Chapter 62: Eczema regimens

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BASIC CONCEPTS
- Dry skin affected by eczema is characterized by loss of intercellular lipids which results in barrier deficits.
- Moisturizers are an important part of eczema treatment as they provide an environment optimal for barrier repair.
- Moisturizers function by impeding transepidermal water loss with oily occlusive substances, such as petrolatum, mineral oil, vegetable oils, and dimethicone, and by attracting water to the dehydrated stratum corneum and epidermis with humectants, such as glycerin, sodium PCA, propylene glycol, lactic acid, and urea.
- Moisturizing ingredients can be delivered to the skin surface by emulsions, liposomes, and niosomes.
- Careful moisturizer selection is key to the treatment and prevention of eczematous skin disease.

Introduction

Eczematous skin disease is one of the most commonly treated dermatologic conditions. While topical prescription corticosteroids and calcineurin inhibitors are the mainstay of therapy, cosmeceutical moisturizers are key to the treatment and prevention of disease. Moisturizers enhance the skin barrier, decreasing stinging and burning from a sensory standpoint and improving the look and feel of the skin. Moisturizers can also smooth desquamating corneocytes and fill corneocytes gaps to create the impression of tactile smoothness. This effect is temporary, of course, until the moisturizer is removed from the skin surface by wiping or cleansing. From a functional standpoint, moisturizers can create an optimal environment for healing and minimize the appearance of lines of dehydration by decreasing transepidermal water loss. Transepidermal water loss increases when the “brick and mortar” organization of the protein-rich corneocytes held together by intercellular lipids is damaged. A well-formulated cosmeceutical moisturizer can decrease the water loss until healing occurs.

Etiology

Eczema is characterized by barrier disruption, which is the most common cause of sensitive skin. The barrier can be disrupted chemically through the use of cleansers and cosmetics that remove intercellular lipids or physically through the use of abrasive substances that induce stratum corneum exfoliation. In some cases, the barrier may be defective because of insufficient sebum production, inadequate intercellular lipids, or abnormal keratinocyte organization. The end result is the induction of the inflammatory cascade accompanied by erythema, desquamation, itching, stinging, burning, and possibly pain. The immediate goal of treatment is to stop the inflammation through the use of topical, oral, or injectable corticosteroids, depending on the severity of the eczema and the percent body surface area involved. In dermatology, topical corticosteroids are most frequently employed with low potency corticosteroids (desonide) used on the face and intertrigenous areas, medium potency corticosteroids (triamcinolone) on the upper chest and arms, high potency corticosteroids (fluocinonide) on the legs and back, and ultra high potency corticosteroids (clobetasol) used on the hands and feet. Newer topical options for the treatment of eczema-induced sensitive skin include the calcineurin inhibitors, pimecrolimus, and tacrolimus.

However, the resolution of the inflammation is not sufficient for the treatment of eczema. Proper skin care must also be instituted to minimize the return of the conditions that led to the onset of eczema.

Moisturizer mechanism of action

Moisturizers are incorporated into eczema treatment regimens to reduce transepidermal water loss. There are three cosmeceutical ingredient categories that can reduce transepidermal water loss: occlusives, humectants, and hydrophilic matrices [1]. The most common method for reducing transepidermal water loss is the application of an occlusive ingredient to the skin surface. These are oily sub-
stances that create a barrier to water evaporation. The more commonly used occlusive ingredients in current formulations and their chemical category are listed in Table 62.1 [2].

The most popular and effective occlusive ingredient is time-tested petrolatum, which blocks 99% of water loss from the skin surface [3]. This remaining 1% transepidermal water loss is necessary to provide the cellular message for barrier repair initiation. If the transepidermal water loss is completely halted, the removal of the occlusion results in failure to repair the barrier and water loss quickly resumes at its preapplication level. Thus, the occlusion does not initiate barrier repair [4]. Petrolatum does not function as an impermeable barrier, rather it permeates throughout the interstices of the stratum corneum allowing barrier function to be re-established [5]. Moisturizers for eczematous disease must contain several occlusive moisturizing ingredients.

