

Occupational Dry Skin

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Introduction

Dry skin (xeroderma or xerosis) is a very common skin condition which occurs when the water content of the stratum corneum (SC) falls below normal, inducing morphological and functional skin changes (Spencer 1988; Rudikoff 1998). There is a loss of smoothness with flaking, scaling and cracking of the most superficial epidermal layers; this is felt as an uncomfortable sensation of tightness, roughness and pruritus often associated with erythema, fissures and eczema (Spencer 1988; Thune 1996a).

Water in the SC is necessary to maintain its pliability, elasticity, extensibility and resistance to trauma (Rawlings et al. 1994; Cork 1997) and to control the function of several enzymes that control desmosome degradation and the formation of natural moisturizing factors (NMF) (Rawlings et al. 1994). When water falls below 5–10 mg/100 mg of the SC dry weight (Schurer et al. 1991; Thune 1996b), the SC loses suppleness and cracks easily (Rudikoff 1998), the process of desquamation is altered and, instead of the usual unicellular and invisible cell detachment, corneocytes are shed in large visible blocks (Spencer 1988; Marks 1997; Rudikoff 1998).

Although SC water is relentlessly lost to the environment by *perspiratio insensibilis* (about 2–8 ml/m²/h at rest) (Forslind 1994; Rudikoff 1998), an almost constant amount of water is retained both inside the protein-rich keratinocytes (20%) and in the intercellular space (10%) (Imokawa et al. 1991). A highly specialized and dynamic permeability skin barrier controls the movement of water across the SC as well as the penetration of environmental chemical, physical and biological hazards (Kerscher et al. 1991; Cork 1997), allowing the body to suffer little change while encountering the different environments that are a part of daily life (Spencer 1988).

When disruption of the skin barrier occurs, either due to environmental insults, intrinsic constitutional defects, deficient reparative mechanisms or a combination of these factors (Thune 1996a), excessive

amounts of water are lost to the environment, as measured by transepidermal water loss (TEWL), and the skin gets “dry”. In case of persistent barrier disruption, besides the loss of the water-holding capacity of the SC, the skin becomes less competent in the protection from environmental hazards, and the manifestations of dry skin worsen and develop into dry erythema, erythema craquelé, eczema craquelé or other inflammatory and eczematous reactions (Thune 1996a; Rudikoff 1998).

Dry skin and its complications are very frequent problems in several occupational settings, although they are often underestimated and seldom included in the lists of occupational skin diseases. In order to understand how dry skin develops, how the main environmental factors induce it and how we can prevent or treat this condition, we have to understand the constitution and physiology of the permeability skin barrier.

Permeability Skin Barrier: Constitution and Physiology

The permeability skin barrier, a highly specialized structure responsible for retaining skin moisture, is localized mainly at the stratum corneum (Rudikoff 1998); however, its formation begins deeper in the epidermis and its constituents are progressively modified during the process of keratinization until they reach their highest efficiency in the five layers of the stratum compactum (Rawlings et al. 1994). The modified keratinocytes – the corneocytes – and the intercellular complex lipid matrix in which they are embedded form this specialized structure, which Elias compared to a “bricks and mortar” model, in which the corneocytes are the bricks and the lipid matrix the mortar (Elias 1983).

The corneocytes are the main constituent of the stratum corneum and hold tightly most of its water. The intercellular lipids are the main obstacle to the outward movement of water from inside our body to the environment, but they still retain a smaller amount

of less tightly bound water within their layers (Imokawa et al. 1991).

The Corneocytes

In the corneocytes at the upper stratum granulosum, keratin filaments are aggregated with filagrin. As they move further into the surface, depending on the degree of skin hydration, keratins and, especially, filagrin, they are proteolytically cleaved into nitrogen-rich amino acids and derivatives, namely glutamine, further converted into 2-pyrrolidone-5 carboxylic acid (PCA), histidine, converted then into urocanic acid, and urea (Rawlings et al. 1994; Rudikoff 1998). These water-soluble and highly hygroscopic compounds, which constitute about 10% of the dry weight of SC cells, are collectively called the natural moisturizing factor (NMF) of the epidermis (Rawlings et al. 1994; Rudikoff 1998). They retain a large amount of water (about 20%) that is tightly bound and difficult to extract by solvents (Imokawa et al. 1991). For water retention within the corneocytes, the plasma membrane is replaced by a cornified envelope, an insoluble proteinaceous structure cross-linked irreversibly by transglutamination (Smack et al. 1994), and further protected by an external continuous lipid monolayer of ceramide 1 that binds covalently to glutamate residues of the proteinaceous envelope (Chapman et al. 1991).

In the outer 15 layers of the SC, corneocytes adhere to one another by rudimentary desmosomes – the corneosomes – (Chapman et al. 1991) and by the intercellular lipid bilayers bound tightly to ceramide 1 of the envelope, which work as the scaffold for these intercellular lipids (Schurer et al. 1991) and for their correct orientation along the surface of the corneocytes (Ponec et al. 1997). At the stratum disjunctum, ceramide 1 is probably hydrolyzed by ceramidases or surfactant-like lipids (Rawlings et al. 1994) and the desmosomes are degraded by humidity-dependent proteases, allowing the normal unicellular corneocyte desquamation (Rawlings et al. 1995; Rudikoff 1998).

