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REVIEW

Xerosis

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The skin is the biggest organ in the body with many roles. The skin provides a barrier to maintain the steady state of the cellular environment inside the body;[1] functions as the body's first line of defence against physical and chemical stimuli from the external environment; and plays an important role as part of the immune system, protecting against microbes and irradiation.[1]

To further understand the skin and how to treat impaired skin barrier function, we need to know the normal structure and function of the skin. It is made up of three layers, these being the epidermis which is the topmost layer; the dermis which is the middle layer which contains skin organelles, is rich in vasculature, elastic and collagen fibre bundles; and the subcutaneous fat layer. The epidermis forms the impermeable barrier that protects the cellular environment from the external environment. The epidermis is made up of four layers: the stratum corneum (cornified layer), stratum granulosum (granular layer), stratum spinosum (spinous layer) and the stratum basale (basal layer).

The basal layer provides replicating cells necessary for the regeneration of the layers of the epidermis.[3] The cells in this layer are mitotically active, which is necessary for normal epidermal turnover and wound healing.[3] The spinous layer contains visible cell-cell adhesions between keratinocytes called desmosomes. Desmosomes give the spiny appearance in histological sections.[3] The granular layer contains granules composed of keratins, profilaggrin, filaggrin, loricrin, and other proteins that make up the stratum corneum.[1] Filaggrin is a keratin filament aggregating protein that is involved in the process of keratinisation.[1] Filaggrin is derived from a large precursor protein, profilaggrin, that is synthesised in the granular layer.[1] Filaggrin is broken down into free amino acids and urocanic acid (natural moisturising factor [NMF]) which has good water-binding properties.[3] NMF assists in hydrating the outer layers of the cornified layer.[1] Ceramide synthesis also occurs in the spinous and granular layer. The top layer of the epidermis is the stratum corneum, which consists of a "brick and mortar" arrangement made up of acellular, anuclear

