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By Gerda Endemann, PhD; Month Day, 2023

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# [H1] Introduction

<u>The skin barrier</u> is a highly specialized structure that helps keep microbes and toxic chemicals from entering the body and water being lost from the body. But a healthy skin barrier is also key to skin that looks and feels good. Healthy, well-functioning skin is soft, pliable, and smooth, and bounces back after being prodded and poked. Dry, flaky, thin skin and red, itchy rashes may be the result of a poorly functioning skin barrier. And a dysfunctional barrier <u>causes symptoms of skin diseases</u> including eczema, acne, keratosis pilaris, and psoriasis.

We take for granted that our skin is able to keep harmful substances outside of the body and precious moisture inside, all while enduring frequent physical and chemical insults and constantly renewing its smooth, sensitive, waterproof surface. Considering the large area of our skin, the demands put on it, and the energy and materials required to maintain skin structures, it's not surprising that functionality may sometimes break down.

And we regularly subject our skin to potentially harmful soaps, chlorine, cosmetic ingredients, detergents, hot water, and fragrances. Our lifestyle, beauty, and hygiene routines may be damaging our skin and hindering barrier function. Understanding the effects of skincare, lifestyle, and environmental factors on our skin may help us support a well-functioning skin barrier whether it's to maintain a healthy, functioning barrier or as part of therapy for skin conditions.

#### [Design note: box]

[H2] SKIN HEALTH GLOSSARY

- <u>Allergens</u> are substances—usually proteins— that elicit an allergic reaction.
- <u>Atopic dermatitis</u>, a type of eczema, is a chronic condition with rashes and itchy, irritated, inflamed, and dry skin. It is not contagious.
- <u>Clinical research</u> refers to studies that test an intervention in people, with the most conclusive ones being double-blinded, placebo-controlled.
- <u>Comedogenic</u> ingredients are those that clog pores and cause blackheads.
- Contact dermatitis is a type of eczema where the skin becomes irritated and inflamed after contact with an irritant or an allergen such as poison ivy.
- Corneocytes are dead skin cells in the outermost layer of skin.
- Desquamation is when dead corneocytes are shed.
- <u>Eczema</u> refers to a group of skin conditions—including atopic dermatitis and contact dermatitis— where there may be dryness, itching, and inflammation. Rashes may be red in light skin tones and brown, grey, or purple in dark skin tones.
- Emollients protect, moisturize, and lubricate the skin.
- Humectants are substances that are water-attracting.
- Keratinocytes are skin cells.
- Lipids is the technical term for fatty substances including fats, oils, triglycerides, ceramides, fatty acids, sphingomyelin, squalene, phospholipids, and cholesterol. Fats and oils both consist primarily of triglycerides, which are three fatty acids attached to one glycerol molecule. With mostly saturated fatty acids, fats like butter and lard are solid at room temperature. With more unsaturated fatty acids, oils are liquid.

- <u>NMF, or natural moisturizing factor</u>, is a collection of small molecules found in corneocytes that help protect cells from changes in water content. NMF contains modified amino acids, lactic acid, sugars, urea, and glycerol.
- Occlusive agents provide a physical barrier to prevent water from evaporating.
- <u>Preliminary or preclinical research</u> refers to studies in animals, cells, and test tubes. Findings may or may not be predictive of what goes on in the human body.
- <u>Pruritus</u> is itchy skin which is often due to skin being dry.
- <u>Sebum</u> is an oily lubricant secreted by sebaceous glands.
- <u>TEWL</u>, or trans-epidermal water loss, is one way that researchers assess how well the skin barrier is functioning. A device is used to measure the amount of water lost from the skin by evaporation. When the barrier is not functioning well, water loss is increased. **[End box]**

# [H1] How Do You Know If Your Skin Barrier Is Damaged? (TOC)

In the skin, appearance and functionality are closely intertwined. The skin barrier contributes in complex ways to beauty and to the health of the skin and entire body.

[H2] A DYSFUNCTIONAL SKIN BARRIER CONTRIBUTES TO:

- Skin that is dry, thin, rough, flaky, red, inflamed, or itchy.
- <u>Symptoms of eczema</u>, psoriasis, acne, keratosis pilaris, rosacea, and contact dermatitis, and signs of aging.

[H2] AN INTACT <u>SKIN BARRIER HELPS</u> MAINTAIN HEALTHY-LOOKING, PLUMP, ELASTIC, SMOOTH, EVENLY COLORED SKIN:

- By keeping the skin hydrated; it's a moisture barrier.
- By producing fats and proteins and cells for skin thickness and elasticity.
- By maintaining a synchronized cycle of skin cell shedding and replacement to prevent skin shedding in scales.
- By collaborating with immune cells in the skin to prevent inflammation, redness, and itching.

[H2] Some of the things that OUR SKIN BARRIER HELPS PROTECT US FROM:

- Irritants and allergens
- Bacterial and fungal infections

- Ultraviolet (UV) radiation
- Chemicals in skincare, beauty, household, and industrial products, and in the air and water.
- Physical harm
- Food allergies

Potentially harmful chemicals may enter the body through a "leaky" or damaged skin barrier. But even a healthy skin barrier is not impervious, which is why it's important to use clean products that have been screened for possibly toxic ingredients. Ingredients from chemical sunscreens are have been found inside the body and in the blood.