The Intercellular Lipid Matrix

The corneocytes are embedded in a complex lamellar lipid matrix forming 20% of the volume of the SC (Forslind 1994) and 8–10.3% of its total dry weight (Schurer et al. 1991; Martini 1995). The main epidermal lipids are the ceramides ($\pm 49\%$), fatty acids ($\pm 26\%$) and cholesterol ($\pm 20\%$) (Forslind 1994). Within the deeper keratinocytes, these lipids are collected in the epidermal lamellar bodies or Odland bodies, already disposed in lamellae, and are then discharged to the extracellular space at the upper layers of the stratum granulosum. They are synthesized either “de novo” or from rearrangement of polar lipid precursors, as

glucosylceramides are transformed into less polar or nonpolar ceramides (Kerscher et al. 1991; Abeck et al. 1997). For the skin to adapt to a low-humidity environment, the percentage of ceramides and other nonpolar lipids increase progressively from the inner to the outer SC layers (Bonté et al. 1997), opposing mucosal epithelia that face an aqueous media in which the hydrophilic lipids, like glucosylceramides, are abundant in the outer layers (Holleran et al. 1993).

Ceramides play a very unique role in the skin permeability barrier. They are a heterogeneous group of sphingolipids with a polar sphingosine or a phytosphingosine base to which a nonpolar long non-hydroxy or α -hydroxyacid is linked (Kerscher et al. 1991; Abeck et al. 1997). Apart from ceramide 1, which is an *O*-acylceramide esterified usually with linoleic acid, the other five classes of skin ceramides (C2–C5, 6-I and 6-II) have very long nonpolar tails and the more polar head, corresponding to the sphingosine-related base. Due to this structure, and especially because of the geometry of ceramide 1, ceramides arrange themselves with their long intermingled tails forming nonpolar layers, limited on both sides by the small polar ceramide heads (sphingosine base) that form a narrower polar layer (Kerscher et al. 1991; Forslind 1994). The nonpolar layers are stabilized by fatty acids and cholesterol (Martini 1995) and are organized in a crystalline or gel phase (Forslind 1994) that is inflexible, impermeable to water and highly resistant to heat and oxidation (Kerscher 1991). The alternating narrower polar layers, formed by the heads of the ceramides and fatty acids, are in a fluid state, have the capacity to handle some molecules of water and are responsible for the bilayers pliability (Forslind 1994; Martini 1995).

This multilamellar structure with stable alternating nonpolar crystalline hydrophobic layers and polar hydrophilic fluid layers, is the main component of the permeability barrier of the skin that prevents excessive water loss, although it still allows some movement of water and hydrophilic substances through the fluid phase (Forslind 1994). The molecules of water retained within this structure and the nearby resident corneocytes are responsible for maintaining the pliability and extensibility of the SC (Forslind 1994; Cork 1997) and for coordinately regulating the activity of SC enzymes, such as the proteases that degrade corneosomes (Rawlings et al. 1995; Rudikoff 1998) and proteases that cleave profilagrin and filagrin into the NMF (Rawlings et al. 1994).

Dynamics of the Skin Barrier

To keep up its efficiency, the skin barrier has sensitive sensors that detect minor barrier disruptions and induce reparative mechanisms: loss of the extracellular

Ca^{2+} and K^+ concentration gradient in the epidermis due to the outward movement of water, production of cytokines by subcorneal "less-protected" keratinocytes [tumor necrosis factor alpha (TNF- α), interleukin (IL)- 1α and β , and granulocyte-macrophage colony-stimulating factor (GM-CSF); and feedback signaling by modified ceramides and sphingosine (Elias et al. 1993).

Reparative mechanisms are activated within minutes after an aggression and consist of the following (Elias et al. 1993; Mao-Quiang et al. 1993): (1) almost immediate extrusion of the content of the preformed lamellar bodies to the extracellular space, forming competent bilayers as early as 2 h after an insult (Elias et al. 1993); (2) sequential increase in the synthesis of cholesterol, fatty acid and ceramides (Ghadially et al. 1995; Abeck et al. 1997; Harris et al. 1997); (3) formation of new lamellar bodies and their replenishment by newly synthesized lipids; and (4) DNA synthesis and keratinocyte proliferation (Elias et al. 1993; Abeck et al. 1997). These processes seem to occur in two sequential phases: an acute recovery phase mainly dependent on cholesterol and FFA synthesis (first 6 h in mice), and a late recovery phase that is much slower and is dependent on ceramide and DNA synthesis and epidermal proliferation (Ghadially et al. 1995; Harris et al. 1997).

