Skin Disorders During Menopause

Gleison V. Duarte, MD, PhD; Ana Cláudia Moura Trigo, MD; Mária de Fátima Paim de Oliveira, PhD

PRACTICE POINTS
- Frontal fibrosing alopecia may respond to finasteride or dutasteride.
- Acute and chronic telogen effluvium may be associated with iron deficiency, mostly related to malabsorption or chronic gastrointestinal bleeding, during perimenopause.
- Oral and topical isoflavones may reduce skin aging in menopausal women.
- The use of estrogens as hormone replacement therapy in menopausal women promotes an increase in skin thickness and/or collagen content.

Menopause is the cessation of menstrual periods due to the loss of ovarian function. Among the various phases of a woman’s life, menopause has the greatest impact on health and has been one of the most neglected areas of research. Hormonal changes caused by menopause can lead to problems in the skin and its annexes, and despite the high frequency of dermatologic signs and symptoms, studies on this topic are limited. In this article, we review the skin disorders that result from the hormonal changes of menopause and other common dermatoses observed during this period and assess possible therapeutic approaches.


In 1983 the Brazilian Ministry of Health launched the Program for Integrated Women’s Health Care following a worldwide trend to adopt multidisciplinary approaches that consider the complexity of women’s health. Although menopause may have the greatest impact on women’s health among all the stages of life, research on this topic is limited. Due to the aging general population, both the proportion of women who are menopausal and the total population of menopausal women have increased. On average, women in developed countries spend one-third of their lives in menopause; thus, the physiology of menopause has become a matter of public health. In a survey of 87 women attending a specialist menopause clinic, more than 64% reported prior skin problems. Despite the high frequency of dermatologic signs and symptoms associated with menopause, few studies have been conducted on the subject. In this article, we review some of the common skin disorders that occur during menopause and assess possible therapeutic and preventive skin care approaches.

Stages of Menopause

During perimenopause, irregular menstrual cycles and a series of clinical manifestations occur that may precede menopause by 2 to 8 years. The term menopausal transition is used by the World Health Organization to describe the phase of perimenopause prior to the end of menstrual periods. The World Health Organization also suggests that the term...
climacterium should be substituted for perimenopause in the period ranging from just before the onset of menopause to 1 year after menopause. Climacterium is the period of transition between the last years of the reproductive stage and postreproductive life, which begins with the gradual disappearance of ovarian function.8

Menopause is the cessation of menstrual periods due to the loss of ovarian function and is a normal physiologic process in women when it occurs after the fifth decade of life. The mean age at menopause is 51 years, and the clinical criterion used to establish the diagnosis is complete absence of menstrual periods for 12 months.6 Throughout a woman's life, the total number of primordial ovarian follicles decreases and most become refractory to the actions of pituitary gonadotropins. As a result, the circulating level of estradiol progressively decreases and progesterone production by the corpus luteum becomes irregular and subsequently ceases.8 Increased production of follicle-stimulating hormone and luteinizing hormone occurs as a consequence. Conversely, the changes in circulating androgens are more complex and controversial.9 It has been documented that testosterone production is lower in postmenopausal patients and that sex hormone–binding globulin decreases and the free androgen index increases. Dehydroepiandrosterone sulfate linearly declines as a function of age, but it lacks an obvious relationship with ovarian function.10

The Importance of Hormones on the Skin

Ovarian failure and the resulting hormonal changes during menopause affect almost all aspects of women's health and may present with signs and symptoms in nearly every body system.1 Symptoms are experienced differently according to ethnic, educational, and sociocultural variability. Asian American women report a low frequency of physical, psychological, and psychosomatic symptoms compared with black women.11 Brazilian women have a higher prevalence of vasomotor symptoms compared to women in other developed Western countries.12 Also, medications used during perimenopause to prevent and treat osteoporosis are capable of inducing hot flashes.13

Estrogens are essential for skin hydration because they increase production of glycosaminoglycans, promote an increased production of sebum, increase water retention, improve barrier function of the stratum corneum, and optimize the surface area of corneocytes. As a result, concerns about dry skin are more frequent among menopausal women who are not taking hormone replacement therapy (HRT).2 Decreased estrogen reduces the polymerization of glycosaminoglycans, while elastin experiences granular degeneration and fragmentation, forming cystic spaces. In addition, there is a reduction in the microvasculature and thinning of the epidermis.14,15

