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Dry skin also is called xerosis. Complex factors contribute to dry, flaky skin, and several of these change with age. Environmental factors such as ambient dryness, irritants, or bathing habits may be involved, as well as individual characteristics related to medical conditions, genetics, or aging. As the biochemistry of dry skin becomes better understood, we are better able to treat this problem.

THE BIOCHEMISTRY OF DRY SKIN

The structure of the epidermis, the outermost layer of skin, and the stratum corneum, the outermost layer of the epidermis, are of greatest importance in determining who develops dry skin and when it develops. The epidermis is composed of 4 layers. The cells of the inner layer migrate upward from the basal layer to the granular layer, until they reach the outer layer of the stratum corneum. Through this migration, the cells change, losing their nuclei (the inner portion containing DNA) and becoming keratinized, thus forming the outer protective keratin layer of the stratum corneum. This outer layer provides a barrier function; it keeps important substances, such as cellular fluids and blood, within the body. It also helps keep out substances that might harm the inner organism if allowed to pass through the skin, such as too much water, invading micro-organisms, and toxins. When no longer functional, skin cells of the outer stratum corneum are shed, in a process called desquamation.

Junctional bridges called desmosomes hold all cells together, including those of the stratum corneum. When the cells are no longer functional, the desmosomes break down so the cells are no longer held together and can be shed from the skin surface. Desmosomes that are "too tight" do not allow for proper shedding of discarded cells. Several enzymes degrade desmosomes and allow nonfunctional cells to detach from each other and desquamate. Genetic differences in the amount or efficiency of these enzymes also determines the efficiency of this process. Aging processes also change enzyme activity and synthesis. If desmosomes are not degraded properly and the outer nonfunctional cells are held together longer than optimal, dry, flaky sheets of skin develop in which the cells are still attached to one another. In a normal process, friction causes very tiny clumps of nonfunctional cells to be shed; in an abnormal process, these clumps are larger since the cells cannot detach from each other, causing them to be more visible, flaky, and unattractive.

The spaces between the outer skin cells and around the bridges are filled with lipid-rich (fatty) material that provides the primary barrier to water loss. The lipid-rich composition of this substance is very important in protecting against excessive skin dryness. There are primarily 3 critical compounds in this substance: ceramides, cholesterol, and fatty acids. The total amounts of these 3 compounds, as well as their proportions to each other, are all very important in healthy function of the skin barrier.

Ceramides, cholesterol, and fatty acids are further classified as to type. For example, there are 9 different chemical classes of ceramides, each doing something a little different from the others. We actually do not understand the exact roles of all of these subtypes as yet, and much more research needs to be done in this area. We do know that the ceramides present as longer chains provide a better water barrier than the short-chain ceramides. People with dry skin (and with diseased skin) have too much of the short-chain ceramides and not enough of the long-chain ceramides. Linoleic acid, an essential fatty acid that must be provided in the diet, is especially important in

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the synthesis of long-chain ceramides. Essential fatty acids are found in the omega-3 and omega-6 groups, in coldwater fish (salmon, herring, and mackerel) and in nuts, avocados, and flaxseed oil.

Some shapes of lipids in the skin act as better barriers than others. The "packing" of these molecules against and around each other determines how much water is let through. The amount of water allowed through a barrier is referred to as the barrier's permeability. High permeability means a lot of water is let through, and low permeability means less water is allowed through. Contrary to what might be expected, water loss through the epidermis, measured as transepidermal water loss (TEWL), is actually lower with increasing age. As the cells of the epidermis migrate upward, the substance between them composed of these lipids changes configuration, so that the barrier is weaker at the outermost layers of the stratum corneum. The deeper layers contain lipids that are more tightly packed against each other and less permeable to water; the outer layers have more loosely packed lipids and are more permeable to water. The more tightly packed lipids have rhomboid shapes (looking like slightly squashed rectangles), and the loosely packed lipids have hexagonal shapes.

