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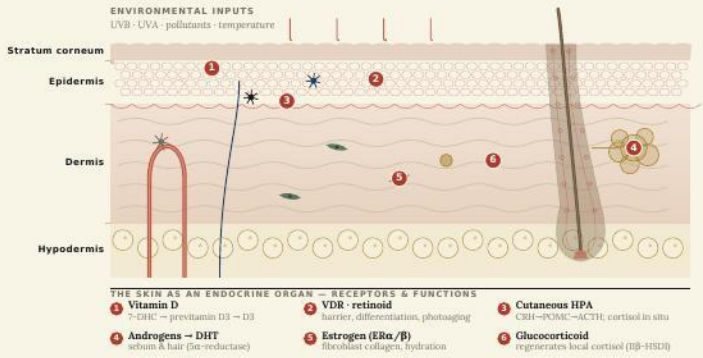
2026

A CLINICIAN'S POCKET GUIDE

Aesthetic & Regenerative Endocrinology

Optimizing the skin–endocrine system.



THE SKIN AS AN ENDOCRINE ORGAN

FADY HANNAH-SHMOUNI, MD FRCPC

Endocrinologist & Biochemical Geneticist
University of British Columbia

Founder & CEO, Hormonaly.ai

FIRST EDITION

A HORMONALY PRESS POCKET REFERENCE · 2026

Aesthetic & Regenerative Endocrinology

A pocket guide for the practitioner — optimizing the skin–endocrine system.

A concise, clinician-focused reference covering the physiology of endocrine aging, the decline of hormones and peptides over the lifespan, the organs of aging, and the evidence-graded interventions — peptides and bioregulators, hormone optimization, the gut, supplements and senotherapeutics, lifestyle and circadian medicine — through to the regenerative frontier of endocrine tissue replacement. With strength-of-evidence ratings and references throughout.

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How to use this guide

This pocket guide is built for the clinician who wants a clear, current picture of **aesthetic and regenerative endocrinology** — the optimization of skin, gut, and the endocrine axes for healthspan — without wading through a textbook. It moves in four parts: foundations, the organs of aging, interventions, and the regenerative frontier with a framework for practice. It is designed to be read in an afternoon or consulted at the point of care.

HOW EACH CHAPTER IS BUILT

- A one-line statement of the chapter's clinical idea, then focused prose with key terms in **bold**.
- **Inline citations**[1] point to a numbered *References* block at the foot of each chapter. Numbering *restarts at 1 in every chapter*, so a citation always refers to its own chapter's list, never a running total.
- **Strength-of-evidence pills (** GRADE A GRADE B GRADE C GRADE D **)** mark how good the evidence is for the *specific use* described — not the elegance of the biology, nor its marketing.
- Callout boxes carry the practical takeaway — and, in every chapter, **clinical pearls** for both testing and therapy.
- A closing "three things to remember" strip distills each chapter to its core.

STRENGTH OF EVIDENCE AT A GLANCE

FROM ESTABLISHED TO SPECULATIVE, WITH REPRESENTATIVE INTERVENTIONS · SCHEMATIC, NOT TO SCALE

SCOPE & INTENT

Evidence grades reflect evidence quality for the specific indication discussed, not biological plausibility or mechanistic elegance. This field attracts genuine advances and considerable hype; the guide states plainly what is established, what is a useful adjunct, and what remains investigational or unapproved. It is a reference, not a protocol, and not medical advice for any individual — it informs clinical reasoning but does not replace specialist input, formal guidelines, or individualized judgment. Approvals, compounding rules, and the evidence base change quickly: verify against current sources, and confirm every citation against the primary literature, before acting.

