When to pour oil on troubled dry skin

What we know about the barrier function of the skin has increased in the past 20 years. This has led to better understanding of dry skin conditions and the development of more sophisticated moisturising products

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The importance of the barrier function of skin is illustrated by the patient who has third degree burns and dies of dehydration. As well as preventing dessication, the skin also prevents invasion by micro-organisms, and guards against mechanical and chemical insults and ultraviolet radiation.

Readers will know that skin is composed of an inner dermis, which provides structural support, and an outer epidermis, which is composed of several layers of developing cells. Keratinocytes are produced from basal cells in the stratum basale and have a life cycle of four weeks. As these migrate towards the outermost layer of the epidermis, the stratum corneum, they undergo maturation and differentiation into corneocytes — anucleated, flattened, hexagonal cells that are filled with water-retaining keratin and surrounded by a thick proteinaceous envelope.

The structure of the stratum corneum has also been likened to a brick wall, with the

KEY POINTS

- Factors affecting skin dryness include genetics, temperature and humidity, contact with irritants, medicines (eg, retinoids), disease (eg, hypothyroidism) and ageing.
- Research into skin barrier function has revealed the potential importance of skin lipids, enzymes called kallikreins and a protein called filaggrin.
- People with dry skin should be advised to avoid prolonged periods in centrally heated or air-conditioned rooms.
- It is advisable to recommend people with dry skin, especially those with eczema, to avoid soaps because they raise skin pH, increasing dryness and promoting growth of Staphylococcus aureus.
- People with diabetes should be encouraged to take good care of their skin.
- Moisturisers contain humectants, occlusives and emollients.
- Effects of products on skin barrier function can be measured using transepidermal water loss, capacitance and conductance.

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cereamides (sphingoloids) are produced from the combination of fatty acids and a sphingoid base (an amino alcohol). (There are at least nine subclasses of cereamides in human skin, synthesised by at least two enzymes: \( \beta \)-glucocerebrosidase and sphingomyelinase.) Cholesterol is produced by the action of steroid sulphatase from lamellar bodies on cholesterol sulphate in the stratum corneum. Fatty acids are derived from phospholipids via the action of phospholipases, again from lamellar bodies.

In 1991, Imokawa et al found that there was a marked reduction in cereamide levels in the skin of atopic individuals compared with healthy controls. In 2004, Cho et al found an inverse correlation between cereamide levels and clinical severity of psoriasis lesions. (It has been suggested that the reduced cereamide levels in psoriatic skin down-regulates the apoptotic pathway and that this leads to epidermal proliferation.)

The lamellar bodies are also known to secrete various peptides that are required for the antimicrobial function of the skin.

### Natural moisturising factor

The water content of a healthy stratum corneum is between 15 and 20 per cent. Water retention is required not only to maintain skin flexibility but also to allow proper functioning of enzymes.

Corneocytes contain “natural moisturising factor” (NMF), a mixture of hygroscopic agents and humectants, including amino acids (40 per cent), pyrrolidone carboxylic acid, lactate, urea and various other salts that absorb atmospheric water and draw in water from the water layer. The source of the amino acids in NMF is filaggrin (an acronym for filament aggregating protein), which is derived from profilaggrin, a high molecular weight protein. Profilaggrin is made and stored in keratinocytes. When these die and change into flattened corneocytes, profilaggrin is converted into filaggrin, stored within the corneocytes, and protected from further breakdown by forming a complex with keratin. This filaggrin-keratin complex exists only in the deeper layers of the stratum corneum and, under normal circumstances, will not be present in the superficial layers. Complete hydrolysis of filaggrin into amino acids occurs in response to low relative humidity. At higher humidities there is less need to provide intrinsic humectancy in the stratum corneum.

Reduced levels of filaggrin (and hence NMF) disrupt the mechanisms that maintain skin hydration, leading to dry skin. In 2006, researchers identified that null mutations in the gene that codes for profilaggrin, FGL3, were responsible for ichthyosis (see Panel 1 for more on this condition). Further work revealed an association between null mutations in FGL3 and the development of atopic eczema and there are now several epidemiological studies showing that as much as 50 per cent of Europeans with atopic eczema have null mutations in the FGL gene.

### Abnormal desquamation

Under normal circumstances, the stratum corneum thickness is kept relatively constant and the flattened corneocytes are continuously shed (desquamated) and replaced.

It has been estimated that an adult human loses nearly a billion cells each day from the skin surface. The process is not completely understood but involves progressive proteolytic breakdown of the corneodesmosomes at the outer surface of the skin.

The shedding of individual corneocytes proceeds unnoticed but when abnormalities in the desquamation process occur, the corneodesmosomes are not properly degraded. As a result, corneocytes are not detached as single cells but as clumps that are visible as white flakes or scales on the surface of the skin.

Some evidence suggests that a series of enzymes called kallikreins (KLKs) are involved in desquamation, in particular KLK7 and KLK5. It has been shown that application of inhibitors of these enzymes give rise to dry and scaling skin conditions and that the activity of KLK7 in abnormally dry (xerotic) skin is reduced.