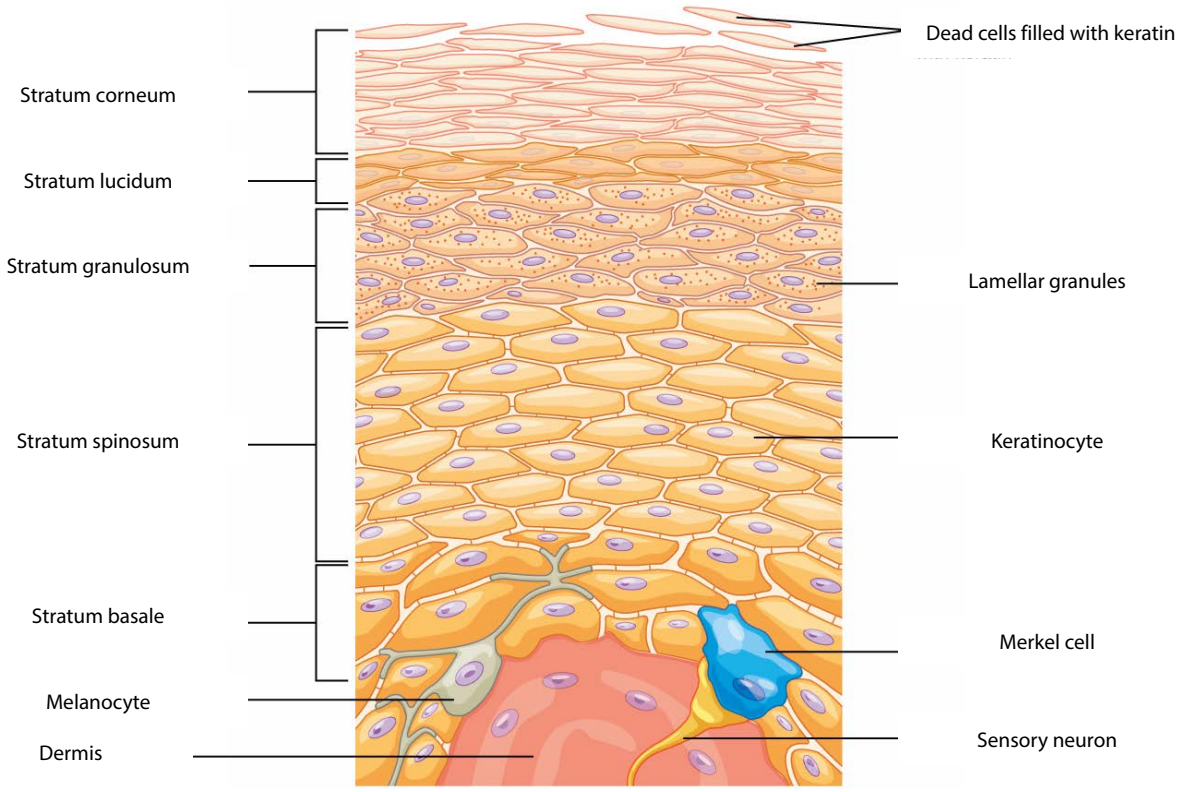


Figure 1: The epidermis showing five layers: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.
Figure from J. Gordon Betts et al. (2013).[2] Anatomy & Physiology, Connexions Web site. http://cnx.org/content/col11496/1.6/, Jun 19, 2013.

corneocytes (the brick) wrapped with a lipid rich layer (the mortar).[3]

Lipids play an important role in the formation of the epidermal water permeability barrier.[4] Amongst these, ceramides contribute to the formation of the permeability barrier;[1] fatty acids in the form of non-hydroxy, α-hydroxy or ω-hydroxy acids contribute to the formation of glucosylceramide;[1] linoleic acid, an essential fatty acid forms α-hydroxyl of the glucosylceramide, the deficiency of which results in dry skin;[1] cholesterol and cholesterol esters contribute to the lipid envelope.[1] The corneocyte coating by the acylceramide protects the cornified cell from attack by proteolytic enzymes secreted by microorganisms.[1] The crosslinking of proteins and the presence of specialised lipids result in mechanical stability and relative impermeability of the epidermis.[4]

Xerosis or xerosis cutis refers to disruption of the skin's epidermal barrier with trans-epidermal-water-loss (TEWL).[5] Clinically this presents as dry, flaky, sensitive skin.[6] The aetiology of xerosis is multifactorial and can be divided into intrinsic, including genetics, and extrinsic factors.[7] Intrinsic factors that contribute to xerosis include physiological ageing, menopause, endocrine disorders (i.e. hypothyroidism, diabetes), chronic illness, malnutrition, existing skin disorders such as eczema, psoriasis, ichthyosis.[5] Extrinsic factors include photoinduced ageing, dry climates, windy conditions, excessive air conditioning, excessive bathing, hand washing, over-use of detergents and soaps, poor diet, excessive alcohol consumption, smoking, pharmacological therapy.[7]

Clinical presentation of xerosis

Chronological aging

In the elderly, xerosis is the most common cause of pruritus.[8] Aging skin has reduced sebaceous gland activity thus less sebum production.[9] There is altered lipid and filaggrin production in the epidermis thus leading to a disrupted epidermal barrier.[9] This leads to TEWL and increased permeability of allergens into the skin.

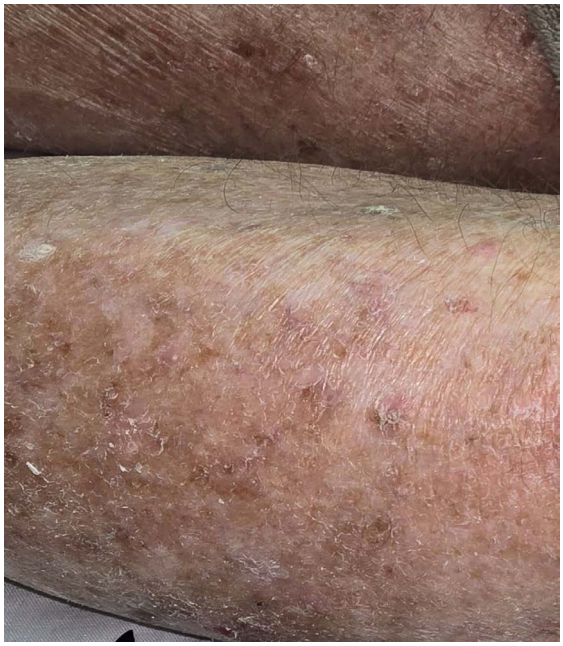


Figure 2: Xerosis in ageing skin

Menopause

Menopause results in decreased oestrogen production. The effect of reduced oestrogen on the skin includes decreased sebum production by sebaceous glands, thinning of hair and epithelial atrophy.[9] Menopause causes changes to lipids and ceramides in the epidermis worsening physiological xerosis.[10]