Contents

PART I · FOUNDATIONS

1 What is regenerative endocrinology? 4
2 The aging endocrine system 6
3 Peptides & bioregulators 8
4 Circadian & neuroendocrine timing 11

PART II · THE ORGANS OF AGING

5 The skin as an endocrine organ 13
6 The skin as a neuro-immuno-endocrine organ 19
7 The endocrine atlas of skin 25
8 The skin-glucocorticoid axis 29
9 Estrogen & skin aging 32
10 Endocrine disruptors, clean beauty & the skin 35
11 Adipose tissue as an endocrine organ 38
12 The gut-endocrine axis 41
13 Inflammaging & metabolic aging 44

PART III · INTERVENTIONS

14 Hormone optimization 47
15 Peptides & bioregulators for regeneration 50
16 The gut toolkit 54
17 Supplements & senotherapeutics 56
18 Lifestyle & circadian optimization 59

PART IV · FRONTIER & PRACTICE

19 Regenerative organ & tissue replacement 61
20 Putting it together 65

REFERENCE

The guide at a glance 67
Clinical pearls 68
Testing & interpretation reference 70
Drug safety, monitoring & contraindications 72
The regenerative-endocrinology consult 75
Regenerative therapy referral pathway 76
Clinical evidence hierarchy 77
Clinical algorithms 78
Appendix: inherited endocrine syndromes & the skin 83
Key references & further reading 87
About the author 88
Colophon 89

PART I · FOUNDATIONS — CHAPTER 1

What is regenerative endocrinology?

Using endocrine biology to extend the years lived in good health — not merely to chase a number.

Regenerative and aesthetic endocrinology applies the tools of endocrinology — hormones, signaling peptides, nutrient-sensing pathways, and the cell biology of repair — to the central goal of modern preventive medicine: extending **healthspan**, the span of life spent free of chronic disease and disability, rather than lifespan alone.[1] The aesthetic dimension is not vanity; the skin is the most visible readout of systemic endocrine and metabolic health, and the same processes that age it age the vasculature, the brain, and the bone.

The field rests on a unifying insight from geroscience: aging is driven by a finite set of interacting **hallmarks** — among them genomic instability, epigenetic drift, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem-cell exhaustion, altered intercellular communication, and chronic inflammation.[2,3] Hormonal decline both reflects and accelerates several of these. That is why an endocrine lens is powerful — and why it must be disciplined.

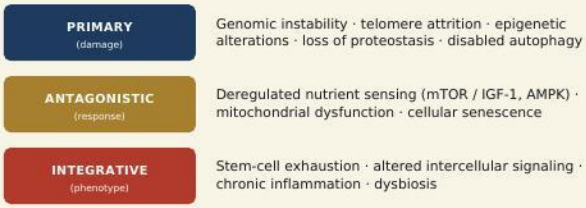

FIGURE 1.1 · THE HALLMARKS OF AGING — THE SUBSTRATE EVERY INTERVENTION IN THIS GUIDE ACTS UPON · SCHEMATIC

A FIELD THAT ATTRACTS HYPE

Few areas of medicine generate more enthusiasm — or more unproven product — than "regenerative" and "anti-aging" practice. This guide holds a deliberate line: it states what is **established** and clinically actionable, what is **emerging** and reasonable to discuss, and what remains **investigational** or frankly speculative. Every major claim carries a strength-of-evidence rating, and the regulatory

status of each agent is named plainly. The clinician's job is to separate biology that is real from a market that often outruns it.

CLINICAL DATA

~9 years — average lifespan–healthspan gap worldwide — years lived in poor health.[4]

1.0 → 2.1 billion — projected rise in adults aged 60+ between 2020 and 2050 (WHO).[5]

12 hallmarks — interacting aging processes in the 2023 update, expanded from the original nine — the substrate every intervention acts on.[3]

THREE THINGS TO REMEMBER

- Regenerative endocrinology aims at healthspan — disease-free, functional years — using hormonal, metabolic, and cellular tools.
- Aging is organized by interacting hallmarks; endocrine decline both signals and accelerates them.
- The discipline is in the rating: state what is established, what is emerging, and what is investigational — and never blur them.

