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PERSPECTIVES

Skin Care Supports Overall Well-Being

Tingting Zhu[1], Fumin Fang[1], Hao Li[2], Dongyun Lei[2], Mao-Qiang Man[3]

[1]Department of Dermatology, the First Affiliated Hospital of Soochow University, Suzhou, 215006, People's Republic of China; [2]Department of Dermatology, Tianjin Academy of Traditional Chinese Medicine Affiliated Hospital, Tianjin, 300120, People's Republic of China; [3]Dermatology Hospital of Southern Medical University, Guangzhou, 510091, People's Republic of China

Correspondence: Mao-Qiang Man, Dermatology Hospital of Southern Medical University, 2 Lujing Road, Guangzhou, Guangdong, 510091, People's Republic of China, Email mqman@hotmail.com

Abstract: Skin is more than a physical barrier; it plays a crucial role in overall health, emotional well-being, and social interactions. Beyond its primary function in protection and sensation, the skin actively influences extracutaneous systems through immune regulation, endocrine signaling, and microbiome interactions. Dermatological conditions such as psoriasis, eczema, and rosacea are linked to systemic inflammation, cardiovascular risks, and metabolic disorders, demonstrating the skin's far-reaching impact on overall health. Additionally, skin appearance affects psychological health, self-esteem, and social engagement, reinforcing its significance beyond physiology. Maintaining skin integrity in aging populations may help mitigate the progression of systemic diseases associated with inflammation and aging. Enhancing epidermal function in neonates, particularly pre-term neonates, lowers the risk of infections and mortality rates, while promoting the weight gain. Understanding these broader influences of skin can lead to more holistic therapeutic strategies, emphasizing dermatological health as a component of overall well-being. This perspective explores the connection between the cutaneous and extracutaneous conditions, and highlights the importance of improvement of cutaneous conditions in the management of some health conditions.

Keywords: stratum corneum hydration, epidermal permeability barrier, inflammaging, keratinocytes, diabetes, obesity, cardiovascular diseases, metabolic syndrome

Introduction

The skin (surface area ≈2m^2 and 15% of body weight) is not the largest organ in the human body in terms of size because skeletal muscle weighs 40% of body weight and mucosal area of the digestive tract is ≈32 m^2 in humans.[1–3] But the skin is subject to extra stress, including UV irradiation, air pollution, microbes, and chemical and physical insults, compared to other organs. Thus, the skin suffers from more disorders than any other organs. Some skin disorders are linked to extracutaneous conditions. While some dermatoses are the manifestations of extracutaneous disorders, some dermatoses can provoke or exacerbate extracutaneous conditions. For instance, the link of atopic dermatitis to obesity, type 2 diabetes mellitus, cardiovascular disease and metabolic syndrome has been well-documented.[4–7] The severity of atopic dermatitis is positively associated with some systemic conditions (diabetes mellitus, metabolic syndrome and dyslipidemia).[7–9] Similarly, psoriasis is a risk factor for type 2 diabetes mellitus, obesity and cardiovascular disease.[10] Moreover, psychiatric conditions such as depression and anxiety are also linked to some skin disorders, including atopic dermatitis, psoriasis and acne.[11–13] Effective treatment of skin diseases improves psychological symptoms.[14] Likewise, both coronary plaque burden and metabolic syndrome are also improved following the effective treatment of psoriasis.[15–17] However, one study showed that biologic agent-induced reductions in psoriasis severity and area index are not accompanied by the improvement in body mass index.[18] Nevertheless, a handful of evidence indicates a link between cutaneous conditions and extracutaneous functions, suggesting that proper management of cutaneous conditions can benefit extracutaneous conditions.

In addition to the treatment of skin disorders, daily application of skin care products can also benefit extracutaneous conditions, including improvements in constipation and mild cognitive impairment in the elderly and reduction in

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neonatal mortality rate.[19–21] In this perspective, we briefly outline the benefits of managing cutaneous conditions in relation to extracutaneous conditions and discuss the clinical implications of skin care for human health.