Hypothyroidism

Patients with hypothyroidism have dry skin and the stratum corneum is poorly hydrated.[9] The dry skin resembles acquired ichthyosis and often affects the arms and legs with fine wrinkling of the skin.[9]

Diabetes mellitus

Diabetics often present with xerosis. Diabetes causes changes in skin homeostasis by either primary diabetes-induced changes of skin metabolism and by associated complications, such as vasculopathy and neuropathy.[11] It has been found that diabetic patients have altered keratinocyte functions due to the influence of insulin on keratinocyte proliferation, differentiation and migration, resulting in impaired epidermal barrier function and delayed wound healing.[11] Impaired epidermal barrier predisposes the patient to infections which contribute to the development of diabetic foot amongst other complications.

Common dermatology conditions that present with xerosis

Atopic dermatitis (AD) is a genetic chronic inflammatory skin condition. Xerosis accompanied with pruritus is one of the fundamental clinical features of AD and results from an impaired epidermal barrier.[12] The pathogenesis of AD is divided into three major categories: impaired epidermal barrier; immune dysregulation; and alteration of the skin microbiome.[13] Each of these can be modified by genetic and environmental factors.[13]

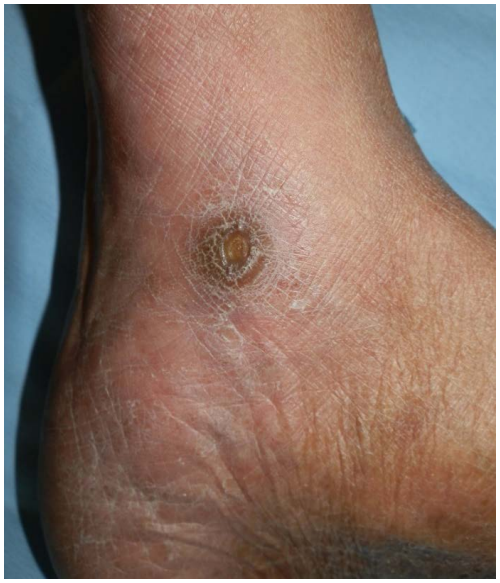
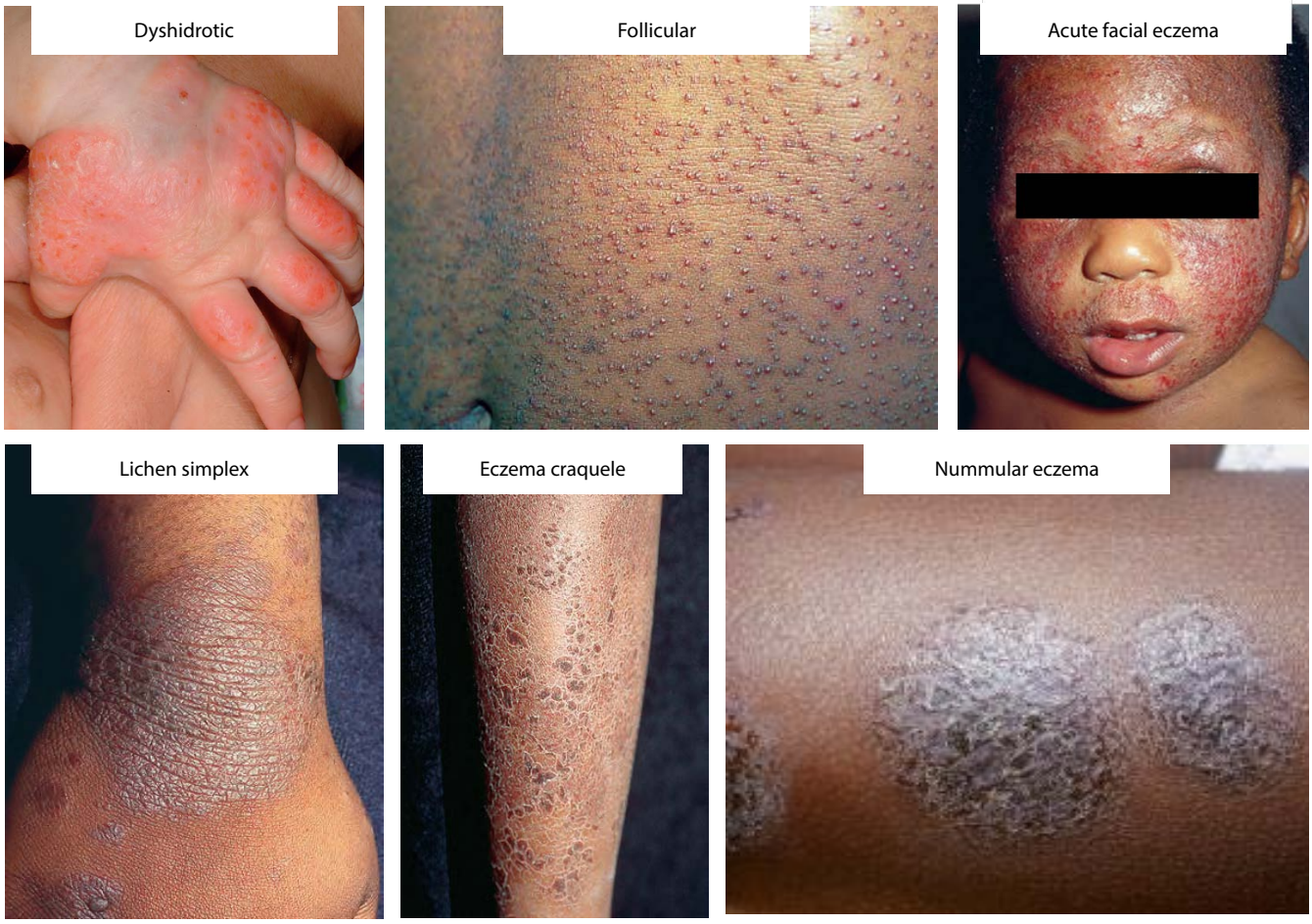