Albright et al16 noted that the skin of menopausal women with osteoporosis showed considerable atrophy, a finding subsequently supported by a study from Brincat et al.17 In menopausal women, the decrease in estrogen promotes a reduction in type I and type III collagen and a reduction in the type III collagen to type I collagen ratio compared with nonmenopausal women.18 Healthy skin is made up of type I collagen (80%, responsible for strength) to type III collagen (15%, responsible for elasticity).2 However, a decrease in androgens is partially responsible for the reduction in sebum secretion, xerosis, and skin thinning or atrophy, accompanied by a reduction in blood vessels, oxygenation, and nutrition of the skin as well as increased transepidermal water loss.19,20 Regarding skin annexes, the decrease in estrogen causes a reduction in axillary and pubic hair. The reduction in elastic fibers results in a loss of firmness and elasticity. Moreover, with a relative predominance of androgenic hormones, vellus hair may be replaced by thicker hair.21

Anagen hairs have estrogen receptors in both sexes. In contrast to the α-receptor, the β-receptor largely is expressed in the papillary dermis and the hair's bulb region; this expression could account for the occurrence of androgenetic alopecia in menopausal women. These receptors are not expressed in telogen hairs, and their role in regulating the hair cycle is unknown.20 The aging of the follicular unit, resulting from the reduction of active melanocytes, promotes the appearance of gray hair. It is estimated that in 50% of men and women, half of their hair will be gray by 50 years of age.21 The age of onset for graying hair appears to be influenced by heredity and ethnicity. Unlike the skin, hair aging is more affected by intrinsic than extrinsic factors.22,23

In women, hormonal changes during menopause are the main source of alterations in hair characteristics.24 The identification of high concentrations of hydrogen peroxide and low levels of catalase in the stems of gray hairs have shed light on the biochemistry of hair whitening and opened new possibilities for its prevention and treatment. A change in the balance of oxidation/reduction reactions may lead to DNA damage and melanocyte apoptosis.22,25

Osteoporosis and Vitamin D

Concerns about the worsening of or induction of osteoporosis after menopause due to the excessive use of sunscreens and vitamin D (VD) deficiency are controversial. Middle-aged women with low serum
25-hydroxyvitamin D levels (<20 ng/mL) have an increased risk of fracture during menopausal transition. A study that measured the UV index in São Paulo, Brazil, demonstrated that environmental levels ensure sufficient production of VD from unintentional sun exposure throughout the course of the year. Thus, concerns about the use of sunscreen affecting VD levels are not justified.

In a study that specifically focused on postmenopausal women in Recife, Brazil (which is located 10º south of the equator), a considerable prevalence of VD deficiency was found, ranging from 30% to 83% depending on age. Despite the abundance of sunlight, the researchers emphasized that the VD prevalence rates found in the study were similar to those observed in nontropical countries, such as the United States and Canada; however, the period of intentional exposure to the sun was not assessed. Moreover, the lack of consensus on the appropriate levels of sun exposure makes it difficult to compare different countries, and thus it is recommended that minimum normal limits be regionally established.

Although it has been suggested that the use of sun protection factor 15 could, in theory, promote a 99% reduction in the synthesis of VD, other studies have failed to identify such an insufficiency. In practice, the disparity may be explained by the large variation in the amount of sunscreen applied, by the body areas to which it is applied, and by the fact that duration of sun exposure usually is greater when using sunscreen.

Considering all the evidence and taking into account that the safe limit for sun exposure that allows maximum synthesis of VD without an increased risk for skin cancer remains unknown, the American Academy of Dermatology states that intentional exposure to the sun should not be considered a main source of sun exposure and the use of sunscreen should not be discouraged. Instead, the Academy recommends using dietary sources of VD or artificial VD supplementation at doses that vary by age: between 1 and 70 years, a dose of 600 IU daily is recommended; older than 70 years, 800 IU daily.

**Primary Skin Disorders of Menopause**

**Pruritus**—Pruritus is the primary skin concern in women older than 65 years. Given that xerosis is the most prominent cause of pruritus, consider the possible role of menopause-related transepidermal water loss. Regardless of the underlying cause, however, some general measures are recommended for managing pruritus in menopausal women such as using low-pH moisturizers daily, preferably after bathing; keeping nails short; wearing loose and light clothing; maintaining a comfortable ambient temperature; using humidifiers or air-conditioning devices; restricting bathing time; and avoiding hot water and high-pH sanitizers.

