



MENOPAUSE AND THE SKIN



The impact and potential mitigation of estrogen loss

BY JENNIFER B. PEARLMAN, MD, CCFP, NCMP, FAARM, ABAARM, CFA

Of all the hormones affecting the skin, estrogens are perhaps the most influential. Estrogens have widespread proteogenomic effects on the skin's structure and function. Estrogen binds both cellular and nuclear receptors and modulates epidermal keratinocytes, dermal fibroblasts, melanocytes, and skin appendages, including hair follicles and sebaceous glands.¹

Estradiol is the predominant form of estrogen throughout a woman's reproductive lifespan and is integral

to supporting healthy skin. Estradiol promotes collagen and elastin production, accelerates wound healing, reduces skin inflammation, and protects against skin photoaging and photocarcinogenesis.^{2,3,4} Throughout the menstrual cycle, skin thickness varies in relation to changes in estradiol levels and is thickest mid-cycle during ovulation.

MENOPAUSE AND THE SKIN

At menopause, a precipitous decline in estrogen leads to an acceleration

of aging. The loss of ovarian estradiol production results in deleterious effects in many tissues, including the brain, heart, vasculature, bone, gastrointestinal system, and skin. Rapid skin aging occurs during menopause, as the hypoestrogenemic state is marked by increased skin wrinkling, laxity, dryness, and vascularity. The barrier function of the skin is diminished due to loss of estrogen, resulting in higher risk of UV-associated aging and skin cancer.

The menopausal loss of estrogen produces accelerated aging of the peri-oral region. The oral lips, much like the vaginal labia, can be considered a biomarker of tissue estrogen levels. Estrogen loss leads to perioral rhytids, aging of the lips with volume loss, dryness and pallor, elongation of the nasal tip to lip distance, and downward descent of the lateral commissure, extending into a deep furrow in the marionette region and eventually forming the jowl. Together, these changes can be considered the "sag sign" of menopause.

The collagen content of skin decreases by 30% in the first 5 years after menopause,⁵ occurring in tandem with a decrease in bone density. Estrogen therapy after menopause has been shown to increase skin hydration

and thickness along with collagen and elastin content, and reduce photoaging. Women who take estrogen after menopause with or without progesterone demonstrate significantly fewer wrinkles.

A new generation of hormone modulating cosmeceuticals aims to leverage estrogen's beneficial effects on the skin. The use of exogenous estrogen therapy, estrogen metabolites, selective estrogen receptor modulators (SERMs), and activators of non-genotrophic estrogen-like signaling molecules (ANGELs) holds promise for mitigating menopause-associated accelerated skin aging.

BIOREGENERATIVE THERAPIES AND HYPOESTROGENEMIC SKIN

The emerging field of regenerative medicine is unlocking the secrets to reversing aging. Cellular therapies and genomic medicine aim to harness the retained potential of adult somatic cells to be reprogrammed to a younger, healthier state. Treatments such as stem cells, exosomes, and biostimulators activate the regenerative potential of dermal fibroblasts to produce more collagen and elastin fibers,



as well as support the extracellular matrix. Poly-L-lactic acid (PLLA), marketed as Sculptra® in North America, has been approved for cosmetic use since 2008 by the US Food and Drug Administration. PLLA is widely used to treat skin wrinkling and aging, and its

ability to activate collagen remodeling and promote adipogenesis of subcutaneous fat has been confirmed through genomic studies. The increase in subcutaneous fat serves as a peripheral source of estrone in estrogen-depleted post-menopausal women. The enzyme aromatase converts circulating androgens into estrone in the adipose tissue and skin, providing a local and systemic source of estrogen. Thus, triggered peripheral estrogen biosynthesis by aromatase in adipocytes and dermal fibroblasts plays an important and underrecognized mechanism through which bioregenerative therapies exert their rejuvenating effects.

ESTROGEN AND BIOREGENERATIVE COMBINATIONS

Hormonal optimization and estrogen repletion play an important role in addressing skin health, appearance, and aging in the post-menopausal or estrogen-depleted patient. Systemic estrogen used in combination with progesterone for women with an intact uterus is a cornerstone to

AT A GLANCE

- Rapid skin aging occurs during menopause, as the hypoestrogenemic state is marked by increased skin wrinkling, laxity, dryness, and vascularity.
- The use of exogenous estrogen therapy, estrogen metabolites, selective estrogen receptor modulators (SERMs), and activators of non-genotrophic estrogen-like signaling molecules (ANGELs) holds promise for mitigating menopause-associated accelerated skin aging.
- The use of systemic estrogen in conjunction with bioregenerative aesthetic treatments such as biostimulators and exosomes can mitigate the accelerated aging of post-menopausal skin.

addressing symptoms, disease risk, and accelerated aging at menopause.

The use of systemic estrogen in conjunction with bioregenerative aesthetic treatments such as biostimulators and exosomes can mitigate the accelerated aging of post-menopausal skin.

ESTROGEN AND SKINSPAN

In addition to the arsenal of aesthetic medical interventions, menopausal hormone optimization therapy (HOT) can play an important role in enhancing healthy lifespan and skin's health, appearance and aging.

Aging is not inevitable. The health, appearance, and aging of our skin can be proactively managed with a targeted and multi-modal approach. ■

1. Stevenson S, Thornton J. Effect of estrogens on skin aging and the potential role of SERMs. *Clin Interv Aging*. 2007;2(3):283-97.
2. Shah MG, Maibach HI. Estrogen and skin. An overview. *Am J Clin Dermatol*. 2001;2(3):143-50.
3. Archer DF. Postmenopausal skin and estrogen. *Gynecol Endocrinol*. 2012;28 Suppl 2:2-6.
4. Cahoon EK, Kitahara CM, Ntowe E, Bowen EM, Doody MM, Alexander BH, Lee T, Little MP, Linet MS, Freedman DM. Female Estrogen-Related Factors and Incidence of Basal Cell Carcinoma in a Nationwide US Cohort. *J Clin Oncol*. 2015;33(34):4058-65.
5. Thornton MJ. Estrogens and aging skin. *Dermatoendocrinol*. 2013;5(2):264-70.

JENNIFER PEARLMAN, MD, CCFP, NCMP, FAARM, ABAARM, CFA

- Medical director and owner, PearlMD, Toronto, Ontario, Canada
- Staff physician, Mount Sinai Hospital Toronto, Ontario, Canada
- Financial disclosure: None

