET

HORMONE **IMBALANCE**

Menopausal hormone therapy (MHT) is the foundation of perimenopausal hormone care. This bucket covers the non-MHT peptide adjuncts that support it, growth hormone secretagogues plus hormonal tools like kisspeptin and PT-141, not a replacement for it.

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BUCKET THREE: HORMONE IMBALANCE

Hormone **Imbalance**

WHERE THIS BUCKET SHOWS UP

You may be in this bucket if you're noticing: low libido, poor sleep quality even without night sweats, loss of muscle tone or strength, mood changes, or a general sense that your body isn't responding the way it used to.

This is the bucket most people expect when they think "perimenopause," and it's an important one, but it's worth being direct about something up front: menopausal hormone therapy (MHT) is the foundation of perimenopausal hormone care, not an alternative to it. Estrogen, progesterone, and in some patients testosterone, remain the most evidence-based, highest-impact intervention available for this transition.[24]

Cortisol rises and GH falls together across this transition, driving much of what shows up here: poor sleep, low libido, loss of muscle tone. GH secretagogues restore more youthful GH pulsatility to address this directly. Kisspeptin and PT-141 are different, hormonal adjuncts chosen by menopausal stage and symptom.

Peptides used in this bucket, ranked by priority:

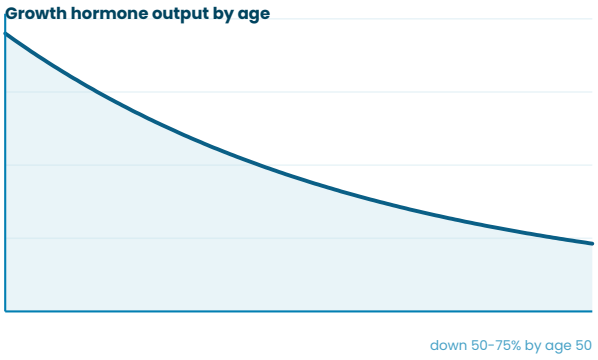
01 **Tesamorelin**

02 **CJC-1295 & Ipamorelin**

03 **Sermorelin**

04 **Kisspeptin**

05 **PT-141**



Growth hormone declines continuously from your 30s.

Growth Hormone, and Why Timing Matters

Growth hormone is a big part of what's covered in this bucket, and it deserves its own framing before we get into individual peptides. GH secretion peaks during the first phase of slow-wave sleep, and it declines continuously from your 30s onward. By 50, output can be down 50 to 75 percent. That decline shows up as:

- ☐ Poor sleep
- ☐ Elevated cortisol
- ☐ Visceral fat
- ☐ Joint pain
- ☐ Muscle loss

Which is exactly why this bucket overlaps so heavily with the other three.

Why Not Just Replace GH Directly?

Exogenous growth hormone is not selective. IGF-1, the growth factor GH triggers the release of, is one of the main anabolic hormones in the body, which is why it builds muscle and helps modulate GH's effects on cartilage and bone. But it can also stimulate tissue in the liver, kidneys, spleen, and heart, not just muscle, and it can potentially increase growth of underlying tumor or cancer cells. That's a real mechanism, not a theoretical risk, and it's exactly why growth hormone peptides get monitored clinically rather than treated like a supplement, and why I always recommend sourcing them through a qualified 503A or 503B compounding pharmacy rather than the gray market. These are strong medications, not something to fool around with.

Secretagogues, the class covered in this bucket, get around part of that problem: they stimulate your own pituitary to release GH in its natural pulsatile pattern, rather than overriding the system with a flat, continuous dose.

Timing matters here more than in almost any other bucket. Estrogen and progesterone aren't declining together in a straight line, they're fluctuating rapidly and unevenly through this transition, and which peptide makes sense depends heavily on where a patient actually is in that fluctuation.

Choosing a GH Secretagogue

All three stimulate your own pituitary rather than replacing GH directly. Strength trades off against tolerability, and where a patient lands depends on which one she needs more. All three also indirectly lower cortisol by blunting cortisone-to-cortisol conversion.

1. **Tesamorelin.** The strongest option, a GHRH analog FDA-approved for HIV-associated lipodystrophy. Decreases visceral fat specifically, and supports deeper sleep, faster recovery, steadier energy, and preserved muscle.[18] Tradeoff: more side effects, anxiety, palpitations, flushing. Tolerability, not efficacy, is usually the limit, which is why microdosing is common here.

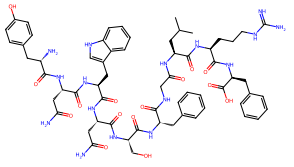
2. **CJC-1295 and Ipamorelin.** A GHRH analog paired with a ghrelin receptor agonist for a stronger, more sustained pulse than either alone.[19,20] My preferred combination for most patients: tolerability and efficacy fall right between tesamorelin and sermorelin.