There are conflicting results concerning the time necessary for complete recovery: in mice it occurs within 24–36 h (Mao-Quiang et al. 1995), whereas studies conducted in man, using TEWL as a measure of barrier function, showed a 50% recovery by 24 h but complete recovery occurred only by day 7, independently of the acute insult that induced a similar degree of barrier disruption (Ghadially et al. 1995). Inter-study variations can be due to individual differences or external influences that delay or even abrogate barrier recovery. Nevertheless, there is a variable period of transient barrier incompetence, when an environmental aggression may further disrupt the fragile skin barrier and induce skin lesions, such as dry skin or dry eczema.

Dry Skin in Occupational Settings

There are occupational settings in which dry skin occurs frequently, due to different types of aggression – physical, chemical, mechanical – that separately, concomitantly or sequentially disturb the epidermal skin barrier. However, dry skin does not uniformly affect all workers; it occurs mainly in winter and only in more susceptible individuals, namely older ones (Ghadially et al. 1995; Rogers et al. 1996) or those with intrinsic defects in the skin barrier, such as atopics (Imokawa et al. 1991; Elias et al. 1993; Di Nardo et al. 1996; Abeck et al. 1997).

Dry skin, which is difficult to define, has subjective and objective clinical symptoms, and morphological modifications on histology (Rudikoff 1998). It can be quantified by bioengineering methods such as conductance and capacitance, which are directly dependent on the water content of the SC and, indirectly, by TEWL (Berardesca and Borroni 1995), which is the best measure for epidermal skin barrier efficiency, especially on dynamic studies (Reed et al. 1995).

Dry skin complaints often begin as a sensation of tightness and/or pruritus that develops spontaneously or on contact with woolen clothing, and especially at night. The objective signs of xerosis are a rough skin with a dull grayish-white accentuation of normal skin furrows, scaling and erythema with linear excoriation or tiny superficial cracks in a retiform pattern (as cracked porcelain or cracks in the dry mud) with polygonal scales adherent in the center and with slightly elevated borders – "erythema craquelé" (Rudikoff 1998; Thune 1996a).

In cases of prolonged exposure to a hot, low humidity ambient or to cold, dry wind in winter, dry skin occurs mainly in air-exposed areas such as the dorsa of the hands and the face, particularly the beard area, where there is the extra daily insult of shaving. The anterior shins, lateral aspects of the thighs, forearms, upper arms, and lower back are frequently involved, eventually due to the rubbing effect of clothing or to over cleaning attitudes in the bath (Marks 1992). In the hands, it is the palms and fingertips near the lateral nail margins which are mainly affected, especially when hand washing and contact with detergents and surfactants is frequent, as in health care workers, restaurant professionals or hairdressers (Rudikoff 1998). This occurs because in the palmar SC, lipids are scarce, making it more susceptible to agents that disturb lipid lamellar arrangement (Schurer et al. 1991; Abeck et al. 1997).

Environmental Insults to the Barrier

The main environmental occupational factors that interfere with barrier function and cause dry skin are: (1) physical factors, e.g., temperature, relative humidity of the air and ultraviolet rays (UVRs); (2) mechanical factors, e.g., repeated skin rubbing and strain; and (3) chemical factors, e.g., solvents, surfactants and water.

Physical Insults

Epidermal lamellar lipids, namely ceramides, show little structural change with supra-physiologic temperatures from 37 °C to 40 °C (Forslind 1994), but sequential exposure to cold and hot temperatures may disturb the barrier. This occurs in office workers who stay for prolonged periods in the warm atmo-

sphere of their office and then leave into the cold, dry winter outdoors or, during summer months, when they stay in the cold, dry air-conditioned atmosphere of their office and then leave into the humid and hot outdoor weather (Rudikoff 1998).

Exposure to very low temperatures has profound effects on skin barrier function and is a frequent cause of occupational dry skin, namely in the fish-processing industry. During work, while individuals manipulate frozen fish or fish stored in ice, the skin of their hands has a very low temperature (20 °C) and they do not complain of dry skin but, as soon as they warm their skin, hands get dry with highly increased TEWL. As shown by complementary animal studies, cold blocks the formation of new lamellar bodies interfering with barrier formation and recovery and it also abrogates the signals for barrier disruption. Consequently, during working hours, no symptoms are perceived by patients; after work, when the temperature returns to normal, the cold-disrupted skin barrier allows too much water loss and the skin gets dry before the reparative mechanisms become effective (Halkier-Sorensen 1996b).

Low relative humidity of the air, namely in air-conditioned office buildings, hospitals or aircraft, facilitates the loss of the water that is less tightly bound to the SC (Rudikoff 1998). However, normal skin does not modify its water content when it stays for short periods in environments with low relative humidity, such as commercial aircraft (7–12%) (Rudikoff 1998), and it can stand environments with a relative humidity around 30–35% for long periods (Wahlberg and Stenberg 1991; Eberlein-Konig et al. 1996). However dry skin can develop in an environment with 35% relative humidity if there are additional insults, such as airborne fiber glass or degreasing trichloroethylene vapors (Rycroft and Smith 1980).