In addition to occlusive ingredients, a therapeutic moisturizer for eczema must contain humectants. Humectants are substances that attract water to the viable epidermis and stratum corneum through swelling [8,9]. Therefore, a moisturizer recommended for eczema must combine both occlusive and humectant ingredients for optimal efficacy and patient esthetics. Occlusive and humectant moisturizers are the formulations most beneficial in the treatment of eczema and include the majority of those found in the dermatologic sample closet (Eucerin Cream and Lotion, Beiersdorf; Norwegian Formula Moisturizers, Neutrogena; Aveeno Cream and Lotion, Johnson & Johnson; Olay Daily Facial Moisturizer, Procter & Gamble, Plentitude, L’Oréal; Cetaphil Cream and Lotion, Galderma; CeraVe Cream and Lotion, Coria).

A third type of moisturizing formulation is known as the hydrophilic matrix. Hydrophilic matrices are large molecular weight substances that create a film over the skin surface thereby retarding water evaporation. The first hydrophilic matrix developed was an oatmeal bath (Aveeno Oatmeal Bath, Johnson & Johnson). The colloidal oatmeal created a film that prevented water from leaving the skin to enter the bath water. Newer hydrophilic matrices include peptides and proteins, but they do not provide meaningful skin moisturization in the eczema patient.

### Moisturizer goals in eczema

The goal of all moisturizing emulsions is to accomplish skin remoisturization, which occurs in four steps: initiation of barrier repair, alteration of surface cutaneous moisture partition coefficient, onset of dermal–epidermal moisture diffusion, and synthesis of intercellular lipids [10]. These steps must occur sequentially in order for proper skin barrier repair. Once the barrier has repaired, there must be some substance that holds and regulates the skin water content. This substance has been termed the natural moisturizing factor (NMF). The constituents of the NMF have been theorized to consist of a mixture of amino acids, derivatives of amino acids, and salts. Artificially synthesized NMF has been constructed from amino acids, pyrrolidone carboxylic acid, lactate, urea, ammonia, uric acid, glucosamine, creatinine, citrate, sodium, potassium, calcium, magnesium, phosphate, chlorine, sugar, organic acids, and peptides [11]. Ten percent of the dry weight of the stratum corneum cells is composed of NMF in well-hydrated skin [12]. Cosmeceutical moisturizing emulsions try to duplicate the effect of the NMF.

### Moisturizer delivery systems

Another method for optimizing the ability of moisturizers to create an environment for healing in eczema patients is through novel delivery of the ingredients. This has led to the development of delivery systems that can time release substances onto the skin surface and improve product esthetics. For example, petrolatum is the most effective ingredient for skin healing, yet it leaves an easily removed, sticky, greasy film on the skin surface. A delivery system could allow small amounts of petrolatum to be released onto the skin surface avoiding the esthetic drawbacks. Examples of delivery systems relevant to eczema treatment include emulsions,
Moisturizing emulsions
Most moisturizers developed for the treatment of eczema are emulsions [13]. An emulsion is formed from oil and water mixed and held in solution by an emulsifier. Most emulsifiers are surfactants, or soaps, which dissolve the two non-miscible ingredients. The most common emulsions are oil-in-water, where the oil is dissolved in the water [14]. This emulsion is the most popular among patients because the water evaporates leaving behind a thin film of oily ingredients. If the emulsion can be poured from a bottle, it is considered a lotion. These moisturizing products are popular for eczema treatment, but may make the eczema worse as the repeated wetting and drying of the skin results in further maceration. Cream oil-in-water emulsions are preferred because the environment created for barrier repair is far superior.