**Hyperhidrosis**—Night sweats, hyperhidrosis, and hot flashes (flushing) are common concerns in 35% to 50% of perimenopausal women and in 30% to 80% of postmenopausal women. Menopausal hyperhidrosis is classified as secondary hyperhidrosis, the symptoms of which may be alleviated by HRT, suggesting that the cause is decreasing levels of estrogen.

In addition to HRT, other treatments such as gabapentin, serotonin-norepinephrine reuptake inhibitors, and acupuncture are used to treat menopausal hyperhidrosis. One study evaluated the use of oxybutynin for 3 months in 21 patients with menopausal hyperhidrosis, and the authors concluded that the drug was effective and well tolerated in women who were nonresponsive to HRT.

**Senile Alopecia**—Starting at 50 years of age, scalp hairs show varying degrees of change in pigmentation, growth, and diameter. Despite the normal ratio of telogen to anagen hair, there may be a considerable reduction in follicular density. The clinical distinction between senile alopecia and androgenetic alopecia can be challenging, and the conditions may coexist.

**Androgenetic Alopecia**—Up to 50% of women experience androgenetic alopecia, or female pattern hair loss (FPHL), during their lives. It is the main cause of hair loss in women, and women in perimenopause are the most affected. Hair regrowth is difficult when treatment is not instituted early in perimenopausal FPHL. The pathogenesis involves a progressive reduction in the hair cycle, resulting in shrinkage of the hair follicles. Unlike the pathogenesis of androgenetic alopecia in men, little is known about the role of androgens in FPHL. The measurement of androgen levels is not recommended in the absence of symptoms of virilization or in the absence of abnormal clinical patterns or progression.

Three clinical forms of FPHL have been described: (1) Ludwig classification (diffuse central thinning concentrated in the parieto-occipital region with the frontal hairline intact), (2) Olsen classification (thinning of the central line and a consequent Christmas tree pattern), and (3) Hamilton classification (frontotemporal or vertex recession, which is seen less often than the other 2 forms). Female pattern hair loss primarily is treated with a 2% to 5% minoxidil solution, which is able to interrupt hair loss or induce mild to moderate regrowth in 60% of patients with FPHL. The effectiveness of
the treatment should only be assessed after 1 year of use. Contact dermatitis is the main adverse effect, but its incidence may be reduced by up to 82% by using vehicles that do not contain propylene glycol. If the use of minoxidil solution is not possible, good results also have been reported with antiandrogen medications, such as spironolactone. These drugs are especially useful in cases of hyperandrogenism.

Conventional doses of finasteride 1 mg daily, as used in men, have shown discrepant results in menopausal women. Improvement of FPHL has been shown in studies using doses of 2.5 mg or higher for a minimum of 12 months. The use of dutasteride, an inhibitor of 5α-reductases I and II, promotes greater inhibition (100%) of dihydrotestosterone activity than finasteride (70%) in men; however, it has not yet been approved by the US Food and Drug Administration for treatment in women.

Impaired Wound Healing—Wound healing also is affected by aging. Delays in healing may be more closely related to the decrease in estrogen levels than to intrinsic aging. A comparison between the expression of genes associated with healing in young and elderly men showed that most of the genes are regulated exclusively by estrogen, which could explain the higher incidence of chronic ulcers in elderly men compared to women. However, menopausal women also are at risk for development of chronic ulcers. Ashcroft et al showed that the use of topical estrogen accelerates the healing of acute incisional wounds by increasing transforming growth factor β.

Healing of the oral mucosa is associated with a higher rate of complications and longer recovery time in women than in men. Estrogens produce anti-inflammatory effects, whereas progesterone demonstrates a proinflammatory effect. Testosterone has anti-inflammatory effects and is able to modify the proinflammatory state in the oral mucosa of menopausal women. Wound healing in menopausal women who are not receiving HRT tends to be slower than in those who are receiving HRT. Age is not necessarily an important factor in wound healing. Premenopausal and younger women have shown no notable differences in healing. Nevertheless, after menopause, differences in wound healing have been found, indicating that hormonal status may be more crucial to wound healing than age.