3. **Sermorelin.** The gentlest, most established GHRH analog in the group.[21] Fewer side effects, still clinically meaningful, and often the right starting point before stepping up.

Strength trades off against tolerability across the three secretagogues.

Kisspeptin

Acts upstream of everything else in the reproductive hormone axis. It stimulates a specific population of hypothalamic neurons that drive the pulsatile release of GnRH, which in turn drives LH and FSH release from the pituitary.[22]



Kisspeptin

Kisspeptin-10 (KP-10), the shortest bioactive fragment of the native peptide.

CLINICAL NOTE

Because kisspeptin works by stimulating the hypothalamus to signal the ovaries, it depends on the ovaries still having follicles left to respond. In early perimenopause, when ovarian reserve is still meaningful, it can be a useful tool. In late perimenopause and post-menopause, when follicular reserve is essentially depleted, the mechanism has little left to work with, and kisspeptin becomes far less effective. A great example of why the right peptide depends on exactly where a patient is in the transition.

PT-141 (Bremelanotide)

Works centrally, in the brain, through melanocortin receptors (MC3R and MC4R), rather than through the vascular mechanism used by medications for erectile dysfunction.[23] For women, this makes it a meaningful option for low libido and sexual dysfunction related to perimenopause, addressing desire and arousal at the level of brain signaling rather than blood flow.

PT-141

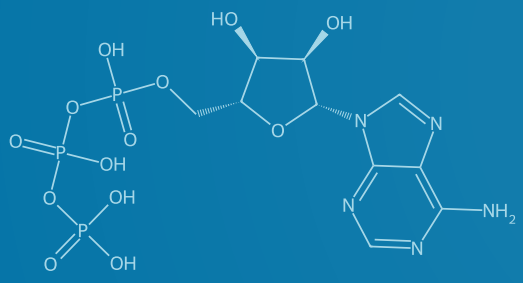
Bremelanotide, a cyclic heptapeptide melanocortin receptor agonist.

04

CLINICAL BUCKET

CELLULAR & **MITOCHONDRIAL**

Every cell in your body runs on energy produced in the mitochondria, and inflammation at the cellular level is regulated there as well.



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Cellular & **Mitochondrial**

WHERE THIS BUCKET SHOWS UP

You may be in this bucket if you're noticing: persistent fatigue that doesn't track with sleep, brain fog, slower recovery from exercise or illness, or a general sense of aging faster than your peers.

Every cell in your body runs on energy produced in the mitochondria. As we age, and especially as estrogen declines, mitochondrial efficiency drops and oxidative stress, damage from reactive oxygen species, rises. This bucket is about supporting that machinery directly.

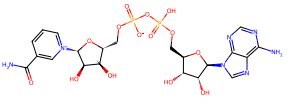
Peptides used in this bucket, ranked by priority:

01	**NAD+**
02	**Glutathione**
03	**SS-31**
04	**MOTS-c**
05	**5-Amino-1MQ**

NAD+ and Glutathione: The Foundation

NAD+ and glutathione are the base of every cellular protocol I build, not just for perimenopause but for longevity generally.

NAD+ is a coenzyme found in every cell of the body, necessary for energy production. At the cellular level, it's required for mitochondrial function



NAD+

Nicotinamide adenine dinucleotide, the coenzyme

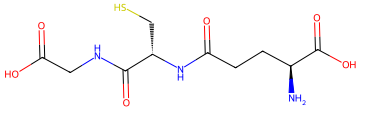
behind cellular energy production and DNA repair.

and the electron transport chain that produces ATP. As we age, NAD+ drops to about 50 percent of what it is in our youth, and when that happens, you tend to see lower energy, higher inflammation, and higher reactive oxidative species. It's also the substrate sirtuin genes need, and sirtuin proteins are associated with longevity, which is part of why NAD+ gets tied to anti-aging alongside telomere shortening and mitochondrial dysfunction generally.[25]

Glutathione is the body's master antioxidant. It directly neutralizes reactive oxygen species and supports the liver's detoxification pathways.[26] Left unchecked, reactive oxidative species drive damage to your DNA, proteins, and cellular structures, and that damage is what actually shows up as:

- Accelerated aging
- Inflammation
- Cell damage
- Mitochondrial inefficiency and damage
- Over time, increased risk of cancer and chronic disease

Reducing oxidative stress at the cellular level is foundational to nearly everything else in this guide, since oxidative damage compounds insulin resistance, inflammation, and hormone dysfunction alike. Glutathione and NAD+ both have strong evidence behind them specifically for reducing the risk of neurocognitive decline, which is exactly why they're the foundation of this bucket rather than an afterthought.



Glutathione

A tripeptide of glutamate, cysteine, and glycine, and the body's primary intracellular antioxidant.