The kallikreins are regulated by enzyme inhibitors derived from a protein called LEKTI (lympho-epithelial Kazal type inhibitor), which is encoded by the SPINK5 gene. Loss of function (“null”) mutations in the SPINK5 gene is thought to be responsible for Netherton syndrome, a rare disorder that involves in overdesquamation and flaking red sore skin.

### Disturbing the skin barrier

The stratum corneum provides a relatively impermeable barrier, due to its hydrophobic intercellular lipids, but a small amount of water is lost to the environment and this is referred to as transepidermal water loss (TEWL). The skin is assaulted daily by detergents, hot water and various chemicals. If the barrier cannot remain intact, the organism is at risk of desiccation through increased TEWL.

When the skin barrier is disturbed, the epidermis mounts an almost immediate response to aid recovery. This involves the rapid release of pre-formed lipids from the lamellar bodies, followed by synthesis of new lipids. Studies using inhibitors of the enzymes involved in lipid synthesis reveal that barrier recovery requires the presence ceramides, fatty acids and cholesterol. Absence of any one of these retards the recovery process.

The time taken for complete recovery varies with age. Full recovery occurs in as little as three days in young people but can take up to a week in aged skin.

Measurements in children with atopic eczema have shown that the severity of the eczema correlates with the magnitude of TEWL (ie, the barrier impairment).
suitable.

Topical or oral isotretinoin found that twice daily application of the cream for 15 days significantly increased transepidermal water loss, which indicates a reduction in the strength of the skin barrier function. Any moisturising agent applied to acne-prone skin has the potential to be comedogenic, making the acne worse. Facial moisturisers are sometimes referred to as “oil-free” but this is a misnomer because all moisturisers contain lipids. However, the term is generally reserved for preparations that do not contain mineral or vegetable oils and instead rely on silicone-based agents, such as dimethicone and cyclomethicone, for their occlusive properties. These are hypoallergenic and non-comedogenic.

One study using Cetaphil moisturising cream (Galderma) for patients with acne prescribed topical or oral isotretinoin found that twice daily application of the cream for 15 days significantly improved skin dryness, roughness and desquamation, but any oil-free moisturiser would be suitable.

**PANEL 2: RETINOID CASE STUDY**

An 18-year-old with acne is being prescribed a topical retinoid. Although this is helping, his skin has become dry. He wants to know whether or not to use a moisturiser and if so which one would be suitable.

Retinoids are known to cause dryness and to irritate the skin (“retinoid dermatitis”). This effect is a type of irritant contact dermatitis, characterised by erythema, burning, dryness, scaling and pruritus. It is associated with an increase in transepidermal water loss, which indicates a reduction in the strength of the skin barrier function. Any moisturising agent applied to acne-prone skin has the potential to be comedogenic, making the acne worse. Facial moisturisers are sometimes referred to as “oil-free” but this is a misnomer because all moisturisers contain lipids. However, the term is generally reserved for preparations that do contain mineral or vegetable oils and instead rely on silicone-based agents, such as dimethicone and cyclomethicone, for their occlusive properties. These are hypoallergenic and non-comedogenic.

A skin barrier function after acetone treatment (the application and removal of adhesive tape) recovered more quickly in rodents kept in low humidity conditions than in high humidity conditions.

A reduction of relative humidity reduced corneocyte release (a measure of desquamation) in pig skin.

The skin of people living in a dry climate (e.g., Arizona) compared with people in New York has much lower TEWL, less scale and higher amounts of ceramides.

Exposing human skin to low humidity for as little as six hours results in decreased water content and increased roughness.

Differing levels of stratum corneum lipids have been observed with season changes as well as increasing age, with reduced lipids in winter.

In xerotic skin ceramide levels are decreased and fatty acid and corneodesmosome proteins increased. Corneodesmosome degradation is reduced at low relative humidity.

**PANEL 3: INFERENCES FROM SKIN STUDIES**

- When hairless mice are exposed to a relative humidity below 10 per cent, there is an increased synthesis of epidermal lipids and epidermal hyperplasia.
- Low humidity resulted in a 31 per cent reduction in transepidermal water loss (TEWL) compared with animals kept at high relative humidity (>80 per cent).
- Skin barrier function after acetone treatment or tape stripping (the application and removal of adhesive tape) recovered more quickly in rodents kept in low humidity conditions than in high humidity conditions.
- A reduction of relative humidity reduced corneocyte release (a measure of desquamation) in pig skin.
- The skin of people living in a dry climate (e.g., Arizona) compared with people in New York has much lower TEWL, less scale and higher amounts of ceramides.
- Exposing human skin to low humidity for as little as six hours results in decreased water content and increased roughness.
- Differing levels of stratum corneum lipids have been observed with season changes as well as increasing age, with reduced lipids in winter.
- In xerotic skin ceramide levels are decreased and fatty acid and corneodesmosome proteins increased. Corneodesmosome degradation is reduced at low relative humidity.

**Dry skin**

There is no precise definition of xerotic skin although the sensation is often described as “tightness”. Other descriptors include painful, itchy, stinging or tingling. flakes are visible and the skin feels rough and uneven. In more severe cases fissures and cracks develop, which provide entry points for irritants and potentially harmful organisms.