UVRs, both UVA and UVB, in suberythemogenic doses improve barrier function (Rawlings et al. 1995). They increase all SC lipids (Lehmann et al. 1991), especially ceramides (Rawlings et al. 1995), and enhance lamellar body extrusion from the corneocytes to the extracellular space (Fartasch et al. 1992). However, after exposure to higher doses of UVR (>3 or 4 MEDs – Minimal Erythema Dose), there is a delayed disruption of the permeability barrier with a significant increase both in TEWL and in the penetration of xenobiotics (Haratake et al. 1997b). Opposing the immediate surfactant and solvent-induced barrier disruption, which is dependent on their effect on corneal lipids, UV-induced skin barrier defects occur later (>48–72 h); they are due to the UV-induced inflammatory T-cell response, epidermal proliferation and an effect on the deeper layers of the epidermis with the delivery of UV-damaged “permeability-incompetent” keratinocytes to

the SC (Haratake et al. 1997a). This explains more frequent dry skin complaints after a sunburn, particularly in younger individuals whose skin is more prone to UV-barrier disruption (Haratake et al. 1997b).

Chemical Insults

Dry skin, often as the precursor lesion of an irritant contact dermatitis, is induced mainly by organic solvents and surfactants that disturb the skin barrier either by acute or repeated smaller insults (Shmunes 1990; Rudikoff 1998). Organic solvents (aliphatic, aromatic or chlorinated hydrocarbons, alcohols, ethers and ketones) are extensively used in industries for chemical reactions in organic synthesis, for chemical extraction processes and as degreasing and dewaxing agents. Direct contact with skin is usually avoided, as cutaneous and systemic harmful effects of solvents absorbed through the skin are well known, but due to their good degreasing properties, workers sometimes use them incorrectly as a cleaning agent for their skin or their clothing (Shmunes 1990; Svendsen and Hilt 1997). Also, volatile hydrocarbons can contaminate the occupational environment and induce dry skin in air-exposed areas (Rycroft and Smith 1980) and, in this way, facilitate allergic contact dermatitis. This occurred among us in a small histopathology department of our faculty: after a long period of dry skin complaints attributed to environmental contamination by xylol, formol and methanol, one doctor and a laboratory technician developed allergic contact dermatitis from an epoxy resin present in the immersion oil for microscopy.

Solvents, such as acetone or chloroform, reduce the water-holding capacity of the SC by dissolving and extracting intercellular lipids (Thune 1996b; Abeck et al. 1997). Lipids can be completely removed, and then the corneocytes adhere tightly to one another by the single ceramide 1 outer layer of the involucrum, which prevents corneosome destruction (Chapman et al. 1991) and disturbs desquamation (Rawlings et al. 1995).

Cutaneous application of a surfactant, such as sodium lauryl sulfate (SLS) or dodecyl sulfate, induces dry, scaly skin (Thune 1996b) with decreased skin capacitance and a dose-dependent increase in TEWL, which is significant by 24 h and maximal by 48–72 h (Di Nardo et al. 1996; Welzel et al. 1996). There are contradictory results concerning the capacity of surfactants to remove epidermal lipids in the same way as solvents do (Thune 1996b; Di Nardo et al. 1996), and most studies suggest that they mainly disturb the multilamellar layered lipid structure and facilitate lipid removal, especially after prolonged skin contact (Thune 1996b; Kawasaki et al. 1997). Actually, sur-

factants bind to the lipid membranes (Kawasaki et al. 1997), disturb the arrangement and the mobility of the lipid bilayers (Thune 1996b; Kawasaki et al. 1997) and increase the water-permeable fluid phase of the intercellular lipids, which significantly reduce the SC water-holding properties (Forslind 1994; Kawasaki et al. 1997). They also affect lipid-protein interactions, disturb the corneocyte envelope and allow the loss of intracellular water and NMF molecules (Rawlings et al. 1994), and interfere with epidermal lipid synthesis (Lóden and Andersen 1996) reducing the ceramide fraction, especially ceramides 2, 3 and 4 (Di Nardo et al. 1996).

Surfactants, present in household and industrial detergents and in skin hygiene products, are one important cause of occupational dry skin, namely in hairdressers or dish washers, who contact the detergent in their work, or in occupations where hand washing is frequent, such as hospital workers, food handlers and typists. In these settings, dry skin develops due to repeated and cumulative insults of the surfactant and often by concomitant high temperature, e.g. skin cleaning with hot tap water, or mechanical friction, e.g. over cleaning attitudes in surgeons preparing for the operating theater.

Mechanical Insults

Mechanical factors, such as repeated skin rubbing or friction induced by clothing or other devices used at work, can remove the outermost SC layers, as in tape stripping, and induce dry skin or increase the effect of other aggressive factors. Prolonged use of occlusive clothing or occlusive protective measures, such as impermeable gloves, especially over a previously damaged dry skin, may further disturb barrier function and aggravate dry skin (Halkier-Sorensen 1996a; Ramsing and Agner 1996). Although there are contradictory results showing no interference on human skin (Welzel et al. 1996), most studies have shown that impermeable occlusive dressings over barrier-disrupted skin are harmful. Water accumulates in the SC, which inhibits the feedback signals that control barrier repair (Elias et al. 1993; Harris et al. 1997) and, due to SC overhydration, the conversion of profilagrin to filagrin and NMF does not occur at the upper stratum granulosum. When the occlusive effect is removed, NMF will be formed only on the innermost SC layers, while the most external layers that are deficient in NMF lose water (Rawlings et al. 1994). Usually workers use impermeable gloves or other impermeable clothing, especially if they have already experienced some symptoms of dry skin, and this often aggravates their skin condition (Halkier-Sorensen 1996a; Ramsing and Agner 1996).