Water-in-oil emulsions, where the water-soluble substances are dissolved in the oil-soluble substances, are less popular because of their greasy esthetics. Most ointments are water-in-oil emulsions, but they leave the skin feeling warm and sticky. Ointments deliver higher levels of moisturization because the water phase is small, leaving behind a proportionately larger concentration of ingredients capable of retarding transepidermal water loss. Even though their efficacy is greater, most eczema patients prefer more esthetic formulations.

Moisturizing serums
A specialized form of emulsion is a serum. Serums are usually low viscosity, oil-in-water emulsions that deliver of thin film of active ingredients to the skin surface. For example, a high concentration glycerin serum can be placed under a high concentration petrolatum oil-in-water emulsion to provide robust skin moisturization. Sometimes a serum will contain cosmeceutical barrier enhancing ingredients, such as ceramides, cholesterol, and free fatty acids.

Moisturizing liposomes and niosomes
Moisturizing ingredients can be incorporated into structures with unique physical properties on the skin, such as liposomes and niosomes (Table 62.2). Liposomes are spherical vesicles with a diameter 25–5000 nm formed from membranes consisting of bilayer amphiphilic molecules, which possess both polar and non-polar ends. The polar heads are directed toward the inside of the vesicle and toward its outer surface while the non-polar, or lipophilic tails, are directed toward the middle of the bilayer.

Liposomes are based on the natural structure of the cell membrane, which has been highly conserved through evolutionary change. The name is derived from the Greek word “lipid” meaning fat, and “soma” meaning body. Liposomes are primarily formed from phospholipids, such as phosphatidylcholine, but may also be composed of surfactants, such as dioleoylphosphatidylethanolamine. Their functionality may be influenced by chemical composition, vesicle size, shape, surface charge, lamellarity, and homogeneity.

The liposome is an extremely versatile structure. It can contain aqueous substances in its core, or nothing at all. Hydrophobic substances can dissolve in the phospholipid bilayer shell, which allows liposomes to deliver both oil-soluble and water-soluble substances without need for an emulsifier. Thus, the internal moisturizer payload plus the phospholipid membrane can both function as moisturizers.

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<tr>
<th>Table 62.2</th>
<th>Special moisturizer delivery systems.</th>
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<td>Delivery system</td>
<td>Structure</td>
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<tr>
<td>Liposomes</td>
<td>Spherical vesicles consisting of bilayer amphiphilic molecules with polar and non-polar ends</td>
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<td>Multivesicular emulsion (MVE)</td>
<td>Liposome within a liposome within a liposome to form concentric liposomes</td>
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<tr>
<td>Niosome</td>
<td>Liposome composed of non-ionic surfactants, such as ethoxylated fatty alcohols and synthetic polyglycerol ethers</td>
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<td>Nanoemulsions</td>
<td>Emulsions with 20–300 nm droplets</td>
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It is unlikely that liposomes diffuse across the stratum corneum barrier intact. The corneocytes are embedded in intercellular lipids, composed of ceramides, glycosylceramides, cholesterol, and fatty acids, which are structurally different from the phospholipids of the liposome. It is postulated that liposomes penetrate through the appendageal structures. They may also fuse with other bilayers, such as cell membranes, to release their ingredients. This is the mechanism by which liposomes can function as moisturizers, supplementing deficient intercellular lipids.

Niosomes are a specialized form of liposome composed of non-ionic surfactants. These are detergents, such as ethoxylated fatty alcohols and synthetic polyglycerol ethers (polyoxyethylene alkylester, polyoxyethylene alkylether). These liposomes do not deliver the moisturizing phospholipids to the skin surface.

**Multivesicular emulsions**

Another variant of the liposome is a multivesicular emulsion (MVE) (Figure 62.1). The MVE is created through a physical mixing technique, which makes them more stable, but also less expensive to produce. An MVE can be thought of as a liposome within a liposome within a liposome. Thus, with the release of each liposome, additional moisturizing ingredients can be deposited on the skin surface. MVEs can deliver glycerin, dimethicone, sphingolipids, and ceramides to the skin surface simultaneously.