SS-31: A Note on How It's Used

SS-31 (Elamipretide) works by binding cardiolipin, a lipid unique to the inner mitochondrial membrane, stabilizing the membrane's structure and reducing the reactive oxygen species generated during energy production.[27]

SS-31 (Elamipretide)

Cardiolipin-protective peptide

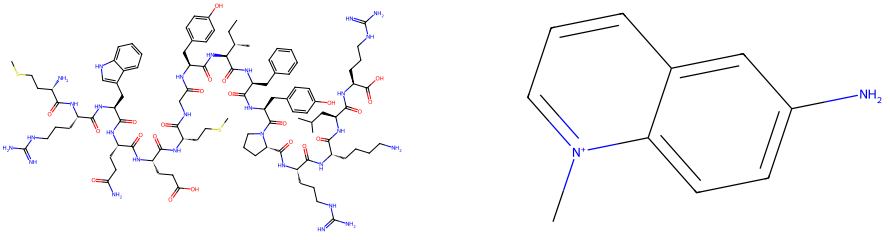
CLINICAL NOTE

I want to be direct about something here, because I think the peptide community has gotten this one wrong. There's a common belief that SS-31 needs to be used before, or alongside, other mitochondrial peptides like MOTS-c, as though it's a prerequisite. In my clinical view, that's not accurate for most patients. Unless someone has a significant autoimmune condition, a significant inflammatory condition, meaningful chronological aging beyond typical perimenopause, or a history of chemotherapy or other mitochondrially toxic drug exposure, SS-31 usually isn't necessary. For the average perimenopausal patient, MOTS-c and the other tools in this guide do the job without it.

MOTS-c and 5-Amino-1MQ, Revisited

Both of these were introduced in the insulin resistance section, and both belong here too, because their mechanisms are fundamentally mitochondrial. MOTS-c's AMPK activation and 5-Amino-1MQ's NNMT inhibition both directly support mitochondrial function and energy output, which is exactly why they show up in both buckets.

MOTS-c's relevance here goes beyond glucose handling. It also supports mitochondrial function within skeletal muscle itself by reducing myostatin signaling,[31] and muscle is genuinely one of the organs of longevity,[32] which is exactly why protecting muscle-level mitochondrial health matters as much here as it does on the insulin resistance side. This overlap between buckets isn't a coincidence, it reflects how tightly insulin resistance and mitochondrial dysfunction are linked.



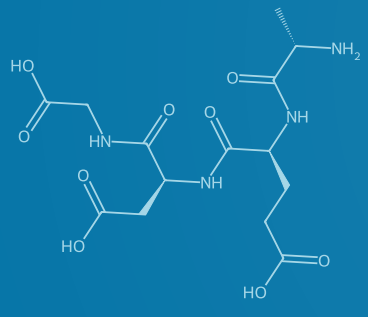
MOTS-c and 5-Amino-1MQ both act directly on mitochondrial function.

05

CLINICAL BUCKET

SKIN & **LONGEVITY**

This section draws on tools from every bucket above, because skin health and longevity aren't separate systems, they're downstream of the same metabolic, inflammatory, hormonal, and cellular processes covered in this guide.



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Skin & **Longevity**

This section draws on tools from every bucket above, because skin health and longevity aren't separate systems, they're downstream of the same metabolic, inflammatory, hormonal, and cellular processes covered in this guide.

Peptides used in this bucket, ranked by priority:

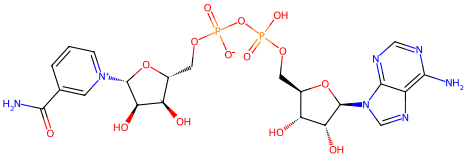
01 **NAD+**

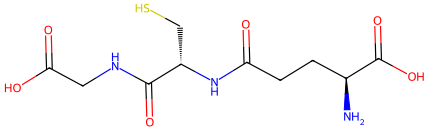
02 **Glutathione**

03 **Growth hormone secretagogues**

04 **Epitalon**

05 **GHK-Cu**





NAD+ and glutathione anchor every cellular and longevity protocol.

NAD+ and Glutathione, Again

Same foundation as the cellular section. Reducing oxidative stress and supporting mitochondrial energy output isn't just relevant to how you feel day to day, it's foundational to how you age. Both also

carry strong evidence specifically for reducing the risk of neurocognitive decline, which is exactly why they anchor this bucket rather than sitting on the sidelines of it.

Worth a brief mention here too: GLP-1s at a microdose, covered in the insulin resistance bucket, carry longevity relevance of their own, better cardiometabolic markers and early evidence of reduced cognitive decline risk, which is why they're worth considering even in patients who aren't using them for weight loss.