[H2] Some of the things our skin barrier helps retain in the body:

- Water
- Extracellular fluid

Keeping water inside the body is about more than keeping skin plump. Without a functional skin barrier, for example when burns are extensive, water loss could be fatal. Additionally, adequate water keeps skin cells healthy and functioning. In research, a common way to assess how well the skin barrier is functioning is to measure loss of water through the skin— trans-epidermal water loss (TEWL).

# [H1] What Is the Skin Barrier? (TOC)

The skin barrier is a highly structured physical barrier made of cells, proteins, and lipids. It has been compared to a brick-and-mortar wall, where the cells are the bricks and the lipids are the mortar. The cells provide structure, and the lipids fill in the cracks, preventing entry or exit of organisms or water. Reinforcement comes from proteins that form rigid filaments, just as rebar steel bars are used for structural support in masonry.

Also contributing to barrier efficacy are compounds that promote immunity, fight bacteria, and help maintain the correct acidity and hydration. Skin cells produce these structural and chemical components. Maintaining the skin barrier is an energy-intensive, and never-ending undertaking – our body is continuously working to maintain skin barrier balance and function. Intact, elastic, protective skin requires good hydration and nutrition. It requires protection from damaging UV radiation and harmful chemicals.

# [H2] THE CELLS OF THE SKIN

The <u>skin barrier is part of the epidermis</u>, the outer layer of skin that is less than a millimeter thick. Underneath the epidermis is the dermis, the thicker layer of skin where nerves, blood vessels, and sweat glands are found.

The primary cell type in the epidermis is the keratinocyte. Keratinocytes are linked to each other—by structures called tight junctions—to form impermeable chains of cells. in addition, keratinocytes make antimicrobial peptides that contribute to the antimicrobial properties of the skin.

The very outermost layer of the epidermis is called the stratum corneum, and it consists of keratinocytes that have transitioned into cells called corneocytes. These cells are linked into a tough network by structures called desmosomes.

After keratinocytes transition into corneocytes, and the cells make the proteins and fats they need, they die. The stratum corneum contains 15 to 20 layers of flattened dead corneocytes, filled with proteins and embedded in a mixture of fatty substances forming a waterproof structure. This mixture of proteins and fats results in an amazing <u>biomaterial that is thin and soft, but also strong and elastic</u>. To continue with the brick wall analogy, it's as if a brick wall that was reinforced with steel was also flexible.

# [H2] THE PROTEINS OF THE SKIN

Corneocyte cells contain large amounts of a protein called keratin that binds water, preventing evaporation and keeping the skin hydrated. Another protein in the stratum corneum that's important for a functional barrier is <u>filaggrin</u>. Its name is derived from its ability to aggregate keratin into filaments. When filaggrin binds keratin to form filaments, the cells collapse and flatten into the dense structures found in the stratum corneum.

After it's completed its work with keratin, filaggrin is repurposed. It's broken down to individual amino acids that are used to make <u>natural moisturizing factor</u> (NMF), a mixture of water-attracting (humectant) substances that keeps the stratum corneum hydrated and the skin moist.

# [H2] NATURAL MOISTURIZING FACTOR

<u>NMF is a unique collection</u> of small molecules in the stratum corneum that helps maintain skin hydration and elasticity. Levels of NMF may be low in atopic dermatitis and in very dry skin. And NMF may be lost as a result of bathing or soaking. (Even some skin lipids may be lost from washing with water.)

NMF contains special amino acids like pyrrolidone carboxylic acid (PCA), lactic acid, sugars, urea, and glycerol. These components act as both humectants and osmolytes. Humectants attract water to the skin, from deeper layers of skin or from the air.

Osmolytes help buffer the cells from changes in water content, and are crucial in skin, which may be subject to dry or wet conditions. In very dry conditions, osmolytes will essentially replace water that's lost, preventing cells from dying.

Urea is an important component of NMF. In addition to supporting skin hydration and elasticity, <u>urea stimulates keratinocytes</u> to grow, make skin barrier proteins such as filaggrin, and produce antimicrobial peptides.

# [H2] THE LIPIDS OF THE SKIN

The technical term for fatty substances is lipids, and the lipid matrix surrounding the corneocytes contains cholesterol, fatty acids, sterols, waxes, and ceramides. Ceramides play a particularly important role, as each cell is surrounded by a thin layer of this lipid. Ceramides are made of molecules called sphingosines linked to fatty acids.

The lipids in the stratum corneum are uniquely suited to their jobs of waterproofing and providing structure. Ceramide makes up about 50 to 60 percent, and cholesterol and fatty acids each make up about 20 to 25 percent <u>in the barrier</u>. In the right proportions these lipids align in an organized fashion that makes the stratum corneum impermeable. You may hear the term "lamellar structure" to describe how the lipids are lined up in layers.

The fatty acids are not the ones we usually think about. Unlike omega-3, -6, or -9 unsaturated fatty acids in most oils, the ones in skin <u>are largely saturated fats</u>. And for saturated fats they are unusually long, mostly 22 and 24 carbons long. The longer and more saturated fatty acids are, the more rigid they are, and the more hydrophobic, meaning that they repel water. However, small amounts of the polyunsaturated fatty acids alpha-linolenic acid (omega-3) and linoleic acid (omega-6) are also essential for barrier function.