Common Dermatoses With No Hormonal Associations

Brittle Nail Syndrome—Brittle nail syndrome (BNS) affects 20% of the population with a female-to-male ratio of 2:1. The pathogenesis of BNS involves factors that affect the adhesion of corneocytes to the nail plate and alter nail formation from its matrix; the former process produces onychoschizia, whereas the latter leads to onychorrhexitis.

The normal nail contains approximately 18% water, and nails with less than 16% water content are more likely to develop weakness. Nail water content appears to be negatively influenced by repetitive occupational exposure to water, and its increase is proportional to the frequency of moisturizer use. The use of certain nail polishes and cuticle removers is considered one of the main reasons for nail weakness in those who have frequent manicures.

Management of BNS requires the correction of the precipitating cause by hydration of the nail blade, cuticle, and proximal nail folds, preferably under occlusion. Supplementation with biotin is considered highly effective by many researchers. In a retrospective study, the use of biotin for 6 months improved BNS in 63% (22/35) of patients. Recommended doses generally are more than 2.5 mg daily. The use of 10% urea in nail polish once or twice daily showed that both regimens improved the morphology, consistency, and reflectiveness of the nail plate.

The use of nail polish containing hydroxypropyl chitosan, Equisetum arvense extract, and methylsulfonylmethane has been reported as a treatment of dystrophic and fragile fingernails. The treatment was evaluated in patients with nail psoriasis and it was shown to be effective in decreasing dystrophy.

Although women are affected twice as frequently as men, there are no known studies comparing the prevalence of BNS in premenopausal versus menopausal women, despite the fact that the ratio of women to men affected has been shown to increase with age. In our clinical practice, BNS predominates among menopausal women. We believe that low estrogen levels may lead to dehydration of the nail plate.

Frontal Fibrosing Alopecia—Frontal fibrosing alopecia has a tendency to affect menopausal women. Frontal fibrosing alopecia is a slow, progressive, lymphocytic cicatricial alopecia that produces symmetrical frontal or temporal recession but rarely affects other areas of the scalp. It often is associated with nonscarring alopecia of body hair or eyebrows. The cicatricial area is atrophic, pale, and surrounded by hyperpigmented skin due to long-term sun damage.

Many investigators believe it is a variant of lichen planopilaris. Others suggest the possibility that hormonal changes characteristic of perimenopause contribute to triggering the disease. Some cases show a partial response to finasteride or...
Telogen Effluvium—Telogen effluvium (TE) is the premature transformation of hair from the anagen phase to the telogen phase. Considered a symptom of an underlying condition (eg, endocrine, nutritional, and autoimmune disorders) rather than a full diagnosis in itself.60-63 TE is characterized by diffuse hair loss confirmed by a pull test in which more than 5 hairs are removed from the scalp on tugging a section of 25 to 50 hairs.56 If there is concurrent TE in women with androgenetic alopecia, more severe hair loss has been reported.24,66 There may be concerns of dysesthesia of the scalp (trichodynia), especially in patients with emotional stress.66

Most often diagnosed in women, TE in its acute form is even more common in menopausal women and lasts less than 6 months.24 The acute form of TE is secondary to hemorrhage, high fever, surgery, drug use, systemic diseases, diet, or great psychological stress and typically occurs 1 to 3 months after the primary event.24,66 The most common cause of iron deficiency at menopausal transition is malabsorption or chronic gastrointestinal bleeding. Ferritin levels below 40 µg/L are associated with hair loss with a 98% specificity and sensitivity.64 Low serum levels of vitamin B12 or vitamin D also are considered important factors.24,65-66

Chronic TE (ie, lasting more than 6 months) predominantly occurs in women aged 40 to 60 years, and its onset is abrupt. Chronic TE is considered a diagnosis of exclusion.24 In 30% of cases of chronic diffuse hair loss lasting longer than 6 months, the cause is unknown.67 The pathogenesis is poorly understood, though it is assumed to result from a reduced duration of the anagen growth phase in the absence of shrinking hair follicles.37-68

Patient education is the most important aspect of TE management. The aim of treatment is to reduce hair loss and correct the precipitating factors. Even if the underlying cause is corrected, hair loss may continue for up to 6 months with the desired cosmetic regrowth occurring after only 12 to 18 months.37,65 In acute secondary TE, the course of the disease is self-limited, and correction of the causal factor is sufficient. In chronic diffuse loss, identification of causal factors is more difficult and treatment involves adequate nutrition (ie, at least 1200 calories daily including 9.8 mg/kg body weight of protein) and multivitamin supplementation, minoxidil, and even antiandrogen medications.37,65-67