Skin Barrier Susceptibility

There are intra- and inter-individual differences in skin barrier susceptibility to aggression and in its recovery capacity; these can best be documented in dynamic studies of barrier function, including TEWL, both at basal conditions and at several intervals after an aggression (Reed et al. 1995). Small differences in the constitution of epidermal lipids may be responsible for such susceptibility. Di Nardo et al. showed that a reduction of SC ceramide content is associated with higher TEWL after surfactant aggression, with a correlation between the type of ceramide deficiency and the response to aggression, e.g., a reduction of ceramide 1 is associated with a higher TEWL at 24 h; ceramide 6II seems to influence later stages of barrier recovery, with increase in TEWL later (72 h), whereas a relative deficiency in ceramide 6I is responsible for increased erythema after surfactant aggression (Di Nardo et al. 1996).

Besides skin diseases that affect the skin barrier and increase susceptibility to environmental aggression (atopic dermatitis, psoriasis, ichthyosis, essential fatty acid deficiency), other barrier modifications occur with age, skin type, dietary factors, seasons of the year and skin localization (Rawlings et al. 1994). There is no significant difference between sexes, but skin type V/VI is more resistant to damage and recovers more quickly from environmental aggression than skin type II/III (Reed et al. 1995). In old age, skin barrier is normal under basal skin conditions, even with reduced TEWL, but it is more easily disturbed and repairs very slowly after external aggression (Ghadially et al. 1995). With increasing age, the SC becomes thinner and the total amount of epidermal lipids decreases progressively (Imokawa et al. 1991; Rogers et al. 1996) with a very significant reduction in ceramides (Imokawa et al. 1991); arrangement of the lipid bilayers is defective (Ghadially et al. 1995) and, mainly after an aggression, lipid synthesis is slower, secretion of lamellar bodies is reduced and they have very few lipid layers or are almost empty of lipids (Ghadially et al. 1995).

In contrast to summer and spring, during winter there is a significant reduction (30%) in the total amount of SC lipids, although the relative percentage of the main lipid fractions is maintained (Rogers et al. 1996). Nevertheless, the more saturated oleate fatty acid replaces the unsaturated linoleate of ceramide 1, which (linoleic acid) is very important for SC flexibility and bilayer fluidity (Rogers et al. 1996). This explains predominance of dry skin complaints in winter, along with winter pruritus and winter eczema (Rudikoff 1998).

In the hands, palmar SC is more susceptible to solvents or surfactants and chapping, hyperkeratosis

and fissuration often affect the palms while sparing the dorsal hand (Abeck et al. 1997). Even though the palmar SC is thicker, it has fivefold less lipid between the corneocytes (2%) (Schurer et al. 1991; Rogers et al. 1996) and the supra-basal highly flexible glycine-rich K1-10 keratin pairs, present in other skin areas, are replaced by the less pliable K6-16 pairs, usually associated with hyperproliferation and barrier disruption (psoriasis) (Smack et al. 1994).

Among skin diseases affecting skin barrier, atopic dermatitis is associated most frequently with occupational dry skin symptoms (Seidenari 1996; Abeck et al. 1997). Atopic dermatitis patients characteristically have a dry skin, especially when exposed to surfactants (Seidenari 1996), hot water and exaggerated cleaning measures, and they are the main individuals to develop dry skin complaints in low-humidity environments (Eberlein-Konig et al. 1996). They have a basal increased TEWL, reflecting a disturbed SC water-holding capacity (Fartasch et al. 1992), a lower resistance to aggression and a slower recovery phase. They have a near 50% reduction in the SC lipid content along with a very significant reduction of ceramide 1, both in lesional and non-lesional skin (Imokawa et al. 1991); sphingomyelin is not committed to ceramide synthesis due to a sphingomyelin acylase deficiency (Murata et al. 1996). Also, in atopic dry skin, lamellar bodies are incompletely fused with the plasma membrane and their content is not regularly extruded to the intercellular space, which explains intercellular lipid reduction (Fartasch et al. 1992).