Lipids on the surface of the skin come from the stratum corneum and from sebum, an oily lubricant that helps with water retention and protection from water and UV radiation. It is secreted by sebaceous glands— mostly via hair follicles—and contains waxes, triglycerides (three fatty acids attached to a glycerol molecule), fatty acids, squalene, and cholesterol. Blocked sebaceous glands are involved in acne, and substances that block pores and cause acne are referred to as comedogenic.

Sebum's fatty acids help maintain the slightly acidic pH of skin— <u>from 4.1 to 6</u>—and have antimicrobial activity. In particular, one unique fatty acid, sapienic acid, is important for antimicrobial defense.

Abnormal sebum composition is linked to poor barrier function, as in the skin condition papulopustular rosacea, where skin may be dry and sensitive.

#### [H2] SHEDDING SKIN: DESQUAMATION

The dead corneocytes on the surface of the skin are constantly shed and replaced by keratinocytes produced in the layer underneath. In healthy skin, small areas of corneocytes are continually shed, but in dry skin this process is slowed down and larger areas—that look like scales—are shed, causing roughness and flakiness.

In the skin disease <u>Netherton syndrome</u>, corneocytes are shed too quickly and the skin barrier is severely dysfunctional. This disease is caused by mutations in a gene

(*SPINK5*) that controls the rate at which structures in the stratum corneum are broken down. Symptoms are similar to eczema with inflammation and allergic reactions.

# [H2] HOW THE SKIN BARRIER VARIES THROUGHOUT THE BODY

There's huge <u>variability in the skin between body parts</u>. Differences exist in the number of layers of corneocytes, amounts of lipids, the ability to retain water, and the permeability to environmental chemicals. The thickest stratum corneum is on the palms and soles of the feet, and by far the thinnest and most permeable stratum corneum covers the genitals.

The skin on the face is very thin—particularly on the lips and around the eyes—and it has poor barrier function and greater water loss compared to the torso and limbs. On the face, water loss is highest from the skin around the mouth, especially on the upper lip, and from the lips.

And facial skin turns over very quickly. It takes only about a week for the stratum corneum on the face to go through its normal shedding and replacement cycle, as opposed to two weeks for most of the body. This cycle is even shorter in skin conditions such as dandruff and psoriasis.

Because of the very thin stratum corneum on genital tissues, water loss is higher from the vulva than from other parts of the body. Chemicals are absorbed readily through thin skin, so absorption of topically applied substances is extremely high in the genitals.

Absorption of chemicals through the skin also depends on the size of the molecule—the smaller the molecule the more readily it is absorbed. Proteins and hyaluronic acid are examples of very large molecules that are not typically absorbed through intact skin, and steroids and hormones are smaller molecules that may enter the body through the skin.

# [H1] Are There Differences in Children's Skin?

The skin barrier is not normally very strong in newborns. Components of the barrier are low and gradually increase, with most components plateauing at around three to four years. The protective moisturizer <u>NMF is low in newborns</u>, and peaks by age one in the elbows and nose, but not until somewhere between ages one and three in the cheeks.

A growing body of research supports the theory that an impaired <u>skin barrier</u> in infancy <u>contributes to food allergies</u>. Children with eczema—which causes barrier dysfunction—are <u>highly likely to develop</u> food allergies. The theory is that a leaky skin barrier allows components of foods to enter the body. Food components will be seen by the immune system as allergens that are foreign and possibly dangerous. An allergic response is mounted, consisting of antibodies and immune cells directed at particular

food components, usually proteins. The next time the body is exposed to that food the immune system is primed for an allergic response.

On the other hand, if the first time the body is exposed to a new food is when a food is eaten, the immune system does not see the food as dangerous. Immune cells in the gut generally learn that when foods come in through the mouth, they do not need to mount an immune response. The body develops <u>tolerance to foods</u> that enter the body via the digestive tract.

The problem appears to be that when food allergens enter through the skin early in life, before the food is eaten, the body has not yet had a chance to recognize the substances as foods and to develop tolerance. Strengthening the skin barrier may help to prevent allergens entering infants' bodies.

# [H1] What Weakens the Skin Barrier? (TOC)

The skin barrier becomes weaker with age, and is impaired in many skin conditions and diseases. It <u>can also be damaged by UV light</u>, high pH, too much friction, prolonged contact with water, and multiple chemicals including chlorine, acetone, detergents, and surfactants. And stress may slow down healing of damaged skin.

# [H2] AGE AND DIABETES

As we age, the skin becomes thinner, its structure changes, and <u>barrier properties</u> <u>gradually decline</u>. Hydration levels and the antimicrobial barrier are reduced. Levels of lipids including ceramides, NMF and glycerol go down. In spite of these changes, <u>water</u> <u>loss is not necessarily increased</u> in aged skin.

There may be at least two things contributing to abnormal lipids in aging skin: lower production of skin lipids, and incorrect processing of those lipids. In people over 80, the production of lipids is low. However, in people ages 51 to 80 the problem seems to be that lipids are not correctly incorporated into the stratum corneum. And this may be due to the skin not maintaining sufficient acidity (low pH).

In 51 to 80-year-olds, the stratum corneum was found to be less acidic than in 13 to 21-year-olds. The enzymes that form the stratum corneum operate best in an acidic milieu, and it appears that <u>the reduced acidity of the skin after 50 may be preventing</u> the formation of new skin barrier. The reduced acidity of the skin also contributes to a poorer antimicrobial barrier.

In type 2 diabetes, changes in the skin barrier and increased permeability are similar to what is observed in aged skin. After being damaged, the <u>skin of people with diabetes</u> takes longer to recover healthy barrier function.