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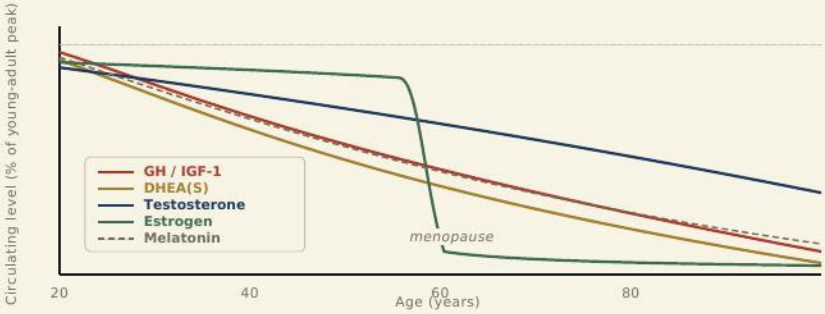
PART I · FOUNDATIONS — CHAPTER 2

The aging endocrine system

Each axis declines on its own schedule — the "-pauses" of endocrine aging.

Aging is not a uniform fade. Each endocrine axis follows a characteristic trajectory, and recognizing them is the first clinical skill in this field.[1] The **somatopause** is the progressive fall in growth-hormone pulse amplitude and IGF-1, beginning in the third decade and among the steepest of all.[2] **Adrenopause** is the parallel decline of DHEA and DHEA-sulfate, which by age 70–80 reach 10–20% of young-adult levels.[3] The **andropause** — better termed late-onset hypogonadism — is a gradual decline in total and (more steeply) free testosterone of approximately 0.5–2% per year, influenced by adiposity, illness, and rising SHBG.[4]

The female **menopause** is the exception: not a gentle slope but a cliff, with the loss of ovarian estradiol and progesterone over the perimenopausal transition, formally staged by STRAW+10.[5] **Thyropause** is subtler — TSH distributions shift upward with age, and modest subclinical changes are common and often benign in the very old. Melatonin amplitude and the robustness of cortisol's diurnal rhythm also blunt with age, themes returned to in Chapter 4.



Schematic; curves are illustrative, not to scale — rates and trajectories vary by individual

FIGURE 2.1 · CHARACTERISTIC ADULT DECLINE TRAJECTORIES OF MAJOR HORMONES — SCHEMATIC, NOT TO SCALE

INTERPRETATION CAVEAT

A low level on a lab report is not automatically a deficiency to be "corrected." Reference ranges are age-stratified for a reason, and much endocrine decline is physiologic. Treatment is justified by symptoms plus confirmed biochemical deficiency against an appropriate range — not by a number alone.

CLINICAL DATA

~0.5–2%/yr — fall in total testosterone after ~age 35–40; free testosterone falls faster as SHBG rises.[4]

~10–20% — of young-adult DHEA-sulfate remaining by age 70–80.[3]

~51 years — median age of menopause; estradiol falls >90% across the transition.[5]

~14% / decade — fall in growth-hormone secretion through adult life after the third decade (somatopause).[2,6]

THREE THINGS TO REMEMBER

- Each axis has its own clock: somatopause and adrenopause are steep and early; andropause is gradual; menopause is abrupt.
- DHEA(S) falls to a small fraction of peak by old age; free testosterone declines faster than total with rising adiposity.
- Physiologic decline is not disease — treat confirmed, symptomatic deficiency, not isolated low numbers.

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PART I · FOUNDATIONS — CHAPTER 3

Peptides & bioregulators

What signaling peptides actually are — and a hard line between mechanism and proof.

Peptides are short amino-acid chains that act as **signaling molecules**: hormones (insulin, GLP-1), releasing factors (GHRH), and local repair and growth factors. The growth-hormone axis is the prototype — GHRH and ghrelin stimulate, somatostatin inhibits, and synthetic **secretagogues** (GHRH analogs like CJC-1295; ghrelin-receptor agonists like ipamorelin) act on these receptors to raise pulsatile GH.[1,2] The mechanistic plausibility is genuine; long-term human evidence in healthy aging is not.

The **"bioregulator"** tradition — short peptides such as epitalon (pineal) and thymalin (thymic), associated with Khavinson — proposes tissue-specific gene-regulatory effects.[3] The mechanistic literature is intriguing, but the human evidence is sparse, largely small and from a single research lineage, and falls short of supporting routine use. No adequately powered, multicenter randomized trials demonstrating improved healthspan or lifespan exist.

Regulatory status reflects June 2026 and may change; verify current FDA guidance before prescribing.

