

Perimenopause and Natural Medicine Approaches to Hormone Health

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Abstract

Perimenopause is a complex and dynamic hormonal transition marked by fluctuations in estrogen and progesterone, leading to widespread effects on neuroendocrine function, metabolism, and structural integrity. Unlike menopause, it is not a fixed state but a variable phase that can begin in early midlife and present with symptoms such as mood disturbances, sleep disruption, metabolic changes, and connective tissue decline. These changes are influenced not only by aging but also by cumulative stress, environmental exposures, and overall physiological health.

At the core of perimenopause is dysregulation of the hypothalamic-pituitary-ovarian axis, resulting in inconsistent hormonal signaling that impacts neurotransmitters, metabolic pathways, and systemic function. This contributes to increased inflammation, reduced mitochondrial efficiency, altered glucose regulation, and heightened cardiometabolic risk.

Natural medicine offers a systems-based approach to addressing these changes by targeting key physiological pathways. Nutritional strategies support estrogen metabolism and detoxification, particularly through liver function and the gut microbiome. Botanicals and nutraceuticals play a role in regulating mood, enhancing stress resilience, improving metabolic flexibility, and reducing inflammation. Additional support for structural health, including bone, skin, and connective tissue, is achieved through targeted nutrients such as silica, vitamins, and collagen-supportive compounds.

While hormone replacement therapy remains effective for symptom relief, it does not fully address underlying metabolic and environmental factors and may not be appropriate for all individuals. Natural medicine approaches can serve as either a primary strategy in early perimenopause or as a complementary intervention alongside pharmaceutical care.

Overall, a comprehensive and individualized approach that integrates nutrition, lifestyle, and targeted supplementation provides a more complete framework for supporting hormone health during perimenopause. This model emphasizes long-term health, improved quality of life, and a shift toward preventative, physiology-driven care.

Introduction

Perimenopause is a dynamic and transitional phase characterized by significant hormonal fluctuation, involving alterations in estrogen and progesterone levels, neuroendocrine restructuring, and metabolic adaptation. Unlike menopause, which represents a state of ovarian senescence and sustained hypoestrogenism, perimenopause is marked by variability and instability in hormonal signaling. This transition can begin as early as the late 30s or early 40s and may continue for several years before menopause is reached (Erdelyi et al., 2024).

Clinically, perimenopause presents with a broad spectrum of symptoms, including mood variability, sleep disturbances, vasomotor symptoms, changes in body composition, insulin resistance, and connective tissue degradation. These changes are not isolated but are influenced by an individual's prior physiological state, including cumulative exposure to chronic stress, environmental endocrine disruptors, and metabolic demands. As a result, hormone-supportive strategies may be relevant not only for aging populations but also for younger individuals experiencing dysregulated endocrine function.

While pharmaceutical interventions such as hormone replacement therapy (HRT) remain effective for symptom management, there is increasing interest in natural medicine approaches. This shift reflects a growing emphasis on safety, personalization, and long-term metabolic health. Natural medicine, incorporating targeted nutrition, botanicals, nutraceuticals, and lifestyle interventions, offers a systems-based model that aligns with the complex and evolving physiology of perimenopause.

Pathophysiology of Perimenopause

The underlying driver of perimenopause is dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis, resulting in impaired follicular recruitment and disrupted gonadotropin signaling. As ovarian reserve declines, feedback mechanisms involving estradiol become inconsistent, leading to elevated follicle-stimulating hormone (FSH) levels and reduced luteal progesterone production (Santoro et al., 2020).

This hormonal variability affects central nervous system function, particularly the regulation of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA). The resulting imbalance contributes to mood disturbances, anxiety, sleep disruption, and cognitive variability.

Beyond the central nervous system, fluctuating estrogen levels influence multiple physiological systems. These include connective tissue turnover, bone remodeling, lipid metabolism, insulin sensitivity, and hepatic detoxification capacity. Estrogen plays a critical role in maintaining collagen synthesis, vascular elasticity, and mitochondrial function. Therefore, inconsistent hormonal exposure increases both structural vulnerability and metabolic instability (Harak et al., 2025).

Additionally, altered cortisol responsiveness during midlife can exacerbate visceral adiposity, impair glucose tolerance, and elevate cardiometabolic risk, particularly in the absence of supportive lifestyle interventions.

Nutritional and Natural Medicine Interventions

Estrogen Metabolism, Detoxification, and the Gut-Hormone Axis

Effective estrogen metabolism becomes increasingly important during perimenopause, particularly in the context of environmental exposures such as bisphenols and persistent organic pollutants. Cruciferous vegetables, including cabbage, kale, and broccoli, contain glucosinolates that are converted into bioactive compounds such as indole-3-carbinol and sulforaphane. These compounds support hepatic phase I and phase II detoxification pathways and promote favorable estrogen metabolite balance (Erdelyi et al., 2024).

The gut microbiome also plays a central role in hormonal regulation through the estrobolome, a collection of microbial genes capable of deconjugating estrogens and allowing their reabsorption. Dysbiosis can disrupt this process, leading to either estrogen excess or deficiency. As a result, prebiotic fibers such as inulin, psyllium, and apple fiber are valuable for supporting microbial balance and

hormonal homeostasis (Li et al., 2022).

Flaxseed, a rich source of lignans, has demonstrated clinical relevance in reducing perimenopausal symptom severity and improving quality of life, likely through its modulatory effects on estrogen metabolism (Shrivastava et al., 2024).