Some skin disorders are associated with extracutaneous conditions, among them, both atopic dermatitis and psoriasis are well-known examples of the link between dermatoses and systemic disorders. Treatment of skin disorders can alleviate their associated extracutaneous conditions. Here, we provide a brief summary of evidence regarding the association between cutaneous and extracutaneous conditions, based on findings from publications retrieved via PubMed and Google Scholar from inception to March 2025.

Psychological Conditions

Changes in psychological conditions are associated with various skin disorders, including atopic dermatitis, psoriasis, hidradenitis suppurativa, rosacea, and acne.[22] For instance, the prevalence of depression is higher in individuals with atopic dermatitis than in those without (20.1% vs 14.8%).[23] The severity of atopic dermatitis is positively associated with both depression and anxiety scores.[24,25] Similarly, psoriasis increases the risk of depression, with an adjusted odds ratio of 1.30 ($p = 0.045$).[26] The severity of psoriasis, measured by the psoriasis area severity index (PASI), is positively correlated with the severity of depression, assessed by the Beck Depression Inventory score.[27] In addition to atopic dermatitis and psoriasis, a higher prevalence of anxiety and depression is also observed in patients with acne and vitiligo;[28] however, one study did not demonstrate differences in either the prevalence or severity of anxiety and depression between patients with and without acne.[29] Moreover, the severity of both anxiety and depression is higher in patients with acne than in those without acne.[30] Additionally, the odds ratios for depression and anxiety in patients with hidradenitis suppurativa are 2.54 and 2.00, respectively.[31] Taken together, this evidence suggests a link between dermatoses and psychological conditions.

Although it remains uncertain whether psychological conditions affect skin disorders or vice versa, the improvement of certain dermatoses can enhance psychological well-being. Treatment of atopic dermatitis with dupilumab for 16 weeks significantly improved skin lesion, accompanied by amelioration of psychological symptoms such as depression and anxiety.[32,33] A large cohort study demonstrated that dupilumab significantly improves anxiety and depression after 2-week treatment.[34] The improvement in depression induced by dupilumab is negatively affected by both a high body mass index and severe depression scores.[35] A small-scale study in patients with atopic dermatitis found that dupilumab is more effective than methotrexate in alleviating depression.[36] Treatment of atopic dermatitis with lebrikizumab for 16 weeks also led to improvements in both anxiety and depression scores.[37] Thus, effective treatment of atopic dermatitis can positively impact associated psychological conditions.

As mentioned above, psoriasis is another dermatosis comorbid with psychological disorders. Although psychological stress and depression can trigger and exacerbate psoriasis, psoriasis increases the risk of psychological disorders.[38,39] Several studies have demonstrated that treating psoriasis can mitigate psychological symptoms. A study in 106 psoriatic patients showed that treatment with biologics (IL-17 and IL-23 antagonist, TNF-α inhibitor) for 6 months decreases the prevalence of depression (from 66% to 40.6%) and anxiety (from 54.7% to 33.6%), along with remarkable reductions in both depression and anxiety scores ($p < 0.005$ for both).[40] Likewise, both PASI and psychological conditions (anxiety and depression scores) were dramatically improved following 4-week treatment with adalimumab.[41] Moreover, biologics can prevent the development of psychological symptoms. A study in 7490 psoriatic patients showed that biologics lowered the rate of suggestive depression with an incidence rate of 3.01 (95% CI: 2.73–3.32) compared to either phototherapy (incidence rate = 5.85, 95% CI: 4.29–7.97) or the conventional systemic therapies, including cyclosporine, methotrexate, mycophenolate mofetil, oral tacrolimus, etc. (incidence rate = 5.70, 95% CI: 4.58–7.10) in patient who were without symptoms suggestive of depression at the beginning of the study. The incidence rate of depression was also lower in biologics-treated group (incidence rate = 0.21, 95% CI: 0.13–0.31) than in the phototherapy group (incidence rate = 0.55, 95% CI: 0.21–1.47).[42] Similar results were obtained in another conventional therapy-controlled study, showing the hazard ratio of depression was 0.83 (95% CI: 0.72–0.97) vs conventional therapy.[43] Thus, biologics lower the risk of depression (hazard ratio = 0.76; 95% CI: 0.59–0.98).[42] Among the biologics, adalimumab is the most effective in reducing the risk of depression (hazard ratio = 0.63; 95% CI: 0.46–0.86 vs conventional therapy).[42] Improvements in anxiety and depression were observed following the treatment of psoriasis with methotrexate, biologics, cyclosporine