These packing states also influence the ease at which discarded cells are shed from the skin surface (desquamation). Higher ceramide content tends to keep the cells together. Aged skin at all times, and everyone's skin during winter, contains a lower ceramide content, which contributes to weakened barrier function. People living in the very hot environment of the Arizona desert have skin with higher ceramide content, which is, therefore, stronger than the skin of those living in New York. A very humid environment causes a similar increase in the amount of ceramides. Lower amounts of ceramides are seen with dry, flaky skin. Changes in the types of ceramides also is seen in persons who develop dry skin very easily, such as those with atopic dermatitis (inflamed, dry skin secondary to allergy and hypersensitivity). People with atopic dermatitis have

decreased skin moisture (impaired skin barrier function) and decreased skin lipids.

<u>Aging</u>

With aging, less functional molecules are synthesized and their ratios also change, critically affecting skin barrier function and contributing to dryness.

In addition to the altered lipid ratios and decreased enzyme levels seen with aging, other factors play a role. The multifactorial etiology of dry skin in older persons is at least part of the reason that this problem is so common in the older age group. Keratinization of the stratum corneum changes due to desmosome dysfunction. After the epidermal barrier becomes impaired in the elderly, it takes longer to reconstitute than in younger individuals. This is partly due to impaired synthesis and partly due to decreased functionality of enzymes and other molecules involved in the process of synthesis. Cytokine function affects inflammatory processes, and immunity is altered. Outermost layers of normal youthful skin are slightly acidic, which strongly augments barrier function. As one ages, this acidification is reduced. Epidermal stem cells responsible for regeneration of the skin are much less robust in the aged.

<u>ltch</u>

Dry skin itches. However, itch is a poorly understood component of dry skin. We know from animal studies that itching relates to individual and genetic differences in the spinal cord and in chemicals that transmit nerve impulses. Animals with genetic defects that spontaneously itch also have a stratum cornea with weakened barrier function.

Environmental Factors

Dry skin tends to worsen during the winter season. As mentioned earlier, there are differences in ceramide synthesis during winter, with a relative deficiency in the long-chain, more protective ceramides. The low humidity of a dry environment, either in the winter or at other times, encourages itch by increasing mast cell



number and histamine content in the skin, both of which contribute to itching. Lower humidity also changes the fatty-acid content of the skin, causing dry skin. Too much exposure of the skin to water also disrupts the ability of the cells to act as an effective barrier. With aging and stress, the skin is less able to accommodate environmental factors that may be present.

Interestingly, some buildings have been associated with the development of dry skin, especially dry facial skin. People with allergies were more sensitive to skin changes in "sick buildings." The more time the person spent inside the building, the more likely he or she was to develop dry skin and itching related to it. Less-frequent cleaning of the building led to more severe symptoms. High ventilation flows, secondhand smoke, and lack of in-room temperature controls also were associated with a higher incidence of dry skin.

Older persons may use diuretic medications, which also can contribute to general dehydration and dry skin. They also tend to overuse heaters or air conditioners. They may apply emollients and skin conditioning products less often.

<u>Summary</u>

Dry skin is characterized by a decreased lipid content and altered ratios of these fats. Ability to reconstitute the epidermal barrier after environmental irritation of any sort is also delayed. Biological processes of the stratum corneum leading to dry skin, as described above, are lower ceramide levels, deficient enzymes that break up desmosomes (which causes shedding skin cells to stick to each other longer than they should, forming flaky sheets), lower levels of long-chain ceramides, disruption in lipid-packing shapes, essential-fatty-acid deficiency, increased itching from a variety of mechanisms, and genetic differences. Dry skin is much more commonly found in aged individuals, due to a number of biochemical and environmental factors.