In aging skin (and in diabetes) it appears to be particularly important to use skincare products that are pH balanced, with a pH around 5 to 6, to help support the production of lipids in the stratum corneum.

### [H2] POTENTIALLY BARRIER DAMAGING SKINCARE

Some things we do to care for our skin may not be supporting skin health over the long term. The skin barrier may be damaged by cleansers, too much exposure to water, and by overuse of acids and exfoliants. It is damaged by laser treatments and chemical peels. Your skin may be sensitive to chemicals and allergens in skincare products—including fragrances, lanolin, and propylene glycol. Some essential oils can cause irritation and contact dermatitis and disrupt the skin barrier.

#### [H3] Skin Cleansers

Skin cleansers contain ingredients to break down and remove dirt and contaminants that don't dissolve in water alone. These ingredients are called surfactants, and old-fashioned soaps are the most well-known type. Soaps are made from animal fats or vegetable oils plus lye; examples are sodium laurate, sodium cocoate, and sodium oleate. Soaps are perceived as natural, but because of the lye they are alkaline (pH 8.5 to 10) and disrupt the naturally acidic pH of the skin. <u>Soaps damage the skin barrier</u>, remove valuable lipids and NMF, cause roughness, disturb the desirable microflora, and allow undesirable bacteria to grow.

The alternatives to soaps are surfactants called <u>synthetic detergents</u>. They are frequently milder than soap, and because of the way they are made they do not have to be alkaline. Whereas washing with soap damages the stratum corneum, washing with synthetic detergents is less likely to damage proteins, strip lipids, and disrupt the barrier. They come in several varieties with many different properties; some may be irritating depending on the concentration and the accompanying ingredients. Two of the synthetic detergents with "sulfate" in their names, sodium lauryl sulfate and sodium lauryl ether sulfate, are stronger and more damaging. Detergents with names ending in isethionate and glucoside are much gentler on the barrier.

#### **Barrier-safe surfactants**

- Sodium cocoyl isethionate
- Cocamidopropyl betaine
- Sodium methyl cocoyl taurate
- Cocamidopropyl hydroxysultaine
- Sodium lauroyl sarcosinate
- Lauryl betaine
- Sodium cocoamphoacetate
- Polyglucosides, coco glucoside, lauryl glucoside, decyl glucoside, caprylyl/capryl glucoside.

#### **Barrier-stripping surfactants**

- Sodium tallowate
- Sodium cocoate

- Sodium palmitate
- Sodium laurate
- Sodium lauryl sulfate (SLS), also called sodium dodecyl sulfate (SDS)
- Sodium lauryl ether (laureth) sulfate

### [H3] Excessive Water Exposure and Washing

As desirable as well-hydrated skin is, prolonged exposure to water may leach out protective compounds such as natural moisturizing factor, and damage the structures that form the skin barrier, leading <u>to irritation</u>, inflammation, and hives. The skin barrier is disturbed by frequent <u>hand-washing</u>, swimming, or soaking. A 30-minute soak was shown to remove some components of the NMF. And when people's forearms were soaked for 10 minutes at 40 °C (104 °F), barrier integrity was affected. Regular hot baths and hot tubs are relaxing and have health benefits for <u>circulation</u>, the arteries, and metabolism, but may weaken and deplete the skin barrier.

Not surprisingly, more frequent <u>handwashing and disinfectant use</u> during the COVID-19 pandemic was associated with increased prevalence of skin conditions.

#### [H3] Irritants and Allergens in Skincare Products

The US FDA has published <u>a list of common allergens</u> that may be ingredients in cosmetic products. They are not labelled as allergens and it is up to the consumer to read ingredient lists and recognize potential irritants. The list includes:

- Rubber
- Latex
- P-phenylenediamine (PPD)
- Coal-tar
- Nickel
- Gold
- Methylisothiazolinone
- Methylchloroisothiazolinone
- Formaldehyde
- Bronopol (2-bromo-2-nitropropane-1,3-diol)
- 5-Bromo-5-nitro-1,3-dioxane
- Diazolidinyl urea
- DMDM hydantoin (1,3-dimethylol-5,5-dimethylhydantoin)
- Imidazolidinyl urea
- Sodium hydroxymethylglycinate
- Quaternium-15 (Dowicil 200; N-(3-chloroallyl) hexaminium chloride).

The FDA also cautions that cosmetic and skincare products may contain natural and synthetic fragrance ingredients that are potentially allergenic and may be identified only

as "fragrances". Some fragrance ingredients that the <u>European Union</u> and <u>Korea</u> require labeling as allergens include:

- Amyl cinnamal
- Amylcinnamyl alcohol
- Anisyl alcohol
- Benzyl alcohol
- Benzyl benzoate
- Benzyl cinnamate
- Benzyl salicylate
- Cinnamyl alcohol
- Cinnamaldehyde
- Citral
- Citronellol (found in rose and pelargonium)
- Coumarin (found in cinnamon)
- Eugenol (found in cloves)
- Farnesol
- Geraniol
- Hexyl cinnamaladehyde (found in chamomile0
- Hydroxycitronellal (found in lavender)
- Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), (also known as Lyral)
- Isoeugenol (found in ylang ylang)
- Lilial
- d-Limonene (found in citrus peel)
- Linalool (found in lavender, pine, peppermint)
- Methyl 2-octynoate
- g-Methylionone
- Oak moss extract
- Tree moss extract

# [H2] DISRUPTION OF SKIN MICROBES

<u>The skin microbiota</u> is the hundreds of species of bacteria, fungi, and viruses that live in human skin. Examples of normal <u>skin residents include</u> *Cutibacterium acnes, Staphylococcus epidermis*, species of *Corynebacterium*, and the major fungal species *Malassezia*.