From Occupational Dry Skin To Eczema

When the barrier function is disturbed, besides excessive loss of water to the environment and consequent dryness, the skin becomes more vulnerable to exogenous hazards: (1) there is an increased penetration of irritants, namely surfactants, solvents and enzymes (Haratake et al. 1997b), with a lowered threshold to induce irritant contact dermatitis (Seidenari 1996); (2) most allergens have an easier access to the stratum spinosum, where they react with living keratinocytes and Langerhans' cells and induce skin sensitization or initiate allergic contact dermatitis in sensitized individuals (Gonçalo 1996); and (3) mites and microorganisms adhere more easily to the skin, as occurs with *Staphylococcus aureus* in atopic dry skin, and their enzymes or other secretion products, their allergens or their superantigens penetrate the SC more easily and induce cutaneous eczematous reactions. This can occur in several ways: by a nonspecific cutaneous inflammation (Murata et al. 1996), by an antigen-specific immune activation mast cells or sensitized T lymphocytes or

by an oligoclonal T-lymphocyte proliferation by superantigens (Hauser et al. 1996).

Also, after acute or chronic barrier disruption, the skin exhibits a subtle state of continuous dermo-epidermal inflammation, with altered cutaneous immunoregulatory mechanisms that may lead to eczema: (1) keratinocytes produce pro-inflammatory cytokines, such as TNF- α , IL-1, IL-8 and GM-CSF (Nickoloff and Naidu 1994; Wood et al. 1992, 1994; Nishijima et al. 1997); (2) epidermal Langerhans' cell density increases proportionally with the degree of barrier disruption, reaching its maximum density by 24-48 h (Proksch et al. 1996); (3) epidermal Langerhans' cells show activation markers, expressing a higher number of the co-stimulatory molecules HLA-II, CD54 and CD86 (Nishijima et al. 1997); and (4) Langerhans' cells isolated from disrupted barrier skin exhibit an increasing capacity for antigen presentation and T-cell stimulation/sensitization (Nishijima et al. 1997).

In atopic dermatitis, there is evidence that dry skin and eczema are related; sphingomyelin is not used for synthesizing the ceramides due to an abnormal sphingomyelin acylase activity. Instead, it is metabolized into the pro-inflammatory sphingosyl-phosphorylcholine that enhances arachidonic acid or eicosanoid release and increases membrane ICAM-1 expression in human keratinocyte cultures (Murata et al. 1996).

Dermal cutaneous vascular response is also altered by barrier disruption: after exposure to SLS for three consecutive days, the skin exhibits an increased cutaneous blood flow after exposure to tap water (Ramsing and Agner 1997), which probably explains frequent patient complaints that water aggravates their dry skin or hand dermatitis.

Therefore, patients with dry skin continuously exposed to an aggressive environment are more prone to develop eczematous conditions, either by non-immune or immediate and/or delayed immune mechanisms. For instance, hairdressers who are exposed continuously to water and shampoos develop dry hands frequently, followed by an irritant contact dermatitis, then allergic contact dermatitis to occupational allergens. Immediate-type allergic contact dermatitis, like protein contact dermatitis or contact urticaria also occur more frequently in patients with dry hands, namely in the catering or fish processing industries (Halkier-Sorensen 1996b) or in surgeons and nurses who are exposed to latex gloves after exaggerated hand cleaning measures.

Also, patients with dry skin, namely those with atopic dermatitis, frequently develop face and eyelid eczema when they are exposed to polluted air and cigarette smoke or simply to the dry and cold winter wind or to hot and dry air-conditioning (Eberlein-Konig et al. 1996). When they abuse hot water baths and

soaps, especially antiseptic soaps, they develop "eczema craquelé" or "aesteatotic eczema". This is present as very pruriginous, ill-defined erythematous patches with roughened and dry skin that cracks superficially, creating red interconnected fissures that form a geometrical 'crazy-paving' aspect (Thune 1996a; Rudikoff 1998), or as circular erythematous plaques with a vesicular or crusted well-limited border and a tendency to central clearing (Wahlberg and Stenberg 1991).

Treatment Of Dry Skin

When considering the treatment of dry skin conditions in an occupational setting, it is most important to correct first any environmental aspect that may be responsible for the chronic barrier disruption (temperature, relative air humidity, cleaning products or protective measures) and this may be sufficient to cure dry skin.

Particular attention should be paid to the prolonged use of impermeable gloves, a frequent complaint among hospital personnel and dentists, especially if the hands have been previously exposed to soaps, detergents, disinfectants or irritants (apart from delaying barrier recovery, impermeable gloves increase the damaging effect of these substances). Cotton gloves used under the rubber gloves prevent the harmful effect of glove occlusion on barrier recovery and ameliorate cutaneous symptoms (Ramsing and Agner 1996).

Exposure to low-dose UVR may benefit other types of dry skin, beyond atopic dry skin and atopic eczema, as it increases ceramides and all other SC lipids (Lehmann et al. 1991; Rawlings et al. 1995; Rawlings et al. 1996). However, even without sun exposure, during summer, barrier function improves due to the increased lipid production (Rogers et al. 1996).