A and tofacitinib.[44] A recent study showed that dupilumab decreased the risk of psychologic conditions (mood and anxiety) in individuals with atopic dermatitis.[45] Interestingly, methotrexate and biologics (Secukinumab, Ustekinumab, and Adalimumab, etc.) display comparable efficacy in reductions in Beck Anxiety Inventory and Beck Depression Inventory scores, although more patients achieve PASI75 in the biologics-treated than in the methotrexate-treated group (83.3% vs 43.3%, p = 0.001).[46] However, one study showed that treatment of psoriasis with either topical, biologics or systemic non-biological therapy increased the risk of depression, with adjusted hazard ratios of 1.19 (95% CI: 1.17–-1.20), 1.50 (95% CI: 1.23–1.84) and 1.19 (95% CI: 1.15–1.23), respectively.[47] Hence, proper management of psoriasis can also improve psychological condition.

Additionally, mild cognitive impairment is common in the elderly, with worldwide prevalence of 15.6% in individuals aged 50 and over.[48] Although the pathogenesis of mild cognitive impairment is unclear, the inflammation theory has been widely proposed.[49,50] Chronologically aged individuals exhibit alterations in epidermal function, including elevated skin surface pH, reduced stratum corneum hydration levels and delayed epidermal permeability recovery, all of which can cause or exacerbate cutaneous inflammation.[51] Persistent cutaneous inflammation can potentially induce an increase in circulating levels of proinflammatory cytokines, leading to the development of inflammation-associated extracutaneous disorders.[52,53] Conversely, improvement in epidermal function with topical emollient lowers circulating levels of pro-inflammatory cytokines.[53,54] A clinical trial demonstrated that improvement in epidermal function with a topical emollient prevents the progression of mild cognitive impairment in the elderly.[20] Moreover, autism spectrum disorder is also likely to be an inflammation-associated condition. In a mouse model of autism, the levels of IL-17A are elevated in both the skin and the brain, while inhibiting the IL-17A signaling pathway with an Nrf2 activator improves autism symptoms.[55,56] Similarly, children with autism exhibit higher circulating levels of IL-17A than neurotypical children.[57,58] Topical applications of an emollient mitigate some of autistic symptoms in children.[59] Furthermore, treatment of psoriasis with IL-17A inhibitor, Secukinumab, also alleviates autistic symptoms in individuals with psoriasis.[60] Additionally, other dermatoses such as rosacea, seborrheic dermatitis and alopecia areata are associated with psychological condition, too.[61–63] Taken together, this body of evidence suggests that improving cutaneous conditions can help alleviate psychological abnormalities.