Figure 3: Leg of a diabetic patient with healing ulcer. Increased skin markings.

Different clinical features of eczema:



Elderly or senile AD is eczema that presents after the age of 60 years.[13] In elderly patients the eczema has less predilection for flexural areas and can present anywhere on the body.[14] It is often characterised by intense pruritus resulting in sleep disturbances, psychological distress and social isolation.[13] First-line treatment of atopic dermatitis is to repair the epidermal barrier using emollients.[12] Topical corticosteroid and topical calcineurin inhibitors, where appropriate, are used to treat the inflammatory response.[12] Newer topical agents to treat inflammation include phosphodiesterase inhibitors (2% crisaborole) which is available in South Africa.

Ichthyosis vulgaris is a genetic autosomal semi-dominant form of ichthyosis.[13] It has a close association with atopic dermatitis, asthma, and allergic rhinitis.[3] Mutations in the filaggrin gene are responsible for ichthyosis vulgaris and are associated with a higher risk of developing atopic dermatitis.[3,13] Clinically, ichthyosis presents with dry skin and mild to moderate scaling appears during infancy or early childhood.[13] Fine scales develop on the extensor surfaces but the groin and flexural areas are typically spared because of increased humidity in those regions.[13] Mild hyperkeratosis of the palms and soles leads to accentuated skin markings.[13] Treatment includes emollients, humectants such as urea and propylene glycol. In severe cases systemic retinoids such as acitretin or isotretinoin may be indicated to remove thick adherent scale.[13]