TREATMENT OF DRY SKIN

Doctors have very inconsistent prescribing practices in treating dry skin. Patients often receive conflicting and confusing advice, which causes difficulty in following a therapeutic regimen. In Great Britain, the "ABC dry skin and eczema management programme" has been developed, with a simple set of guidelines for treating dry skin. However, many substances helpful to dry skin have been described only fairly recently in the research lab and are unknown by many clinicians. Some of the agents that are known to help this problem are described below:

<u>Glycerol</u>

Glycerol helps with moisturization. It does so by helping desmosome bridges between stratum corneum cells to degrade, so the cells can be shed appropriately. Glycerol also helps the lipid molecules between cells provide a better barrier to water. In addition, it somehow assists in the formation of the more effective long-chain ceramides. Urea-containing creams also have been found to moisturize, although they have a higher incidence of irritation associated with them than glycerol.

Hydroxy Acids

Both alpha hydroxyacids and beta hydroxyacids assist with the proper shedding of dead skin cells. Alpha hydroxyacids encourage lipid synthesis in intercellular areas, which improves barrier function and improves dry skin. Lactic acid, an alpha hydroxyacid, particularly improves ceramide synthesis.

<u>Enzymes</u>

Some topical enzymes help the desmosome connections between cells break down, so the cells can come apart and be shed. The pancreatic enzyme chymotrypsin and papain, found in pineapple, both work in this way. Enzymes from a bacterium called Bacillus licheniformis also are being studied in the research lab.



Improving Lipid Synthesis

Placing the correct ratio of a substance containing the 3 major intercellular lipids (ceramides, cholesterol, and fatty acids) on the skin causes an improvement in dry skin. Furthermore, aged skin seems to be more deficient in cholesterol, and providing a lipid mixture with more cholesterol accelerates skin barrier recovery in older persons, but not in younger.

<u>Niacinamide</u>

This vitamin B3 derivative has several beneficial effects on dry skin. It encourages synthesis of ceramides. Niacinamide also has anti-inflammatory activity, which may be helpful if dry skin is associated with irritation and inflammatory processes.

Linoleic Acid

This is an essential fatty acid necessary for proper growth and development of the epidermis. It also is required for synthesis of the important long-chain ceramides necessary to protect against dry skin. "Essential" fatty acid refers to the fact that the substance cannot be made by the human body and must be provided in the diet. Other nonessential fatty acids, such as those found in coriander seed oil, improve dry skin by increasing ceramide synthesis.

Controlling Itch

New topical antihistamines that counteract histamine receptors in the skin will probably decrease itch in the future. Another receptor in the skin related to itching is the cannabinoid receptor (the same one stimulated by marijuana); but, unlike the histamine receptor, it decreases itch. Itching also increases with inflammation, which activates and irritates nerve endings.

Magnesium and Calcium

Salts containing magnesium and calcium improve skin barrier function, and help dry skin or prevent its development.

<u>Vitamin C</u>

Vitamin C increases ceramide synthesis in the skin and causes more of the beneficial long-chain ceramides to be made. Both of these effects help with dry skin.

Botanical Extracts

Only more recently have some plant extracts been investigated for beneficial effects on dry skin. Older recommendations were almost uniformly against use of botanicals. However, new interest and research into natural treatments has supported the effectiveness of some botanicals in supporting the skin barrier and improving lipid synthesis. Many more could be investigated in the future.

Suggested iS CLINICAL® products for dry skin— YOUTH EYE[™] COMPLEX, HYDRA-COOL® SERUM, PRO-HEAL® SERUM ADVANCE●®, MOISTURIZING COMPLEX, CREAM CLEANSER, EYE COMPLEX, BODY COMPLEX, ACTIVE SERUM[™], C EYE SERUM ADVANCE●®, POLY-VITAMIN® SERUM, YOUTH COMPLEX®, and SHEALD[™] RECOVERY BALM.

PRODUCT RECOMMENDATIONS

Suggested iS products for dry skin— EXTREME PROTECT SPF 30, REPARATIVE MOISTURIZER, EXFOLIATING ENZYME TREATMENT, RESTORATIVE EYE COMPLEX, PROTECTIVE MOISTURIZER SPF 15, AGE TREATMENT COMPLEX, and COOLMINT REVITALIZING MASQUE.

Suggested INNOVATIVE SKINCARE® Professional products for dry skin – REJUVENATING MASQUE and RESURFACING MASQUE.

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