REGULATORY REALITY — VERIFY BEFORE PRESCRIBING (STATUS JUNE 2026)

As of June 2026, the U.S. FDA peptide-compounding landscape remains unsettled. Several popular peptides have appeared on, been withdrawn from, or are now under review in relation to the 503A bulk-substance lists: a 2023 round placed many in **Category 2** (restricted), and in 2026 the FDA withdrew several from Category 2 and referred seven — BPC-157, KPV, TB-500, MOTS-c, DSIP (emideltide), semax, and epitalon — to its Pharmacy Compounding Advisory Committee (PCAC) for a 23–24 July 2026 meeting. Crucially, nomination, withdrawal from Category 2, or PCAC review is not FDA approval and does not by itself establish a settled lawful clinical compounding route; "research use only" is not a clinical loophole, and topical GHK-Cu (with limits) is the narrow Category 1 exception. Verify the current FDA 503A/503B lists, PCAC outcomes, and your state-board rules before clinical use.[4]

A DECISION FRAME: IS THIS PEPTIDE USABLE?

CATEGORY	WHAT IT MEANS	CLINICAL STANCE
FDA-approved drug	Approved for a defined indication (e.g. tesamorelin, semaglutide)	Prescribe on-label; standard monitoring.
Pharmacy-compounded (503A/503B)	Made by a licensed pharmacy from a substance on the positive bulks list	Lawful only if the substance is currently listed and criteria are met — verify the live list.
Dietary supplement	Sold as a supplement (e.g. oral collagen peptides); no disease claims	Discuss as a supplement; quality and dose vary.
Investigational / under PCAC review	Nominated or being reviewed; not approved	Trials or IND only — review is not approval.
Research-use-only (RUO)	Labeled "not for human use"; no GMP/QC guarantee	Not a clinical route; impurity, dose, and contamination risk.

CLINICAL DATA

503A status — a 2023 round restricted several peptides; by 2026 several were withdrawn from Category 2 and seven (BPC-157, KPV, TB-500, MOTS-c, DSIP, semax, epitalon) were referred to PCAC for 23–24 Jul 2026. Review is not approval — no settled lawful compounding route yet.[4]

No benefit — no RCT shows functional or healthspan benefit from GH secretagogues in healthy aging adults — body-composition shifts have not translated into clinical gain, and carry metabolic downsides.[2]

Single-lineage — most bioregulator (epitalon) human data come from small, largely one-center studies.[3]

Plausible, not proven — the mechanistic rationale for signaling peptides is genuine, but adequately powered, multicenter healthspan or lifespan trials do not yet exist.

"RUO" is not a route — research-use-only material carries no GMP or quality guarantee and is not a lawful clinical pathway — impurity, dose, and contamination are real risks.

THREE THINGS TO REMEMBER

- Peptides are signaling molecules; mechanistic plausibility is common, long-term human proof in healthy aging is rare.
- GH secretagogues act on the real GHRH/ghrelin axis but lack outcome evidence for "anti-aging" use.
- The FDA 503A peptide landscape is unsettled — substances have moved on, off, and into PCAC review in 2026; nomination, withdrawal, or review is not approval, so no settled lawful compounding route exists yet. Check the current FDA status.

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PART I · FOUNDATIONS — CHAPTER 4

Circadian & neuroendocrine timing

When a hormone is secreted matters as much as how much — and timing is modifiable.

The suprachiasmatic nucleus entrains a body-wide network of molecular clocks that gate metabolism, hormone secretion, and tissue repair across the 24-hour day.[1] Cortisol peaks near waking; growth hormone and most tissue repair are nocturnal and sleep-dependent; melatonin rises in darkness; insulin sensitivity is highest in the morning.[2] Aging blunts the **amplitude** of these rhythms — flatter cortisol curves, lower melatonin, fragmented slow-wave sleep — and that flattening is itself a driver of metabolic and immune decline.