Type 2 Diabetes

Individuals with Type 2 diabetes mellitus exhibit changes in cutaneous conditions, including reduced stratum corneum hydration levels.[64] Meanwhile, inflammatory dermatoses, such as atopic dermatitis and psoriasis, are associated with an increased risk of developing Type 2 diabetes mellitus.[6,65,66] Psoriasis increases the risk of type 2 diabetes mellitus.[67] The risk of developing type 2 diabetes mellitus positively correlates with the body surface area involvement in individuals with psoriasis,[68] but not with Psoriasis Area and Severity Index.[67] Effective treatment of psoriasis improves both psoriasis and insulin resistance,[69,70] although inconsistent findings have been reported.[71] Moreover, acitretin dose-dependently lowers fasting blood glucose levels in individuals with psoriasis.[72] Regarding atopic dermatitis, alterations in several gene expression and signaling pathways are similar between atopic dermatitis and Type 2 diabetes mellitus,[73] suggesting a link between these two conditions. A clinical study showed that topical treatment with either betamethasone or tacrolimus for two weeks improved the severity of atopic dermatitis, accompanied by decreased insulin resistance.[74] This increase in insulin sensitivity is likely due to reduced cutaneous inflammation, as glucocorticoids are known to increase insulin resistance.[75,76] A retrospective cohort study demonstrated that the treatment of atopic dermatitis with dupilumab decreases the risk of type-2 diabetes mellitus (hazard ratio = 0.53; 95% CI, 0.42–0.68; P < 0.001).[77] Thus, treating skin disorders such as atopic dermatitis and psoriasis may provide benefits for managing Type 2 diabetes mellitus.

Obesity

Excessive weight gain can lead to the development of obesity, which is defined as body mass index (MBI) of ≥30 kg/m^2 or ≥27.5 kg/m^2 for Asian.[78] Certain dermatoses, including atopic dermatitis and psoriasis, are associated with an increased risk of obesity, although obesity also predisposes individuals to developing these skin disorders.[5,79,80] Improving these skin disorders can lead to weight loss. For example, weight loss was observed in 53.4% of psoriatic

patients who responded to oral roflumilast treatment,[81] particularly in females who showed an 8% reduction in body mass index at week 48 ($p < 0.001$ vs baseline).[82] Oral roflumilast-induced weight loss is positively correlated with changes in psoriasis area and severity index.[83] Likewise, TNF-α inhibitor-induced weight loss is positively associated with reductions in multiple biomarkers and disease severity in individuals with psoriatic arthritis.[84] Reductions in body weight were also observed following the treatments of psoriasis with either ustekinumab or methotrexate.[85] It is worth noting that individuals with obesity often poorly respond to psoriasis treatment and that weight loss increases the efficacy of treatment.[86–89] However, weight loss alone has been shown to improve psoriasis.[86,90] Thus, whether weight loss results from improved psoriasis or vice versa remain unclear.

Atopic dermatitis is another skin disorder that is associated with obesity.[5,91] Although studies indicate that obesity increases the risk of atopic dermatitis, the risk of obesity is three times higher in individuals with atopic dermatitis than in the controls, particularly in individuals with moderate-to-severe atopic dermatitis whose risk of obesity/overweight is 20 times higher than that of individuals with mild atopic dermatitis (OR 20.4, 95% CI 6.53–90.7).[92,93] In contrast to psoriasis, treatment of atopic dermatitis with biologics has been shown to increase body weight,[94,95] although a reduced risk of obesity has been reported in patients with atopic dermatitis following one year of treatment (hazard ratio = 0.70; 95% CI, 0.58–0.86).[77] This line of evidence suggests distinct pathomechanisms of obesity in atopic dermatitis (primarily Th2 inflammation) and psoriasis (primarily Th1 inflammation).