Structural Integrity: Bone, Skin, and Connective Tissue

Declining and fluctuating estrogen levels accelerate collagen degradation and increase bone resorption, placing individuals at risk for osteopenia and musculoskeletal discomfort earlier than traditionally expected. Bioavailable silica, particularly in the form of orthosilicic acid, has been shown to support collagen synthesis, enhance connective tissue strength, and improve bone mineral density when combined with vitamin D and calcium (Pritchard & Nielsen, 2024).

Vitamin C and trace minerals further contribute to collagen cross-linking and antioxidant protection, supporting structural resilience during periods of hormonal stress. Additionally, vitamin K2 and vitamin D3 work synergistically to direct calcium deposition toward bone tissue while reducing vascular calcification risk.

Emerging evidence suggests that optimal intake of these nutrients not only supports skeletal integrity but also contributes to cardiovascular and immune health in midlife populations (Webster et al., 2023).

Neuroendocrine and Mood Support

Mood disturbances and cognitive fluctuations are among the most commonly reported symptoms of perimenopause. Estrogen plays a significant role in modulating catecholamine synthesis, highlighting the importance of targeted amino acid support.

N-acetyl-L-tyrosine serves as a precursor to dopamine and norepinephrine, supporting motivation, focus, and emotional regulation. L-theanine offers anxiolytic benefits by modulating stress responses without inducing sedation, making it particularly useful during periods of heightened sympathetic activity (Wang et al., 2022).

Botanical and nutraceutical support can further enhance neuroendocrine balance. *Mucuna pruriens*, a natural source of L-DOPA, supports dopaminergic tone, while adaptogenic herbs such as *Panax ginseng* and *Astragalus membranaceus* have been associated with improved stress resilience, immune modulation, and mitochondrial function (Shinde et al., 2024).

Inflammation, Energy Production, and Metabolic Flexibility

Perimenopause is frequently associated with low-grade inflammation and reduced mitochondrial efficiency. Polyphenolic compounds, including curcumin, resveratrol, and pine bark extract, exhibit anti-inflammatory and antioxidant properties that may reduce joint discomfort and lower cardiometabolic risk (Cione et al., 2019).

Resveratrol, in particular, has been shown to activate sirtuin pathways, supporting cellular longevity and metabolic adaptability. Fatigue, a common symptom during this phase, often reflects diminished ATP production. D-ribose contributes to cellular energy synthesis, while NAD⁺ pathways are essential for maintaining mitochondrial repair and metabolic regulation as hormonal signaling becomes less stable (Mishra & Kakhlon, 2025).

Body Composition, Glucose Regulation, and Appetite Signaling

Hormonal fluctuations during perimenopause can disrupt insulin sensitivity, appetite regulation, and energy balance, often leading to weight gain despite minimal changes in diet or activity levels. Altered signaling of estrogen and progesterone affects insulin, leptin, and cortisol pathways, contributing to metabolic inflexibility.

Botanical interventions such as *Gymnema sylvestre* and white kidney bean extract have demonstrated supportive effects in glucose regulation, postprandial carbohydrate metabolism, and glycemic variability (Muddapur et al., 2024).

Ginger root supports digestive efficiency, thermogenesis, and inflammatory balance, while valerian root may indirectly support metabolic health by improving sleep quality, reducing sympathetic nervous system activity, and promoting cortisol regulation.

Skin, Gut Barrier, and Immune Resilience

Estrogen plays a central role in maintaining skin integrity, hydration, immune surveillance, and wound healing by regulating keratinocyte proliferation, collagen production, and sebaceous gland activity. During perimenopause, declining and fluctuating estrogen levels contribute to dryness, reduced elasticity, and increased inflammatory susceptibility.

Bovine collagen supplementation provides bioavailable amino acids necessary for connective tissue repair and has been associated with improvements in skin elasticity, dermal thickness, and joint comfort. Bovine colostrum contains immunoglobulins, lactoferrin, and growth factors that support gut barrier integrity and immune resilience during periods of hormonal stress (Ghosh & Iacucci, 2021).

Topical and adjunctive approaches, including peptide-based formulations, hyaluronic acid, and botanical compounds, further support dermal architecture, hydration, and lipid barrier restoration, helping to mitigate both visible and functional changes associated with early estrogen decline.

Pharmaceutical Options: Benefits and Limitations

Hormone replacement therapy remains one of the most effective interventions for managing vasomotor symptoms and urogenital atrophy. Current clinical guidelines emphasize individualized risk stratification, with transdermal estrogen and micronized progesterone demonstrating improved safety profiles compared to earlier oral formulations (North American Menopause Society [NAMS], 2023).

However, HRT does not directly address underlying metabolic dysfunction, environmental toxin burden, or gut health. It may also be contraindicated in individuals with hormone-sensitive cancers or elevated thromboembolic risk.

Non-hormonal pharmacologic options, including selective serotonin reuptake inhibitors (SSRIs) and gabapentin, can reduce vasomotor symptoms but are often associated with side effects such as fatigue, weight gain, or cognitive dulling (Sahni et al., 2021). Natural medicine approaches may therefore serve as a primary strategy during early perimenopause or as a complementary approach alongside pharmaceutical interventions.

Conclusion

Perimenopause represents a complex endocrine transition involving interconnected changes across hormonal, metabolic, neurological, and structural systems. It is not a singular event but a dynamic physiological process requiring a comprehensive and individualized approach.

Natural medicine strategies grounded in nutrition, botanicals, and lifestyle modification provide evidence-informed tools to support estrogen metabolism, regulate stress response, preserve connective tissue integrity, enhance mitochondrial function, and promote metabolic flexibility.

These approaches offer the potential to improve quality of life, extend healthspan, and complement pharmaceutical interventions when necessary. The integration of natural medicine into perimenopausal care reflects a broader shift toward preventative, patient-centered, and mechanistically informed models of women's health.

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