In the case of more susceptible workers or when the environmental factors cannot be corrected, other measures must be used to prevent and treat dry skin and avoid progression to eczema and increased penetration of harmful xenobiotics. In individuals with predominantly wet work, who contact with surfactants and foods, frequent application of petrolatum or a lipid-rich emollient protects them from developing dry skin, e.g., in experimental conditions previous application of a lipid-rich emollient reduced the SLS-induced TEWL increase (Halkier-Sorensen 1996a; Lóden 1997). Nevertheless, these conclusions cannot be extended to all occupational settings and to every commercial emollient available; different aggressions in the working place need different protective measures, which are not yet well standardized or adjusted for every particular case. In addition, for each protective cream studied, whose complete constitution is seldom known, a small difference in the ingredients

and their relative amount may be responsible for disparate results on barrier protection and recovery. For instance, the addition of 0.1% chlorhexidine to a barrier cream delays the later phases of barrier recovery, very probably by the aggression on deeper keratinocytes that are preparing the lipid bilayers (Halkier-Sorensen 1996a).

There are several topical agents, usually called moisturizers or emollients, that ameliorate the manifestations of dry skin (turn it smoother, more pliable and extensible and less scaly) and also restore or improve the protective barrier against the penetration of environmental hazards (Marks 1997). Moisturizers work mainly via three different mechanisms. Humectants, such as glycerin and sorbitol, urea, lactic acid and pyrrolidone carboxylic acid [PCA], which diffuse and fix themselves into the SC, attract and retain water and, thereby, increase SC water content. Occlusive emollients are formed mainly by lipids from animal fats (lanolin and derivatives), vegetable or vegetable-based oils (olive oil, coconut oil, primrose oil), mineral oils (vaseline and light paraffin oil), synthetic oils (synthetic silicone oils) or waxes (beeswax, paraffin wax). Physiologic lipid mixtures, consisting of ceramides, cholesterol and free fatty acids mixed in physiologic proportions, are incorporated into the nascent multilamellar bilayers therefore helping in the reconstitution of the physiologic skin barrier (Mao-Quiang et al. 1993; Mao-Quiang et al. 1996). Petrolatum, an occlusive emollient constituted mostly by inert lipids, penetrates within the intercellular spaces, takes the place of the lipids in the upper SC layers and has a transient but very efficient occlusive effect, preventing the movement of the water to the environment and promoting its slow accumulation in the SC (Ghadially et al. 1992; Mao-Quiang et al. 1995).

Some substances, usually included in moisturizers, have other potential beneficial effects on dry skin: (1) the L-isomer of lactic acid increases the endogenous synthesis of ceramides and promotes the incorporation of linoleate, instead of oleate, into ceramide 1 (Rawlings et al. 1996); (2) glycerol and other polyols prevent lipid crystallinity (Rawlings et al. 1994), increase SC humidity and promote corneosome digestion and, consequently, the unicellular invisible desquamation (Rawlings et al. 1995); (3) alpha-hydroxy acids improve keratinization and SC hydration (Leyden et al. 1995); and (4) silicones or silicone-based barrier creams may have an extra protective effect on external aggressions.

The combined use of these substances is the rule, as they can have an additive beneficial effect: humectants have a very effective and almost immediate effect of attracting water to the SC and, if we add an occlusive lipid-rich emollient that penetrates the intercellular space, it will keep the water trapped within the SC and

prevent its loss. Because this emollient effect is transient (4–6 h), physiologic lipid mixtures that incorporate themselves within the lamellar layers will have a more delayed but prolonged effect (Mao-Quiang et al. 1996), probably similar to the use of substances that promote ceramide synthesis. Nevertheless, these substances have to be mixed in adequate proportions in order to avoid a deleterious effect on the skin barrier; the use of isolated ceramides or cholesterol or an unbalanced mixture of physiologic lipids in a previously disturbed skin barrier is more harmful than beneficial (Mao-Quiang et al. 1993; Mao-Quiang et al. 1996).

As knowledge increases regarding the skin barrier and how to modify it, the old art of making emollients to treat dry skin, dating back to the 'cold cream' of Galien, is turning into the new, developing science of making moisturizers that clear dry skin, improve disrupted skin barrier, accelerate recovery and protect it from specific environmental aggressions. There are several available ingredients with additive effects that can be mixed in water-in-oil, oil-in-water or more complex emulsions that are more acceptable to the patient and are best adapted to each occupational setting. For the moment, studies clearly show benefits from correct use of adequate moisturizers in protecting against harmful occupational aggressions and in treating dry skin in certain occupational settings. However, there is still much more to do in adapting each emollient to each particular occupation, to each particular patient and either as a preventive or a treatment for dry skin conditions.

For the present, because these rules are not well established, emollients should be used for occupational dry skin, although somehow empirically, and as both a preventive and a therapeutic measure. We should try to adapt the emollient to each patient and to each occupation, let the patient choose the emollient with which he feels best, and use a topical corticosteroid whenever eczematous changes develop on dry skin, as steroids improve inflammation and do not further disturb the skin barrier (Lóden and Andersen 1996; Halkier-Sorensen 1996a).

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Poultry Processors

M. Gonçalo

Introduction

For poultry processing, live animals (chickens, ducks, turkeys) are received in cages and transferred to an area where they are stunned by an electrical shock, hung upside down to incise their neck for exsanguination, plunged in boiling water to become scalded, and plucked, usually by mechanical processes in an assembly-line fashion. Workers usually only assist these operations, but they may get burns or electrical shocks by accident or when the machines need human correction. The animals are then eviscerated manually, cleaned with running water, decapitated, declawed, cut into pieces, deboned and sliced before packaging for sale and/or cold storage.