Two levers are both potent and free. **Light** is the dominant zeitgeber: ordinary evening room light meaningfully suppresses and delays melatonin, degrading sleep quality and downstream repair.[3] The morning is the mirror image: stepping into outdoor light soon after waking — ideally within an hour — advances and stabilizes the central clock, the strongest daily anchor available.[4] Because the entraining signal is **ocular** — melanopsin-containing retinal cells that project to the SCN — the light must reach the **eyes** (go outside rather than rely on glass; never look straight at the sun). Letting it fall on the **body and skin** is a sensible bonus — the skin carries its own peripheral clocks, and morning time outdoors supports vitamin D and mood — but it does not replace ocular light, and it is no license for unprotected midday UV. **Meal timing** is the second: eating in alignment with the active phase — for example early time-restricted eating — improves insulin sensitivity and blood pressure even without weight loss.[5] Circadian alignment is the substrate on which every other intervention in this guide is built.

CLINICAL PEARL

Before adding any peptide, hormone, or supplement for "fatigue" or "poor recovery," fix the circadian basics first: consistent wake time, bright morning light, dim evening light, and a protected sleep window. Many presentations resolve here — at no cost and no risk.

CLINICAL DATA

≥10,000 lux — outdoor morning light, versus ~100–500 lux indoors; get it into the eyes within about an hour of waking.[4]

0.3–0.5 mg — physiologic melatonin dose — far below the typical 3–10 mg in OTC products.[6]

~100 lux — ordinary evening room light is enough to suppress and delay melatonin.[3]

Weight-neutral — early time-restricted eating improved insulin sensitivity and blood pressure without weight loss.[5]

THREE THINGS TO REMEMBER

- Hormone secretion is rhythmic; aging flattens rhythm amplitude, which itself harms metabolism and immunity.
- Bracket the day with light: outdoor morning light into the eyes anchors the clock (body and skin exposure is a bonus, not a substitute), while dim evening light protects melatonin.
- Eating earlier in the active phase improves insulin sensitivity independent of weight loss.

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PART II · THE ORGANS OF AGING — CHAPTER 5

The skin as an endocrine organ

The most visible readout of systemic endocrine and metabolic aging.

Skin aging proceeds on two tracks. **Intrinsic (chronological) aging** thins the epidermis and dermis, reduces collagen by roughly 1% per year, fragments the elastic network, and lowers fibroblast output — changes first quantified decades ago.[1] **Extrinsic aging**, dominated by ultraviolet exposure, drives matrix-metalloproteinase activation that degrades collagen faster than it is replaced, producing the coarse wrinkling and dyspigmentation of photoaging; glycation and smoking compound it.[2]

Crucially, the skin is not a passive recipient of hormones — it is a peripheral **endocrine organ** that expresses receptors for, and locally synthesizes, a broad range of signaling molecules, and performs its own steroidogenesis.[3,4] The table summarizes the major circulating inputs; the sections that follow add the detail and the locally produced peptides that the table cannot hold.

ENDOCRINE INPUT	CUTANEOUS ROLE
Estrogens	Collagen synthesis, dermal thickness, hyaluronan, barrier hydration, wound healing; menopausal loss drives thinning, dryness, lost elasticity
Androgens (T → DHT via 5α-reductase)	Sebaceous size and sebum → acne, seborrhea, hirsutism, androgenetic alopecia; skin is itself a site of androgen metabolism
Glucocorticoids (cortisol)	Dermal atrophy, suppressed collagen, impaired healing, striae; local cutaneous HPA axis (Chapter 8)
Vitamin D (calcitriol)	Keratinocyte proliferation and differentiation, barrier, cutaneous immunity; synthesis begins in skin via UVB
DHEA, progesterone	Modest, largely precursor-driven roles in local steroidogenesis
Thyroid (T3 / T4)	Epidermal turnover, sebum and sweat, hair cycling; hypo → dry, coarse, cool skin; hyper → warm, moist skin
GH / IGF-1	Fibroblast proliferation, collagen, dermal thickness; IGF-1 raises sebum; insulin resistance → acanthosis nigricans

ENDOCRINE INPUT	CUTANEOUS ROLE
Melanocortins (α-MSH, ACTH)	POMC-derived; melanogenesis via MC1R; anti-inflammatory
Prolactin, oxytocin	Cutaneous receptors; hair-follicle biology, sebaceous function, wound healing
PTHrP (local)	Regulates keratinocyte proliferation and differentiation