Cardiovascular Disease

Several skin disorders, including atopic dermatitis, psoriasis and Hidradenitis Suppurativa, increase the risk of cardiovascular disease.[96] A number of studies have demonstrated a reduction in the risk of cardiovascular events in psoriatic patients by either biologic or non-biologic treatment.[97–102] Wu et al reported that TNF inhibitor cohort demonstrated a decreased risk of myocardial infarction with adjusted hazard ratio of 0.50 (95% CI, 0.32–0.79 vs topical treatment).[103] Oral medication and phototherapy also lowered the risk of myocardial infarction (hazard ratio = 0.36; 95% CI 0.22–0.59 vs topical therapy).[104] Interestingly, the benefit of oral medication and phototherapy in reducing myocardial infarction risk was observed only in Caucasians, not in non-Caucasians.[104] The TNF inhibitor-induced reduction in the risk of myocardial infarction does not vary with the length of treatment.[105] Moreover, biologic therapy improves both diastolic function (ie, E/e' ratio, from 8.1 ± 2.1 to 6.7 ± 1.9, $P < 0.001$) and global longitudinal strain (from −16.8 ± 2.1 to −18.3 ± 2.3%, $P < 0.001$), accompanied by reduction in PASI from 12.0 ± 4.1 to 2.8 ± 4.1 ($p < 0.0001$).[97] Dupilumab is an antibody against IL-4 and IL-13, commonly used to treat atopic dermatitis. Treatment of atopic dermatitis with dupilumab decreases the risk of multiple vascular conditions such as peripheral vascular disease (hazard ratio = 0.64; 95% CI 0.45–0.90; $P = 0.011$), deep vein thrombosis (hazard ratio = 0.42; 95% CI, 0.26–0.69; $P < 0.001$), and hypertension (hazard ratio = 0.67; 95% CI 0.58–0.79; $P < 0.001$).[77] In addition to biologics, methotrexate treatment also improves aortic stiffness (AoS), as demonstrated by a reduction in carotid-femoral pulse wave velocity from 50.8 to 23.5 m/s ($p = 0.04$) in patients with severe psoriasis receiving cumulative dose of methotrexate ≥1500 mg.[106] However, another study showed that only a low cumulative dose of methotrexate (<1.56 g) lowered the risk of cerebrovascular disease (HR = 0.53; 95% CI 0.28–1.00; $p = 0.0486$) but not high cumulative dose (≥1.56 g) (HR 0.80; 95% CI 0.11–5.68; $p = 0.8214$).[107] The benefit of biologics and methotrexate in reducing the risk of cardiovascular events is well reviewed in a recent publication.[108] Hidradenitis suppurativa is another common dermatosis with a prevalence of up to 4% in Europeans.[109] The prevalence of cardiovascular comorbidities is 76.5%, while the risk of cardiovascular disease-related death is 58% higher in patients with hidradenitis suppurativa than in patients with severe psoriasis,[110] a skin disorder with a higher cardiovascular risk. Both cardiovascular comorbidities and diabetes mellitus are positively correlated with the severity of hidradenitis suppurativa,[109] suggesting that proper management of hidradenitis suppurativa can potentially lower the incidence of these comorbidities. Overall, current evidence demonstrates that effective treatment of inflammatory skin diseases, such as psoriasis and atopic dermatitis, can reduce the risk of cardiovascular disease.

Others

Metabolic syndrome is associated with several skin disorders, including atopic dermatitis, psoriasis, hidradenitis suppurativa and acne vulgaris.[7,110–112] Effective treatment of psoriasis with ustekinumab improves psoriasis,

accompanied by reductions in serum levels of adipocytokines in psoriatic patients.[113] Similarly, TNF inhibitor lowers circulating levels of cholesterol and low-density lipoprotein[114] and decreases the incidence of metabolic syndrome.[115] However, a retrospective study showed that TNF inhibitor, etanercept, did not significantly alter the circulating levels of total cholesterol, LDL, and HDL levels in psoriatic patients.[116] This evidence suggests that treating skin disorders may help ameliorate metabolic syndrome.

In comparison to full-term infants, preterm neonates have a higher mortality rate and more commonly experience delayed development, in addition to compromised epidermal permeability barrier function.[117–121] Topical emollients improve several cutaneous and extracutaneous functions in preterm infants, including improving the skin barrier function,[122] accelerating the development of fine motor skills and reducing the risk of hearing disability,[123] lowering mortality rate,[124,125] reducing the incidence of bloodstream infections,[126] and increasing weight gain compared to untreated controls.[127,128] Moreover, treatment of atopic dermatitis significantly improves health-related quality of life in children, regardless of whether the treatment regimen is topical, systemic, or phototherapy.[129] Likewise, either topical treatments or systemic biologics improve both disease severity and sleep quality in individuals with psoriasis or atopic dermatitis.[130–133] Collectively, these findings highlight the benefits of skin care in neonatal development, health-related quality of life, and sleep quality.