Microbes in the skin make a number of <u>contributions to the maintenance of the skin</u> <u>barrier</u>. They <u>produce enzymes</u> that help with desquamation, production of the lipid matrix, and renewal of corneocytes. They promote skin cell functions by <u>modulating</u> <u>gene expression</u>. They prevent the growth of harmful microorganisms, both by <u>producing antibiotics</u> and inducing skin cells to produce antimicrobial peptides. They also help encourage the immune system to fight off pathogens. The skin <u>microbiota may be disrupted by antibiotics</u>, detergents and soaps, especially those with a high pH, antimicrobial chemicals in antiseptic soaps, and cosmetic products. <u>Triclosan and other antimicrobial ingredients</u> have been banned in OTC soaps, but may be used in healthcare settings. The disinfectant ingredients <u>benzalkonium chlorides</u> have been banned in personal care products in the EU but are in widespread use elsewhere.

For disinfection, both soaps and alcohol-based hand sanitizers will kill resident microbes, but in one study, although hand sanitizer was more effective at reducing bacteria and fungi, it was less damaging to the skin barrier than soap. Gentle cleansers with a neutral or slightly acidic pH are thought to <u>cause the least disruption</u>.

Changes in skin microbes are associated with skin conditions such as acne, rosacea, and atopic dermatitis. A commonly seen problem is overgrowth of *Staphylococcus aureus*, which contributes to barrier dysfunction: <u>S. aureus can destroy skin barrier</u> components, and <u>its presence is linked to water loss</u>, poor skin hydration, permeability changes, inflammation, and high skin pH. *S. aureus* also produces molecules that sensitize skin and increase the chances of developing allergies. An overgrowth of *S. aureus* is often associated with <u>eczema</u> flare ups and possibly with <u>psoriasis</u> lesions. An *S. aureus* infection—with <u>pimples or boils</u>, <u>possibly with pus</u>—may exacerbate skin conditions.

Probiotics have been shown to reduce inflammation in the skin, to help prevent the growth of harmful bacteria, and to support a healthy skin barrier. Some of the promising probiotics that <u>are being studied</u> are *Lactobacillus reuteri*, *L. acidophilus*, *L. plantarum*, *L. helveticus*, *L. rhamnosus*, *Bifidobacterium breve*, *Nitrosomonas eutropha*, *Streptococcus pneumoniae and S. thermophilus*, *Epidermidibacterium keratini*, and *Pseudoalteromomonas antartica*. However, there is not yet sufficient data to recommend specific probiotic products to help balance the skin microbiota and keep it healthy. Products for topical use are not produced under sterile conditions, so they require preservatives to prevent the growth of undesirable microbes. These preservatives and other ingredients may affect the viability of the probiotic ingredients. Research is ongoing on plant extracts containing prebiotics that may provide food for skin bacteria. Some of <u>colloidal oatmeal</u>'s skin benefits may be from the prebiotics it contains to support the skin flora.

#### [H2] ENVIRONMENTAL FACTORS THAT IRRITATE SENSITIVE SKIN

#### [H3] Detergents, Cleaning Products, and Hard Water

Laundry detergents and other cleaning products contain surfactants that help break down dirt and grease. Even very low amounts of <u>surfactants used in cleaning products</u> <u>can damage the skin barrier</u> resulting in increased water loss and permeability. They may disrupt tight junctions between keratinocytes, increase skin pH, promote inflammation, and prevent keratinocytes from carrying out their specialized functions. Examples are sodium lauryl sulfate and sodium dodecyl sulfate.

And it may be more difficult to wash off detergent residues than you think, especially with hard water. More <u>detergent residue may remain on skin</u> after washing and rinsing with hard water than with soft water, and this residue may be enough to cause skin irritation and reduced barrier function. Using a water softener has been shown to reduce detergent residues on the skin.

It's easy to tell if you have hard water, because when it dries around faucets it leaves a whitish scaly mineral residue that is difficult to dissolve and wipe off.

A meta-analysis of sixteen studies concluded that <u>children who live in areas with hard</u> <u>water</u>— with high levels of calcium and magnesium carbonate—have an increased risk of developing skin irritation and atopic dermatitis. Unhappily, there isn't evidence that water softeners remedy existing skin conditions

Minerals can be removed from hard water using a water softener, reverse osmosis, or other filters. The <u>Minnesota Department of Health</u> has answers to questions about installing a water softener.

### [H3] Swimming Pools

<u>Chlorine and by-products of disinfectants</u> may be irritating to skin and lungs, and swimming in pools has been associated with multiple skin disorders and damage to the stratum corneum. <u>In one study</u>, skin barrier function was assessed by measuring water loss in elite swimmers before and after two hours of swimming. Immediately after swimming and 30 minutes later barrier function was significantly reduced.

<u>Chlorine and chloramine</u> are used at around one to four parts per million (ppm) to disinfect water supplies, swimming pools, and spas. One study asked whether low levels of chlorine in this range adversely affect skin. Researchers concluded that exposure to as little as 0.5 to 2 ppm chlorine in hot water for ten minutes resulted in <u>poorer hydration</u> of the stratum corneum.

