

# Combating xerosis

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During the past few decades, the incidence of dryness related skin problems has been on the increase. More than 75% of people above the age of 65 years suffer from xerosis.

As the skin is the largest organ, it is exposed to the external environment and comes into contact with the sun, chemicals, soap and harsh temperature conditions while acting as a barrier to protect the internal organs in our body.

## Causes of dryness

There are various other causes of dry skin, including genetic and acquired diseases, nutritional deficiencies, use of certain medications and poor lifestyle. One can also not ignore the fact that people now have a longer lifespan, and as one gets older the function of the skin barrier and sebaceous glands decrease, leading to xerosis.

Dryness of the skin is caused by reduced water content of the stratum corneum (outermost layer of the skin).

Water is usually lost through evaporation and is replenished from the lower layers of the epidermis and dermis.

An imbalance between supply and loss of water, leads to xerosis. There are many lipids and derivatives of amino acids in the stratum corneum that regulate the transepidermal water loss.

These are mainly produced by the lamellar granules in the epidermis, as well as the

sebaceous glands, which produce sterol esters. These substances help by keeping the natural moisturising factors (NMF) inside the cells, thus assisting in the retention of water and keeping the cells hydrated. In brief, as the epidermis loses water, the skin appears flaky and small cracks become visible, which get accentuated along the natural skin lines. The xerotic skin can appear inflamed and become very pruritic. The scratching that ensues can lead to the introduction of infections, as well as scar formation.

## Genetics

There are numerous genetic conditions that result in dry skin. Ichthyosis vulgaris is by far the commonest and can affect up to one in 250 individuals. The dryness that occurs as a result of this disease becomes visible in later childhood, and is labelled as a person with overly dry skin.

Keratosis pilaris has been described as being part of this condition and manifests as sandpaper roughness affecting the upper arms, proximal limbs and in rare cases, the face. This disease is caused by a dysfunction of the fillagrin protein, which forms part of the NMF of the epidermis.

Other genetic conditions include x-linked ichthyosis, steroid-sulfatase deficiency and several others. Notably, one should not forget atopic eczema, which is caused by a dysfunction in fillagrin and decrease in ceramides, leading to dryness, inflammation, erythema and pruritus.

## Diseases

Other common diseases that can manifest with dry skin are HIV infections, end-stage renal disease, hypothyroidism, sarcoidosis, hormonal disbalance (like in menopause), neurological disorders, as well as leprosy and syphilis.

There are various other autoimmune diseases including scleroderma and Sjögrens syndrome that can decrease the hydration of the skin through the loss of function of certain glands. Rarely, paraneoplastic syndromes can result in xerosis due to the presence of internal malignancies. Therefore one should always have a high level of suspicion to detect such conditions. Sometimes, the use of radiotherapy to treat the cancers may also lead to dry skin, and thus a good history can be very helpful.

## Medications

Apart from the diseases discussed above, there are several medications that lead to dryness of the skin. The most drastic of them is isotretinoin, which leads to predictable severe xerosis. This medication has its action on certain receptors in the skin, which results in the inhibition of sebum secretion by the sebaceous glands, as well as more regulatory actions on the keratinocytes.

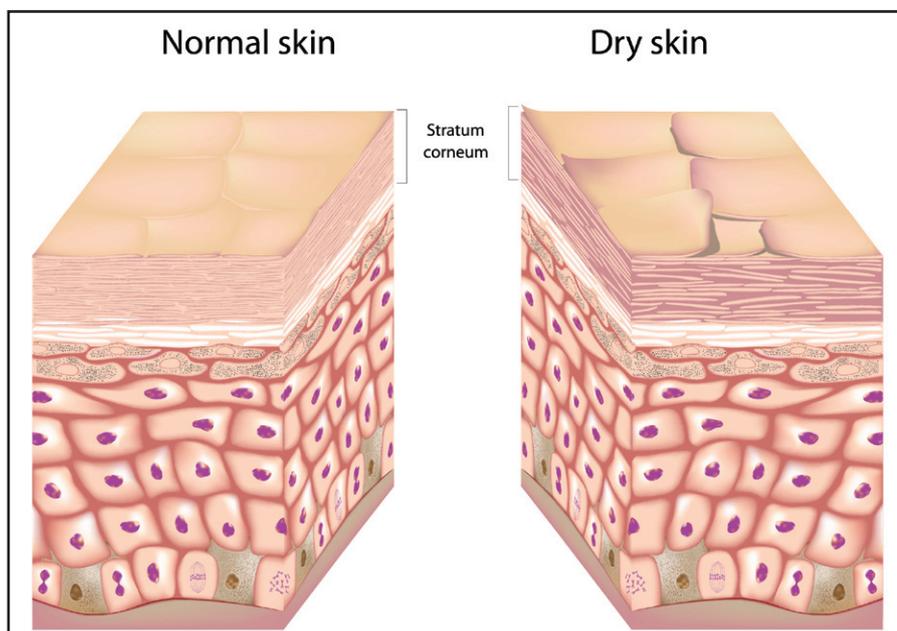
Others include anti-androgens and lipid lowering medications. Various others that have lesser effects on the skin include diuretics and beta-blockers, as well as some chemotherapy agents (EGF-inhibitors).