Prospectives

The skin is the window to the body, and its functional alterations reflect the changes in extracutaneous systems. For example, renal dysfunction can cause dry skin and pruritus.[134,135] Both stratum corneum hydration levels and epidermal permeability barrier are altered in individuals with Type 2 diabetes mellitus.[61,136] On the other hand, cutaneous function also influences extracutaneous organs and systems, as previously discussed. A notable example of the impact of cutaneous function on extracutaneous systems is the link between inflammatory dermatoses and several extracutaneous disorders, including cardiovascular disease, type 2 diabetes mellitus, mental health conditions, and obesity.[5,6,50,137] Thus, skin conditions exert effects that extend beyond the skin itself.

Given the negative impact of skin conditions on overall health, they should be properly managed and treated. To address a specific skin condition, an appropriate therapeutic regimen should be promptly applied. Studies have shown that the severity and duration of skin disorders, such as psoriasis, are linked to an increased risk of extracutaneous diseases.[138,139] Thus, timely and effective treatment of these skin disorders can significantly lower the risk of developing extracutaneous conditions. Additionally, chronologically aged skin undergoes structural and functional alterations in both the dermis and epidermis, possibly leading to the development of inflammaging, a chronic low-grade systemic inflammation.[51,140] This chronic inflammatory state contributes to the pathogenesis of various aging-associated disorders.[51] Enhancing epidermal function with topical emollients may slow the progression of aging-related conditions, such as mild cognitive impairment, while also lowering circulating levels of proinflammatory cytokines.[20,54] Likewise, adequate care of prematurely developed skin supports healthy development and helps reduce the risk of infections and mortality in preterm neonates.[123–128] A recent study showed that topical emollient (Dr. Yu barrier repair lotion) prevented the development of lung inflammation (atopic march) in a murine model of atopic dermatitis.[141] Thus, effective management of diseased or problematic skin can achieve significant health benefits in extracutaneous systems.

In addition, skin care is more than just a superficial concern. Proper skin care benefits overall health and well-being even in individuals with normal skin. Skin care is often associated with beauty and aesthetics, yet its impact extends far beyond appearances. The skin serves as a protective barrier against environmental threats, including UV irradiation, toxins, and pathogens. Proper skin care can reduce the risk of harmful insults to the body. Moreover, beautiful skin can positively impact mental and emotional well-being. Studies show that routine skin care can boost confidence and self-esteem while helping reduce symptoms of depression.[142,143] Thus, routine skin care is also crucial for overall health, even for individuals with normal skin. In addition to properly treat skin disorders, regimens for regular skin care include a. removing the oil and impurities from the skin; b. according to skin condition, topically applying ingredients that benefit cutaneous functions (proliferation, differentiation, lipid and collagen production, antioxidation, etc.); c. restoring the skin conditions such as stratum corneum hydration, epidermal permeability barrier function, elasticity, wrinkles; d. protecting the skin against UV irradiation, chemical and physical insults, and maintaining a balanced microbiome on the skin.

Healthy diets and appropriate physical activity also benefit the skin. Again, the usefulness and selection of these regimens should be based on the individual's condition.

Conclusions

Skin care, a fundamental pillar of overall health, benefits the emotional well-being, social interactions and extracutaneous functions. Whether healthy or diseased, the skin influences extracutaneous conditions. Prompt and effective treatment of skin diseases can help prevent and alleviate dermatosis-associated extracutaneous conditions. Maintaining healthy skin, particularly in aging individuals, may help mitigate the development and progression of certain aging-related disorders in extracutaneous systems.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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