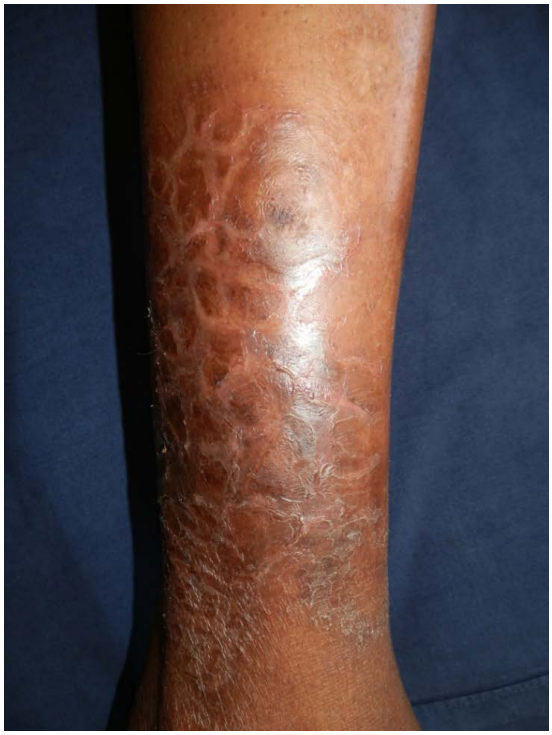


Figure 4: Ichthyosis vulgaris

Papular pruritic eruption (PPE) is associated with human immunodeficiency virus (HIV) infection. It is characterised by skin-coloured to erythematous, non-follicular papules, nodules that are distributed symmetrically on the extremities and trunk.[9]

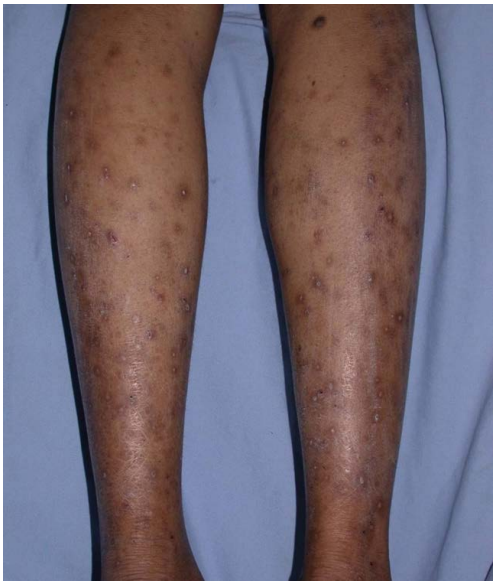


Figure 5: Papular pruritic eruption, with xerosis, excoriations and healing with post inflammatory hyperpigmentation.

It presents with severe pruritus, xerosis, excoriations and heals with post inflammatory hyperpigmentation in patients with dark skin. PPE is a hypersensitivity reaction to arthropod antigens.[9] First-line treatment is initiation of antiretroviral treatment together with oral antihistamines and topical corticosteroids as adjuvant treatment.[9]

Pityriasis rosea is an acute self-limiting erythematous, squamous exanthem with a classical clinical pattern.[9] It is thought to be a hypersensitivity reaction to a viral infection.[9] It has been postulated to be as a result of human herpes virus-7 (HHV-7) or HHV-6.[13] The rash presents 1–2 weeks after a viral infection, with plaques that have a collaret of fine scale at the edge, often arranged along skin folds creating a "Christmas-tree-pattern" on the back.[13] You may or may not see a "herald-patch" which is the initial presenting lesion when the rash appears, usually being the largest lesion. The rash usually spares the face, distal extremities and palms and soles.

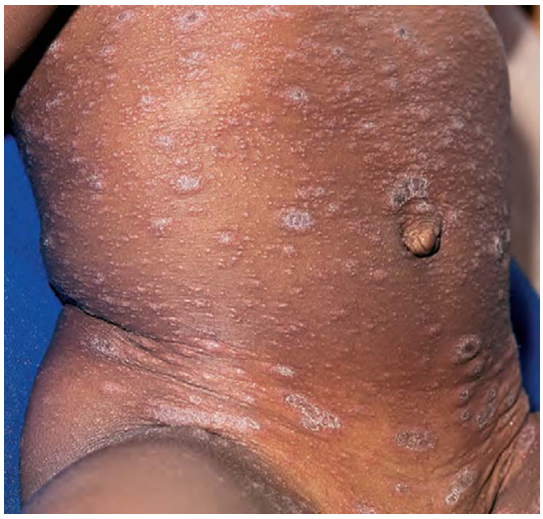


Figure 6: Pityriasis rosea with scaly plaques with collarette of scale at the edge.