In addition to applying sunscreen prior to swimming outdoors, after being in a pool or spa, it's a good idea to shower with a gentle cleanser and apply moisturizer.

# [H3] Pollution

The effects of <u>pollution on skin barrier</u> function have been quantitatively assessed in a number of studies by measuring trans-epidermal water loss (TEWL), with higher water loss indicating a leaky barrier. A review of four studies concluded that air pollution may cause reduced skin barrier function, probably by generating free radicals that damage the skin. Barrier disruption was linked to nitrogen dioxide and particulate matter, and was higher in urban settings than rural ones. Particulate air pollution has also been shown to <u>reduce production of proteins</u> such as filaggrin needed to form the barrier.

Wildfires contribute to air pollution, creating particulates and nitrogen dioxide, and <u>increasing numbers of wildfires</u> in the past few years are affecting skin health as well as health of the respiratory tract. Smoke from the <u>California Camp fire in 2018</u> was found to exacerbate symptoms of atopic dermatitis.

And it's been suggested that <u>nanoplastics in water</u> and cosmetic products could enter the skin, causing inflammation and damage to the skin barrier.

It's particularly important in urban settings to use gentle cleansers to remove pollutants, to support skin barrier function with slightly acidic skin care products, and to keep the skin moist and hydrated.

Air pollution causes damaging free radicals to be generated in the skin, so another important component of skin care is boosting antioxidants that keep free radicals in check. Antioxidants in the skin can be boosted orally and topically: Major players are vitamins C, E, niacin/niacinamide, and multiple polyphenols from plants. This is why plant extracts are such important ingredients in skin care products.

# [H3] Sunlight and UV Light

The consequences of excessive sun exposure include photodamage, damage to DNA, malignancies, loss of collagen, and <u>barrier dysfunction</u> leading to water loss and dry skin. <u>UV light damages the lipid matrix</u> between cells in the stratum corneum and the structures that link cells together, affecting the skin's mechanical properties. Protecting the body, the stratum corneum absorbs most UVB wavelengths and about half of UVA, the remainder penetrating more deeply into the skin.

But sunlight in moderation has benefits, the most obvious one being that a small amount allows our bodies to make vitamin D without damaging the skin. And under controlled conditions, <u>phototherapy with UVB radiation</u> is used to help treat atopic dermatitis.

# [H2] PSYCHOLOGICAL STRESS

As is the case for most health conditions, it's likely that skin diseases may be brought on or made worse by psychological stress.

In one study, the barrier function of skin was tested in medical students during a time of stress (final exams) and during other times of lower stress. In these students, the barrier function of healthy skin was not affected by stress. What was affected was the ability of skin to recover barrier function after it was damaged.

Tape stripping is one way that researchers damage the skin and reduce barrier function. It appears that if you rip cellophane tape off of the forearm 15 to 20 times in a row, the

skin barrier is damaged. This can be assessed by measuring the amount of water lost from the skin.<sup>1</sup>

Tape stripping caused damage equally to stressed and non-stressed students' skin. But when the students were under stress during finals week, the skin took longer to heal after the tape stripping and more water was lost from the damaged skin. This suggests that experiencing stress may compromise the body's ability to maintain a healthy skin barrier.

# [H2] GENETIC FACTORS AFFECTING HUMAN SKIN

There are many mutations in the filaggrin gene that compromise its function, reduce the integrity of the skin barrier, and are linked to skin diseases. Mutations in filaggrin are responsible for the inherited skin disease, ichthyosis vulgaris, characterized by dry, itchy, scaly skin. <u>Mutations in filaggrin</u> are a strong risk factor—along with environmental factors— for developing atopic dermatitis and associated asthma. Fifty percent of people with atopic dermatitis have mutations in filaggrin.

<u>Mutations in the *TGM1* (transglutaminase-1) gene</u> cause the skin disorder lamellar ichthyosis. This gene codes for an enzyme that cross-links proteins, including keratin and filaggrin, into a rigid matrix, strengthening the stratum corneum. In this disorder, without sufficient cross-linking skin becomes red and scaly.

Comèl-Netherton syndrome is a rare, potentially fatal disease caused by <u>mutations in</u> <u>the SPINK5 gene</u> which codes for an inhibitor that blocks proteases, enzymes that break down proteins. In the absence of this inhibitor, protease enzymes digest components of the stratum corneum, including structures that link keratinocytes together, causing severe damage to the skin barrier and resulting in red, peeling, and scaly skin. The enzymes also trigger severe inflammation.

Mutations in the *TMEM79*, *CLDN1*, *FLG2* genes, and in genes encoding hornerin, involucrin, and loricrin proteins may also cause disruptions in skin barrier functions.

# [H1] How to Keep the Skin Barrier Healthy (TOC)

Plenty of hydration, protection from excessive sunlight, a diet of whole foods including essential fats, and a gentle skin care regimen with moisturizers are foundational, whether your skin tends to be healthy, dry, oily, peeling, or red.

<sup>&</sup>lt;sup>1</sup> In this case, the researchers were aiming for 20 to 30 grams (about five teaspoons) of trans-epidermal water loss (TEWL) per hour per square meter of skin. A square meter is about 60% of the area of an adult woman's skin.