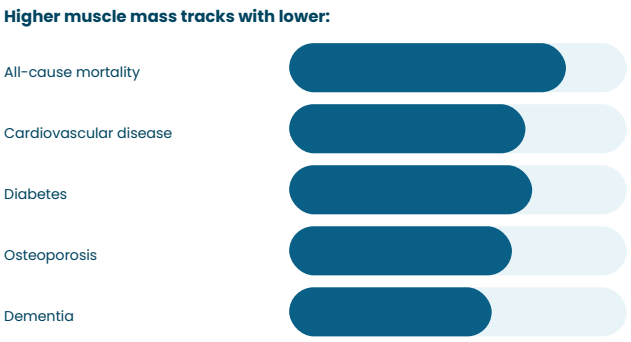
Growth Hormone Secretagogues, Muscle, Bone, and Visceral Fat

Growth hormone decline accelerates with age, and especially after menopause, and here's a hard truth about what that actually costs you: when it comes to longevity, everyone should be trying to build and preserve muscle. Increased skeletal muscle mass is associated with decreased:

- ☐ All-cause mortality, meaning death by any cause
- ☐ Cardiovascular disease risk
- ☐ Diabetes risk
- ☐ Osteoporosis risk
- ☐ Dementia risk

Skeletal muscle is the organ of longevity. Period.

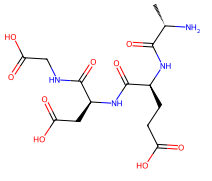
GH secretagogues support this through IGF-1, one of the main anabolic substances in the body. It drives protein synthesis and maintenance of skeletal muscle mass, and it increases bone formation and collagen production too. That's exactly why restoring more youthful GH pulsatility addresses muscle, bone density, and visceral fat all at once, three of the strongest levers you have on how you age.



Skeletal muscle is the organ of longevity.

Epitalon

A synthetic peptide, used sparingly and typically in short courses rather than continuously. It's not a peptide most patients need continuously, but its effect on telomerase, the enzyme responsible for maintaining the protective caps on our chromosomes, is undeniable, and that makes it one of the more compelling tools in longevity medicine.[28] Cellular aging accelerates through perimenopause the same way inflammation and insulin resistance do, which is part of why a peptide aimed squarely at telomere maintenance has a place in this guide.



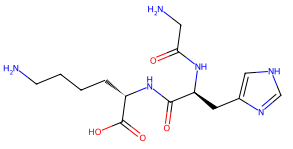
Epitalon

A synthetic tetrapeptide (Ala-Glu-Asp-Gly) studied for its effect on telomerase activity.

GHK-Cu for Skin

Patients using GHK-Cu topically typically see:

- ☐ Fewer fine line wrinkles
- ☐ Fewer dark spots
- ☐ Less acne
- ☐ Better hair growth
- ☐ Better skin and nail growth



GHK-Cu

The same copper-tripeptide complex, shown here for its skin and gene-expression effects.

The mechanism goes beyond collagen. It stimulates collagen and elastin synthesis directly, with human RCTs showing a significant reduction in wrinkle volume and prevalence, [17] but its more remarkable property is shifting gene expression in skin cells toward a more youthful profile while reducing local inflammation.[29] Skin thinning, dryness, and loss of elasticity are visible signs of the same estrogen decline driving everything else in this guide, which is exactly why this combination of collagen support, gene-level rejuvenation, and anti-inflammatory effect shows up in both the inflammation bucket and here.

CLOSING

Which Bucket **Fits You?**

Everything in this guide sorts into four clinical buckets, plus a bonus category for skin and longevity. Start with whichever symptoms feel most like yours:

01 Insulin resistance: new belly fat, rising labs, sugar cravings, a family history of diabetes catching up with you. GLP-1s lead this bucket by a wide margin.

02 Inflammation: joint pain, histamine-type reactions, gut symptoms, or disproportionate hot flashes. BPC-157/TB-500 and GHK-Cu do most of the work.

03 Hormone imbalance: low libido, poor sleep, loss of muscle tone, mood changes. MHT is the foundation, everything else here is additive.

04 Cellular and mitochondrial dysfunction: fatigue that doesn't track with sleep, brain fog, slow recovery. NAD+ and glutathione anchor this bucket.

05 Skin and longevity (bonus): draws on tools from every bucket above.

One thing worth being direct about: the order I've ranked peptides within each bucket reflects how I view their efficacy and importance, based on my own practice, not a rigid formula. What makes sense for you depends on your labs, symptoms, and goals.

NEXT STEPS

This guide is a starting point, not a protocol. What actually makes sense for you requires an individualized approach and protocol.

START WITH A CONSULT

If you're a patient: Book a consult to talk through your symptoms and a personalized plan.

Book a Consult

READY FOR TREATMENT?

Already know what you need? Start treatment built around your symptoms and goals.

Start Treatment

LEARN MORE ABOUT BELLE

See how Belle approaches women's hormone and metabolic care.

Learn More

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APPENDIX

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