The presence of malnutrition due to socio-economic factors cannot be overlooked as a common cause of xerosis in our society. This mainly affects children, the elderly, alcoholics, and people suffering from chronic diseases. Zinc deficiency and lack of vitamin A are frequently encountered in public hospitals.

Various vitamin B deficiencies, as well as protein malnutrition are more prevalent in other African countries. Understanding the underlying cause of the xerosis can help in formulating a more comprehensive treatment. Once these have been addressed, the keratinocytes with their NMF tend to regain normal function and the skin appears smoother.

## Role of moisturisers

In most cases, the cause of xerosis is unknown and therefore, one has to make use of moisturisers to address the dryness. In the past two decades, a better understanding of the NMF, ceramides as well as the function of aquaporin in the epidermis, has led to the development of more effective moisturisers.



Dry skin

The NMF is a collection of water-soluble compounds that are only found in the outermost layer of the skin. They make up to 20% of the weight of the stratum corneum and absorb water from the atmosphere and combine it with their own water content, which results in a hydrated outer skin.

The NMF is composed mainly of free amino acids and their derivatives, like PCA, urocanic acid (a natural absorber of UV rays) and inorganic salts, sugars, lactic acid and urea. NMF components are derived from the breakdown of products from the proteolysis of the fillagrin protein, which starts a profillagrin in the granular layer.

These compounds are highly efficient in attracting and binding water inside the corneocytes (the keratinocytes on the outermost layer of the skin), thus working as humectants. This process is very well

regulated and even low levels of humidity do not affect its function. In addition, the NMF allows the corneocyte to balance the osmotic pressure exerted by the intracellular cement surrounding them.

Keeping the solute concentration balanced is important for preventing excessive water influx, as seen in the wrinkled skin of someone who has been in the bath for too long, or water efflux, which would cause the corneocytes to shrink. The NMF being water soluble makes them vulnerable to being lost by repeated contact with water, thus making the skin dryer.

### Ceramides

Ceramides are the major constituent of the lamellar sheets that help keep the corneocytes bound together. They are a structurally heterogeneous and a complex

group of sphingolipids containing derivatives of sphingoside bases in amide linkage with a variety of fatty acids. They play an essential role in structuring and maintaining the water permeability barrier function of the skin.

Ceramides interact with other fatty acids and cholesterol to form ordered structures that remain in solid crystalline or gel-state, which is less permeable than the liquid crystalline cellular membranes.

### New formulations

Through long term research work, there have been few skin diseases (atopic eczema) where low levels of ceramides have been detected.

This has led to the development of new formulations of moisturisers, containing lipids similar to ceramides present in the skin, which can help in the improvement of the skin barrier. Aquaporins (AQP) are proteins that facilitate the transport of water across the cell membranes of keratinocytes. These include the important AQP3 which is involved in the water maintenance of the epidermis and AQP5 which is involved in sweat secretion.

The APQ3 being the most abundant of them, also helps in the transport of glycerol which plays a role in the hydration of human skin. The glycerol is important for the metabolism of lipids in the skin, as well as the regulation and proliferation of keratinocytes.

The APQ3 is also believed to be important in wound healing, as it facilitates cell migration being a water channel and it enhances keratinocyte proliferation and differentiation.

The expression of APQ3 water channels are strongly affected by age and chronic sun exposure resulting in a defective osmotic equilibrium in the epidermis. This would account for the skin dryness observed in older people in skin areas that are most exposed to the sun.

### Novel moisturisers

The understanding of the function of the NMF, ceramides and aquaporins have led to the development of novel moisturisers, that contain compounds that are similar to those present in the skin. These work by increasing the water content of the stratum corneum, as well as providing an impervious lipid barrier which decreases the evaporation from the outer layer, as well as encouraging the accumulation of water from the lower layers.

This hydration helps to soften the skin surface by flattening out the ridges and by reducing the amount of scaling (through separation of individual corneocytes). It also makes the skin surface soft, more extensible, pliable and more compliant. Moisturisers that contain humectants, occlusive oils or both are widely available and one can choose according to their needs.

References available on request. **SF**

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For full prescribing information refer to the package insert. Naviderm Ointment. Each 1 g of ointment contains 200 mg of cod liver oil (Type A), a natural source of vitamin A and vitamin D. Applicant: Accord Healthcare (Pty) Ltd.

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