# [H2] BARRIER-SUPPORTING SKIN CARE

Skin care products range from barrier-friendly to barrier-disrupting. Choose gentle cleansers, lotions, and creams with a slightly acidic pH (ideally around pH 5 to 5.5) that contain ingredients to reduce water loss and replenish barrier components.

#### [H3] A Slightly Acidic pH Is Best

Depending on how and where on the body skin pH is measured, it typically ranges from <u>4.1 to 6</u>.

This slightly acid pH is optimal for both production of the stratum corneum and for its functioning. The enzymes that make the lipids in the stratum corneum work best at an slightly acidic pH, so <u>when pH is elevated</u> (alkaline pH over 7), lipid supply and barrier integrity are reduced.

A comprehensive review of skin products in people over 50 concluded that pH of products was an important factor in skin health. The use of skin products with a slightly acidic pH of 4 was reported to <u>improve skin barrier health</u>. Soap has a very alkaline pH, but non-soap cleansers are available in a slightly acidic to neutral pH range of 4 to 7. (There's more info on skin cleansers <u>here</u>.)

Skin peel products that are strongly acidic (less than pH 4) may be used occasionally as exfoliating treatments, but they work by damaging the skin and they strongly disrupt the skin barrier. The best products for regular use are neutral to slightly acidic.

#### [H3] A Gentle Cleanser, Not Soap

Soap is not only more alkaline than desirable, but harsher. Compared to soap and water, skin hydration is better when <u>non-soap cleansers</u> like isethionates and glucosides are used.

#### [H3] Moisturizers for Dry Skin

Moisturizing lotions and creams can reduce dryness and itching, improve skin hydration by supplying moisture and reducing moisture loss, and support skin barrier function. The most effective moisturizers contain occlusive agents that prevent water from evaporating, humectants that attract water, lipids, emollients, emulsifiers, antioxidants, and preservatives.

In people over 50, moisturizers containing humectants that attract water have been shown to reduce dryness and itching, and the use of products containing glycerol (a humectant) or petrolatum (an occlusive agent) has been shown to <u>reduce skin tears</u>. Here's a rundown on the basic ingredients in moisturizers.

**Occlusive agents** <u>provide a physical barrier</u> to prevent water from evaporating. Some examples are:

- Mineral oil made from petroleum, which can improve softness and barrier function. The claim that it is comedogenic—clogs pores and promotes acne—<u>has</u> <u>been disproven</u>.
- Petroleum jelly (petrolatum) made from petroleum, which is effective and nonirritating. The Environmental Working Group (EWG), an organization that analyzes and grades ingredients and products for their effects on health and on the environment, does not have concerns about this ingredient other than the <u>need to verify purity</u>.
- Silicone-based occlusive ingredients including <u>dimethicone and cyclomethicone</u>, which are softening and moisturizing and are common in products labelled "oil-free". However, cyclomethicone persists in the environment, may have adverse effects on health, and is given <u>a poor score</u> by the EWG. The EWG also <u>scores dimethicone</u> poorly.
- Oils and fats such as jojoba oil and coconut oil also have occlusive properties.

**Humectants** are substances that attract and absorb water. Glycerol, amino acids, lactic acid, pyrrolidone carboxylic acid (PCA), and urea are humectants used in cosmetics and naturally found in NMF, the moisturizing complex present in the stratum corneum. <u>Allantoin</u> is a natural humectant that is a derivative of urea, and it is effective at lower levels and is less irritating than urea. Other humectants include hyaluronic acid, aloe, propylene glycol (which is linked to <u>contact dermatitis</u>), and sorbitol. The smaller ones like glycerol and urea penetrate more deeply into the skin than larger molecules like hyaluronic acid.

Humectants pull water from the body into the stratum corneum. When the air is moist humectants can also absorb water from the air. But when the air is dry, the water they pull from deep in the body may evaporate and be lost. To prevent this, humectants are used together with emollient and occlusive agents to coat the skin and keep the water in the skin itself.

**Emollients** provide a soft and smooth feel to the skin, and some of them also reduce water loss. <u>Emollient ingredients</u> include jojoba oil, sunflower seed oil, coconut oil, almond oil, and lanolin, which is grease extracted from wool, primarily from sheep. Lanolin is purified and cleaned for use in cosmetics, but may cause allergic contact dermatitis.

**Lipids** are a large category including fats, oils, free fatty acids, waxes, squalene, cholesterol, ceramides, phospholipids, and sphingomyelins. Fatty and oily ingredients act as both emollients that coat and soften the skin, and occlusive agents that form a thin layer to reduce water loss. Lipids generally stay on the <u>surface of the skin</u>, perhaps penetrating into the topmost layer of the stratum corneum, and possibly into the second and third corneocyte layer when skin is very dry.

Natural oils such as jojoba, coconut, and sunflower seed have been used for hundreds of years to promote healthy skin<sup>2</sup>. They help keep water in and irritants out of the stratum corneum. Most oils consist of triglycerides, which are three fatty acids attached to a glycerol molecule.

Free fatty acids help keep moisturizers acidic so that they mimic the pH of healthy skin. And fatty acids work in other ways to reduce inflammation and support the skin's antimicrobial properties. Free fatty acids may also be formed in the skin from fats and oils. The triglycerides in fats and oils can be broken down by bacterial enzymes, releasing fatty acids.