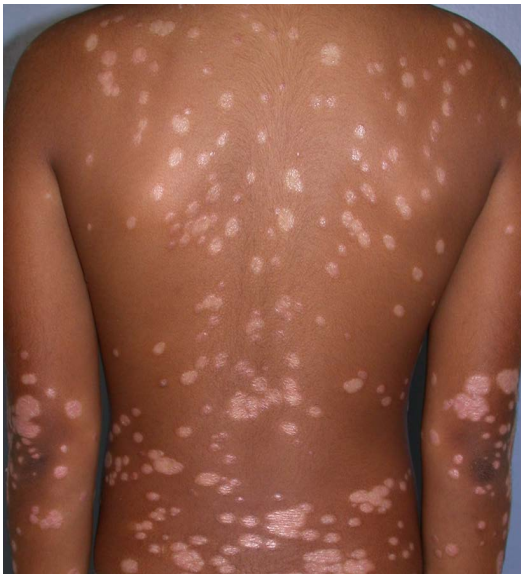


Figure 7: Psoriasis plaques, well demarcated with silvery scale on the surface.

Treatment of pityriasis rosea is often not necessary as it is a self-limiting exanthem. Patients who complain of pruritus are treated with mid-potency topical corticosteroids and oral antihistamines.[9]

Psoriasis is an immune-mediated polygenic skin disorder.[13] Various environmental triggering factors, such as trauma, infections, and medications, may initiate disease in predisposed individuals.[13] Psoriasis presents with sharply demarcated erythematous plaques with thick silvery scale.[9] Often the background skin is also very dry. Plaques may be localised or widespread.

Extracutaneous manifestations include psoriatic arthritis and nail psoriasis. Psoriasis is potentially a multisystem disease featuring extracutaneous manifestations in a subset of patients. Patients with long-standing severe cutaneous psoriasis have an increased risk of developing cardiovascular events.[9] The risk of myocardial infarction is especially increased in young patients with severe disease.[9]

First-line treatment for psoriasis includes keratolytics such as 5–10% salicylic acid to remove thick adherent scale on active plaques by reducing epidermal proliferation.[13] This is then followed by application of topical corticosteroids, occasionally in combination with vitamin D_3 analogues. Vitamin D_3 analogues work by inhibiting proliferation and promoting differentiation of keratinocytes, as well as decreasing production of inflammatory mediators.[13] Coal tar preparations are available in most pharmacies over-the-counter and are a useful adjuvant treatment for psoriasis. Coal tar has anti-inflammatory, antimicrobial and antipruritic effects.[13] It suppresses DNA synthesis, which stabilises epidermal differentiation in conditions such as psoriasis.[13]

Management of xerosis (dry skin)

Effective treatment for xerosis should include ingredients that address factors that are central to increasing and maintaining skin hydration.[15] Moisturisers constitute the main treatment

for xerosis and prevention of trans-epidermal water loss. Moisturisers help repair the damaged epidermal barrier of the skin. Moisturisers that contain emollients (e.g. glycol and glyceryl stearate, soy sterols) lubricate the skin; occlusive agents (e.g. petrolatum, dimethicone, mineral oil) form a layer to prevent evaporation of water from the skin.[12] Humectants (e.g. glycerol, lactic acid, urea) attract and hold water inside the epidermis.[12] Newer moisturisers now contain ceramides and filaggrin breakdown products, mainly urocanic acid, help in hydrating the stratum corneum (epidermis).[12]

Bathing practices can also assist in maintaining skin hydration. Bathing removes excess scale, crust, irritants, and pollutants which may be present on the skin.[12] The so-called soak-and-smear practice is when moisturisers are applied onto the skin soon after bathing, before drying the skin, thus locking water into the skin.[16] For inflammatory skin conditions such as eczema and psoriasis it is recommended that soaking in plain water for 20 minutes followed by the immediate application of pharmacological anti-inflammatory therapies such as topical corticosteroids (TCS) to diseased skin without drying improves outcomes of treatment.[12]

Guidelines recommend limited use of non-soap cleansers that are neutral to low pH, fragrance-free and hypoallergenic.[12] Soaps consist of surfactants that interact with stratum corneum proteins and lipids, resulting in dry skin.[12] The skin's normal pH is 4 to 5.5. Most soaps are alkaline in pH thus disrupting the homeostasis of the skin.[12] Alkaline changes in the skin pH result in disruption of the cutaneous microbiome and enzyme activity in the upper epidermis.[17] Thus non-soap based surfactants and synthetic detergents (syndets) are recommended for better epidermal tolerance.[12]

The cause of xerosis is multifactorial. Treating the underlying systemic or cutaneous condition is paramount. Understanding the structure and functioning of the epidermis has led to targeted effective treatment solutions. As health practitioners we need to assist our patients in selecting treatment that alleviates symptoms, repairs xerosis and is cost effective.

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