Dry skin will occur when the water content of the stratum corneum falls below 10 per cent. Three types of factor give rise to dry skin:

- Internal or genetic
- Environmental, which include changes in relative humidity and temperature
- External, including the use of solvents, surfactants (in soaps), acids or alkalis, retinoids (see Panel 2 for a case study), and UV radiation

Internal factors can include altered or impaired lipid synthesis. For example, in recessive X-linked ichthyosis, there is a deficiency in cholesterol sulphatase. Subsequent accumulation of cholesterol sulphate leads to inhibition of desquamatory proteases. Disorders that have, as part of the clinical picture, an ichthyotic appearance include Sjogren-Larsson syndrome and Refsum disease.

Dry skin can also be a feature of diabetes and thyroid disease (hypothyroidism). In diabetes, it is thought that loss of fluid because of high blood glucose can cause dry skin. According to Diabetes UK, keeping skin in good condition should be a priority for people with diabetes. Ageing is also associated with xerotic skin and it has been shown that aged skin contains lower levels of ceramides and triglycerides.

**Changes in temperature and humidity**

Many people with skin problems, such as eczema and psoriasis, find that their condition worsens with a decrease in temperature and relative humidity. Central heating and air conditioning can also give rise to dry skin.

Panel 3 lists some inferences from various studies of the effects of humidity on skin in the past 20 years. Although the skin can adapt to low relative humidity conditions with time (e.g., barrier function becomes stronger), exposure to such conditions can induce the appearance of visible skin scales in as little as three days. At low humidity the activity of the desquamatory enzymes, which rely on water for their activity, is decreased and this causes the adherence and accumulation of corneocytes, leading to visible skin flaking. It also appears that low humidity can give rise to the early signs of inflammation.

It is now clear that the stratum corneum acts as an important biosensor and is able to respond to changes in the relative humidity of the environment. It seems that modern life (e.g., air conditioning, air travel) has increased the frequency of dry skin. People with dry skin can be advised to avoid prolonged periods in centrally heated or air-conditioned rooms.

**Soaps and detergents**

The skin has a normal pH of between 5 and 5.5. This slightly acidic environment works in conjunction with anti-microbial peptides to protect the skin against micro-organisms. Maintenance of skin pH is important because an elevation reduces the activity of the enzymes involved in lipid synthesis but increases the activity of enzymes involved in desquamation, the net effect of which is to reduce the functional integrity of the skin barrier. The pH of the skin is maintained by the secretion of fatty acids from sebum and from the fatty acids present within the intercellular lipid layer as well as from the amino acids generated from filaggrin.

It has been known for some time that skin cleansers can have a negative impact on the skin, causing dryness. Soaps are the alkaline salts of fatty acids, consisting of a hydrophobic tail and a hydrophilic head, and have an alkaline pH in the range of 9 or 10. Surfactants in soaps can bind with proteins and lipids in the stratum corneum and this interaction can lead to changes in the conformational shape of proteins that ultimately affects biological function, such as ability to hold water, and impairs the barrier function of the skin. Soaps also disturb the lipid structure and because the enzymes involved in desquamation are found within the lipid matrix, this will influence enzyme activity.

The clinical relevance of disturbances in pH becomes apparent in conditions such as atopic eczema. It is known, for example, that skin pH is raised in atopic eczema and that micro-organisms, such as...


**Moisturisers**

The term “moisturiser” has little scientific meaning and is often used interchangeably with “emollient”, although the latter is usually defined as a substance that can smooth or soften the skin.

Despite the wide range of ingredients and formulations available, all moisturisers work in one of two ways:

- Increasing the water holding capacity of the skin
- Trapping water in the skin by providing an occlusive oily water-impermeable layer

A moisturiser will contain humectants, occlusives and emollients (see Panel 4) in varying combinations, working in a complementary manner.

Humectants are able to attract water into the skin (unless the relative humidity is greater than 80 per cent) and absorb that water. Occlusives and emollients are fats but “emollients” and “oils” are the preferred terms since fat (or lipid) has negative connotations.

The first occlusive agent was petroleum jelly (Vaseline; white soft paraffin) and although originally considered as inert, it has been shown to penetrate the stratum corneum and aid lipid biosynthesis.

The occlusive prevents water loss via evaporation and the emollient allows the product to spread on the skin and fills the cracks and crevices between corneocytes.

Moisturisers add water to the skin but increased hydration is transient because the product to spread on the skin and fills the cracks and crevices between corneocytes.

The most commonly used formulations are emulsions — two-phase water-in-oil systems (eg, creams) or oil-in-water systems (eg, lotions).

**Efficacy**

All preparations should achieve skin hydration but, with a greater understanding of some of the factors involved in the pathophysiology of dry skin, some of the newer products claim to correct underlying problems. For example, the most recent development in moisturiser technology is the inclusion of barrier repair lipids (ceramides, cholesterol and free fatty acids).

It is worth exploring which particular ingredients, old and new, have evidence of efficacy demonstrated in clinical studies. Panel 5 describes how moisturisers are tested.

**References**


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