Trichotillomania—Trichotillomania is the compulsive behavior of plucking strands of hair and is considered to be a poor adaptive response to stress. Although trichotillomania most commonly occurs in children, adolescents, and young adults, in older adults it is more often associated with psychopathology and is markedly more common in women.59 The condition usually is refractory to treatment, and although the scalp usually is the primary focus of the behavior, eventually patients may pluck body hair. Menopausal women also may present with trichotileiromania in which hair loss is secondary to repeated friction that has fractured the hair shaft; this condition often is associated with scalp dysesthesia.24 Trichotillomania is considered an obsessive-compulsive disorder, whereas trichotileiromania needs further investigation because it can occur secondary to many psychiatric disorders. The specific psychotherapeutic and pharmacologic treatments likely will depend on the underlying cause of the disease.70

Treatment of Skin Disorders in Menopausal Women

Classic HRT—Several studies have used histologic analysis or ultrasonography to show that estrogens used in HRT thicken the skin or increase collagen content, whether given orally, topically, or transdermally.71-75 In a randomized, double-blind study comparing topical estrogen versus glycolic acid, 6 months of estrogen use on only one side of the face promoted a 23% increase in epidermal thickness (P = .00458), and the use of glycolic acid stimulated a 27% increase (P = .00467). The combined use of estrogen and glycolic acid prompted a 38% increase in epidermal thickness (P = .000181), with significant differences observed for all groups compared with the controls for the reversal of histologic markers of skin aging.76

Finally, collagen synthesis also is increased as inferred by the increase in procollagen type I and II terminal peptides.75 Hormone replacement therapy also affects the skin’s ability to retain water and leads to a reduction in skin wrinkling; however, the effects of HRT on dyschromic alterations have not been well studied.77 The numerous adverse effects of HRT, such as an increased incidence of cancer and cardiovascular morbidity, limit its use.

Isoflavones—Estrogen use is capable of causing morphologic changes in the aged skin of menopausal women.19,77 Given that HRT is contraindicated for some women and can cause adverse effects or pose unacceptable risks for others, Accorsi-Neto et al15 studied the possibility of achieving the beneficial effects of estrogen with plant hormones. Oral isoflavones given to rats that had been irradiated with UV light inhibited the increased expression of UV-induced metalloproteinases, reducing collagen degradation.78
Among the phytoestrogens, genistein, an isoflavone, is notable for its selectivity, with a high affinity for estrogen receptor $\beta$ and low affinity for estrogen receptor $\alpha$, which is found in the uterus and breasts. Accorsi-Neto et al$^{15}$ assessed whether soy isoflavones also would reduce skin aging in women, as observed in the aforementioned rat study. After 6 months of using 100 mg of concentrated soy extract daily, the investigators noted increased thickness of the dermis and epidermis, increased dermal vasculature, an increased number of collagen and elastic fibers, and an increased papillary index. In rats, genistein increases antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione.$^{78,79}$ Topical phytoestrogens also were evaluated, with promising results for increased skin thickness. In animals, the use of isoflavones also offers protection against carcinogenesis in sun-damaged skin.$^{15}$

Some investigators believe that a better understanding of the mechanism of action and possible side effects of phytoestrogens is essential to allow their use as a promising antiaging alternative.$^{80}$ There is no evidence that estrogens (eg, HRT) possess antioxidant or photoprotective properties.$^{78}$ Moreover, it is possible that new selective estrogen receptor modulators will specifically affect the skin without the expected systemic effects of existing estrogens.$^{80}$

**Conclusion**

Although often overlooked, skin disorders are quite common during menopause. Understanding the physiology of this important period in a woman's life is essential for developing an early and effective preventive therapeutic approach. Use of sunscreens has been questioned due to a concern about osteoporosis, but studies have not shown a connection between sunscreen use and reduced VD levels. Intentional sun exposure should not be considered a source of VD; instead, recommend dietary or artificial supplementation. Although studies have shown HRT to positively affect wound healing, reduce signs of aging, increase hydration, and yield other benefits, its use is not recommended for treating skin disorders. Isoflavones could be promising alternatives to estrogen; however, further studies are needed before their use can be recommended.

**REFERENCES**