STEROID HORMONES

Estrogens are probably the single most influential class for skin quality: they stimulate fibroblast collagen synthesis, raise dermal thickness and hyaluronic-acid content, support barrier hydration, and accelerate wound healing, so the post-menopausal estrogen drop drives much of the thinning, dryness, and lost elasticity of aging skin.[5,6] **Androgens** — testosterone and, more potently, DHT generated locally by 5α-reductase — enlarge sebaceous glands and raise sebum, making them central to acne, seborrhea, hirsutism, and androgenetic alopecia; the skin is itself a site of androgen metabolism.[4] **Glucocorticoid** excess thins the dermis, suppresses collagen, impairs healing, and produces striae, through both systemic cortisol and a local cutaneous HPA-type axis — relevant to Cushing's and to chronic stress alike (Chapter 8). The hormonal form of **vitamin D** (calcitriol) governs keratinocyte proliferation and differentiation and modulates cutaneous immunity, and its synthesis begins in the skin under UVB;[7] DHEA and progesterone play more modest, partly precursor-driven roles.

THYROID HORMONES

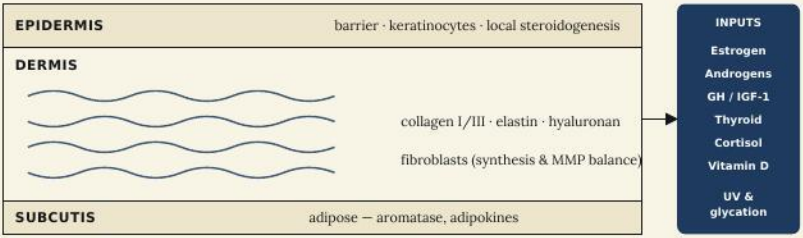
T3 and T4 govern epidermal turnover, sebum and sweat secretion, and hair cycling. **Hypothyroidism** gives dry, coarse, cool skin and myxedema; **hyperthyroidism** gives warm, moist skin and, in Graves' disease, pretibial myxedema.[8]

PEPTIDE AND PROTEIN HORMONES

Growth hormone and IGF-1 promote fibroblast proliferation, collagen synthesis, and dermal thickness; IGF-1 also stimulates sebaceous activity, part of why high-glycemic, high-insulin states track with acne,[9] while marked insulin resistance surfaces cutaneously as acanthosis nigricans. The **melanocortins** α-MSH and ACTH — both POMC-derived — drive melanogenesis through MC1R and are anti-inflammatory in skin.[3] **Prolactin and oxytocin** have cutaneous receptors with roles in hair-follicle biology, sebaceous function, and wound healing,[10,11] and locally produced **PTHrP** regulates keratinocyte proliferation and differentiation.[4]

SKIN AS A SIGNALING TISSUE

A large amount of skin biology runs on paracrine and autocrine peptides rather than circulating hormones: **EGF** and **FGF7/KGF** for keratinocyte proliferation, **TGF-β** for fibroblast activation and scarring, **VEGF** for angiogenesis, and **PDGF** for wound repair.[12] Neuropeptides such as **substance P** and **CGRP** mediate neurogenic inflammation, itch, and vasodilation,[13] while the antimicrobial peptides **cathelicidin (LL-37)** and the defensins anchor barrier immunity — with LL-37 specifically implicated in rosacea.[14,15] Locally synthesized melatonin and β-endorphin add antioxidant and stress-response layers.[3]



The skin both responds to and synthesizes hormones — a peripheral endocrine organ

FIGURE 5.1 · SKIN ARCHITECTURE AND ITS HORMONAL INPUTS · SCHEMATIC, NOT TO SCALE

WHAT THE EVIDENCE SUPPORTS

Among topical agents, **retinoids** have the strongest dermatologic evidence for reversing measurable signs of photoaging and remain first-line GRADE A. For systemic **menopausal hormone therapy**, skin benefit is real but secondary — never an indication on its own.[6] Oral **collagen peptides** show modest improvements in hydration, elasticity, and wrinkle parameters in randomized trials, though most are small and industry-funded GRADE C,[16] and topical **GHK-Cu** has decades of mechanistic and small-trial support for collagen stimulation GRADE C.[17] The familiar "cosmetic peptides" borrow directly from this endogenous signaling: signal peptides such as palmitoyl pentapeptide-4 (Matrixyl) and copper tripeptide GHK-Cu target matrix and collagen, and neuromodulatory acetyl hexapeptide-8 (Argireline) softens expression lines — generally with modest, small-trial evidence GRADE C.[18]