**Moisturizing nanoemulsions**

Nanoemulsions are similar to regular emulsions with an oil-loving hydrophobic phase and a water-loving hydrophilic, except droplets in these emulsions are on the nano scale of 20–300 nm [15]. If the nano droplets are larger than 100 nm, the emulsion appears white, while nanoemulsions with droplets of 70 nm are transparent. Nanoemulsions offer the ability to deliver highly hydrophobic or lipophilic substances into the skin, which could not otherwise penetrate. The stratum corneum is an excellent barrier to lipophilic ingredients.

For example, new nanoemulsions of ubiquinone have been developed. Ubiquinone, also known as coenzyme Q10, is an important antioxidant manufactured by the body and found in all skin cells. It is found in both hydrophilic and hydrophobic cellular compartments, but topical delivery has been challenging. Nanoemulsions have successfully delivered higher concentrations of ubiquinone into the skin with the goal of enhancing the skin’s natural antioxidant capabilities, while leaving beyond a moisturizing film from the other ingredients in the emulsion.

**Developing a moisturizer regimen**

This chapter has discussed the goals of moisturization, the various types of moisturizers, and some of the unique moisturizer delivery systems. The biggest challenge for the clinician is adding moisturizers or combining moisturizers as part of a treatment regimen.

Patients with eczema require basic hygiene. The face and body must be cleansed. There is no doubt that the synthetic detergent cleansers, also known as syndets, provide the best skin cleansing while minimizing barrier damage. Bars based on sodium cocyl isethionate appear to perform the best (Dove, Unilever; Olay, Procter & Gamble). There are some patients, however, who only require the use of a facial syndet cleanser occasionally, because sebum production and physical activity are minimal. For these patients, a lipid-free cleanser is preferable because it can be used without water.
and wiped away (Cetaphil, Galderma; CerVe, Coria). These products may contain water, glycerin, cetyl alcohol, stearyl alcohol, sodium laurel sulfate, and occasionally propylene glycol. They leave behind a thin moisturizing film and can be used effectively in persons with excessively dry, sensitive, or dermatitic skin. They do not have strong antibacterial properties, however, and may not remove odor from the armpit or groin. Lipid-free cleansers are best used where minimal cleansing is desired.

After completing cleansing, the eczema patient requires moisturization. The moisturizer should create an optimal environment for barrier repair, while not inducing any type of skin reaction. For example, the product should not contain any mild irritants that may present as an acneiform eruption in the eczema patient because of the presence of follicular irritant contact dermatitis. The best moisturizers are simple oil-in-water emulsions. The morning moisturizer should provide SPF 30 photoprotection. A variety of sunscreen-containing moisturizers are on the market for this purpose (Olay Complete Defense SPF 30, Procter & Gamble; Neutrogena Daily Defense SPF 30, Johnson & Johnson). If additional hydration is required, a moisturizer can be applied to the face followed by a second sunscreen-containing moisturizer on top. It is possible to layer moisturizers for additive benefit. The sunscreen-containing moisturizer should be applied last, as it does not need to touch the skin to provide optimal photoprotection.

The evening moisturizer provides the best opportunity for barrier repair, because the body is at rest. The best ingredient for barrier repair is white petrolatum, but dimethicone and cyclomethicone are commonly added to decrease the greasiness of a simple petrolatum and water formulation. Basic night creams containing these ingredients, in addition to glycerin, are the mainstay of therapeutic eczema moisturizers. It is important to remember that fewer ingredients are preferred, because more ingredient exposure creates added opportunities for sensitization or an adverse event.

**Conclusions**

Eczema treatment requires the use of prescription medications in conjunction with skincare products. Both must be judiciously selected to insure optimal results. Thorough resolution of eczema requires alleviation of the disease, the treatment phase, and prevention of recurrence, the maintenance phase. This chapter has discussed those concepts that are key to designing a maintenance phase regimen for eczema patients.

**References**