By the end of the 1970s, the poultry-processing industry was considered a high-risk industry for skin diseases (Marks et al. 1983), and nowadays occupational dermatoses are still frequent among poultry-processing workers (Hayashi et al. 1989). Poultry processors are exposed to several biological irritants. They experience almost continuous wet work, including contact with irritant animal liquids, faeces and viscera, and disinfectants and detergents for hand cleaning and for the hygiene of the work place. Workers also suffer frequent cuts by knives, sharp objects and bone fragments, especially the neck bones, which are exposed after chicken decapitation. Hands and, eventually, the forearms are the main affected areas, even though some workers use protective measures like cotton and rubber or vinyl gloves, plastic forearm shields, rubber boots and aprons, and chain-mesh gloves to prevent cuts and abrasions from sharp objects and bones. Although the use of protective gloves is very useful for preventing skin disorders (Hayashi et al. 1989), it is not always possible to wear them due to the subtle tasks that have to be performed.

Biological hazards are very frequent. Susceptible workers, mainly atopics, exposed to animals carrying mites such as *Dermatophagoides* species or *Dermanyssimus gallinae* (red poultry mite) may suffer acute prurigo, mainly of the exposed areas (personal expe-

rience) or scabies-like lesions (Yassien et al. 1996). Skin abrasions and minor cuts by sharp objects, and especially by bone fragments, are often secondarily infected by pyogenic cocci (*Staphylococcus aureus* and *Streptococcus*), eventually with sepsis (Barnham and Kerby 1984), or by *Erysipelothrix insidiosus*, the agent of Erysipeloid. Acute pyogenic paronychia or chronic *Candida albicans* paronychia and onychia, sometimes with interdigital intertrigo, are favoured by the wet work, contact with aggressive chemicals and glove occlusion. In some of these occupational settings, hand or forearm warts and wart-like lesions induced by human papillomavirus (HPV), especially HPV-7, are present in more than 40% of the workers (Stehr-Green et al. 1993), mostly those who handle the blood, claws or skin of raw or unfrozen chicken (Stehr-Green et al. 1993; Keefe et al. 1994). The animals are not infected with the virus, but these working conditions seem to facilitate spread of the virus among workers (by the meat or contaminated instruments that workers manipulate), or there might be some product from these animals that favours virus proliferation and infection (Stehr-Green et al. 1993).

Wet work with regular hand cleaning with soaps, detergents and disinfectants favours dry skin with chapping, and this in turn facilitates irritant and allergic contact dermatitis. Irritant contact dermatitis occurs mainly in the eviscerating section (Marks et al. 1983), and direct skin contact of irritated hands with proteins from the viscera, blood, meat and skin of these animals favours immediate allergic-contact reactions: contact urticaria or protein contact dermatitis. Immediate skin reactions from chicken and turkey meat have been seen mainly in food handlers (Hjorth and Roed-Peterson 1976; Katchen and Maibach 1991), but cases of type-I and -IV allergy to chicken muscle and heart have been described in a poultry eviscerator (Beck and Nissen 1982).

Allergic contact dermatitis in this occupational setting is not very frequent and is mainly due to rubber products used for skin protection (gloves, aprons, rubber boots) or from medicaments used to treat or prevent dry skin (lanolin) or skin infection

[antiseptics, ethylenediamine contained in Mycolog cream (Marks et al. 1983)]. Although rare, allergic contact dermatitis can occur due to exposure to the viscera and blood contaminated with substances from animal feed, like growth stimulants, antioxidants, vitamins or antibiotics (chlorpromazine, terramycin, chlortetracycline or virginiamycin), as occurred with dinitromide (a dinitrobenzene derivative used to control chicken coccidiosis) (Bleumink and Nater 1973).

Irritants

Water (wet work)
Hand-cleaning soaps and detergents
Germicidal solutions
Detergents and cleansing products for the work place
Animal viscera - blood, enzymes, faeces

Standard Allergens

Thiuram mix, 1% petrolatum (pet) (gloves, aprons)
2-Mercaptobenzotiazol, 2% pet (gloves, aprons)
Mercapto mix, 2% pet (gloves, aprons)
N-isopropyl-N'-phenyl-p-phenylenediamine, 0.1% (black rubber boots)
Formaldehyde, 1% aqueous solution (aq) (cleaning solutions)
Ethylenediamine dihydrochloride, 1% pet (medications)
Wool alcohols, 30% pet (medications)

Additional Allergens

Chlorhexidine digluconate, 0.5% aq (antiseptic solutions)
Ammoniated mercury chloride, 1% pet (antiseptic solutions)
Thiomersal, 0.1% pet (antiseptic solutions)
Povidone-iodine, 5-10% aq (antiseptic solutions)
Chicken, duck or turkey meat or viscera (prick test as is for contact urticaria)

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