COSMETIC & AESTHETIC ENDOCRINOLOGY

Although not a formally recognized subspecialty, these threads are increasingly discussed together under the label **cosmetic (aesthetic) endocrinology** — a descriptive framing for a familiar clinical activity. In practice it means treating

endocrine pathophysiology to improve the cosmetically bothersome findings patients present with — most prominently the hirsutism, androgenetic alopecia, and acne of PCOS and hyperandrogenism.[19,20] The skin is its organ, and a growing literature frames the skin explicitly as an endocrine tissue that both produces and responds to hormones.[21]

The estrogen–skin axis is the best-developed lever. Because sex steroids are small lipophilic molecules, they can be delivered topically for local effect with limited systemic exposure;[20] oral or topical estrogen slows — though it cannot reverse — post-menopausal skin aging, improving collagen, thickness, and hydration, and selective estrogen-receptor modulators (SERMs) are being explored to capture that benefit more selectively.[22,23] The axis also runs through stress: psychological stress, acting via the HPA axis and androgens, is associated with acne — a reminder that a cosmetic complaint is often a systemic readout.[24]

The lever cuts both ways. Because each of these findings is downstream of a hormonal driver, treating the endocrine cause is often the most durable cosmetic intervention — more so than a topical measure applied to the surface alone. Suppressing ovarian and adrenal androgen output (a combined oral contraceptive, spironolactone, or 5α-reductase inhibition) improves the acne, seborrhea, and hirsutism of hyperandrogenism; restoring euthyroidism reverses the dry, coarse skin and diffuse shedding of hypothyroidism; and correcting hypercortisolism resolves the dermal thinning and easy bruising it drives. The discipline of the field is to read the skin as a presenting sign, identify the axis behind it, and treat that axis to its guideline target — rather than chase the visible finding in isolation.

CLINICAL PEARL — THE AESTHETIC EXAM IS A SYSTEMIC SCREEN

Sudden skin thinning and easy bruising suggest cortisol excess; coarse, dry, cool skin suggests hypothyroidism; new acanthosis nigricans flags insulin resistance; rapid photoaging tracks UV, glycation, and smoking. Read the skin as a window on the whole endocrine system before reaching for a serum.

CUTANEOUS SIGNS OF ENDOCRINE DISEASE — QUICK REFERENCE

SKIN FINDING	POINTS TO
Acanthosis nigricans	Insulin resistance / hyperinsulinemia (T2D, PCOS, obesity)
Hirsutism, persistent acne	Androgen excess (PCOS, CAH, androgen-secreting tumor)
Violaceous striae, easy bruising, thin skin	Cortisol excess (Cushing syndrome)
Dry, coarse, cool skin; periorbital puffiness	Hypothyroidism
Flushing	Carcinoid, pheochromocytoma, menopause, rosacea
Hair loss (diffuse or patterned)	Thyroid disease, androgen excess, telogen effluvium

REFER TO ENDOCRINOLOGY PROMPTLY IF

Suspected Cushing syndrome (violaceous striae, central obesity, proximal weakness, new hypertension or diabetes). · Rapidly progressive virilization (deepening voice, clitoromegaly, rapid hirsutism) — possible androgen-secreting tumor. · Severe or rapidly progressive alopecia areata. · Unexplained weight loss. · Signs of an endocrine tumor (new galactorrhea, visual-field loss, a neck mass, refractory hypertension).

CLINICAL DATA

~30% in 5 yr — fall in skin collagen in early postmenopause, then ~2%/yr thereafter.[5]

2.5–10 g/d — oral collagen-peptide dose improving skin hydration and elasticity in RCTs.[16]

Topical GHK-Cu — decades of mechanistic and small-trial support for collagen synthesis.[17]