Specific oils and mixtures of lipids are discussed in the section below, <u>Best Skin Barrier</u> <u>Ingredients</u>. Mixtures of triglycerides, fatty acids, waxes, and squalene similar to lipids in sebum are used to mimic lipids naturally coating the skin. And mixtures of ceramides, fatty acids, and cholesterol—mimicking the composition of lipids in the stratum corneum— are also used in moisturizers and for barrier repair.

**Emulsifiers** keep water and oil layers from separating. They are also called surfactants. <u>Examples of</u> clean emulsifiers are:

- Lecithin
- Stearate
- Palmitic acid
- Cetearyl alcohol (cetyl alcohol plus stearyl alcohol)
- Betaine

Emulsifiers to avoid include:

• Polyethylene glycols. The EWG has some concern that any ingredient based on polyethylene glycol (PEG) may contain dioxane, a carcinogen, formed during manufacturing.

Antioxidants are included to maintain freshness of skin care products and to promote skin health by helping to prevent the formation of damaging free radicals. Free radicals called reactive oxygen species (ROS) are formed in the skin upon exposure to sunlight, environmental chemicals, and air pollution, and also as a byproduct of everyday metabolism. Left unquenched, ROS damage lipids, DNA, and proteins in the skin including collagen, contributing to thin skin, loss of elasticity, and a weakened skin barrier.

Vitamin C (ascorbate), tocopherol (vitamin E), and niacinamide are three valuable antioxidant ingredients, and plant extracts provide a wide range of additional antioxidants.

By reducing free radical damage, vitamin C may help prevent damage to collagen and signs of <u>photoag</u>ing. Vitamin E contributes photoprotective and skin-barrier-stabilizing

<sup>&</sup>lt;sup>2</sup> These oils have very different properties from "essential oils", that are aromatic and evaporate at room temperature. Some essential oils may be irritating to the skin.

properties. Topical niacinamide is used to target wrinkles, hyperpigmentation spots, and red blotchiness.

Plant extracts have been used traditionally for many years for their skin benefits including soothing irritated skin, long before scientists identified the bioactive components. We now know that <u>olive oil and olive leaf extracts</u> contain the antioxidants hydroxytyrosol, oleuropein, and luteolin. <u>Rosemary extract</u> contains flavonoids, terpenes, and polyphenols. Grape seed oil (*Vitis vinifera*) <u>contains procyanidin</u> antioxidants.

These plant extracts and antioxidant ingredients are meant to complement, not replace, sunscreen.

**Preservatives** are necessary to prevent microbial growth, since we touch creams and lotions with our hands, introducing bacteria and molds, and we store products at room temperature for long periods of time.

• <u>Phenoxyethanol</u> is an effective and non-irritating <u>preservative used in cosmetics</u>. Europe's Scientific Committee on Consumer Safety (SCCS) has concluded that it is an effective preservative, and safe for consumers–including children of all ages (at concentrations of up to 1%).

Preservatives that may be potential skin irritants include:

- Ethylene diamine-tetraacetate (EDTA)
- Sorbic acid
- Propylene glycol
- Thimerosal
- Several parabens

#### [H2] BEST SKIN BARRIER INGREDIENTS

A poorly functioning skin barrier directly contributes to the symptoms of dry skin, atopic dermatitis, psoriasis, acne, allergies, and contact dermatitis. Therapies for a damaged skin barrier include gentle hygiene, moisturizing lotions and creams, and topical and oral drugs. Of course, while we hope that this information is helpful, if you have a skin condition or disease, you'll want to discuss any questions or treatment with your dermatologist.

Moisturizers have been formulated with mixtures of lipids mimicking those found on the surface of the skin. Lipids on the surface of the skin come primarily from sebum plus smaller amounts from the stratum corneum.

Skin-similar lipids include squalene, waxes, triglycerides, and fatty acids, plus some ceramides and cholesterol. Jojoba oil is used as a source of waxes in skin-similar lipid mixtures. Coconut oil, macadamia oil, or other fats and oils may be used as sources of triglycerides and fatty acids.

Lipid mixtures have also been utilized that mimic those of the stratum corneum and contain ceramides, cholesterol, and fatty acids.

Moisturizers help maintain skin hydration, soothe the skin, and reduce the need for anti-inflammatory drugs. Some moisturizers may increase the lipid content of the stratum corneum by promoting optimal conditions for lipid production, and possibly by supplementing with fatty acids.

In <u>a study</u> described in detail below, a regimen providing a spectrum of skin-similar lipids was shown to increase levels of total lipids, ceramides, and free fatty acids in the skin of 35 to 50 year-old women. In <u>another study</u>, a lotion containing glycerol and free fatty acids was able to increase the levels of ceramides, cholesterol, and free fatty acids in the stratum corneum of people with dry skin. It's likely that some of the free fatty acids in these products were used for the production of other lipids.

### [H3] Squalene

Squalene is a natural triterpene lipid that makes up <u>about 13 percent of sebum</u> secreted by sebaceous glands and is a significant component of skin lipids. In skin care products, squalene provides hydration and is an emollient that provides suppleness and flexibility. Squalene's most important attribute is that it is an antioxidant that prevents free radical

damage. I<u>t's hypothesized</u> that the relatively high level of squalene in human skin, relative to other mammals, is because being relatively hairless we require additional protection from UV radiation. Squalene may contribute to this protection, helping to prevent damage to the skin barrier from the sun and other environmental stressors.

# [H3] Jojoba Oil

Jojoba (*Simmondsia chinesis*) seed oil is an unusual liquid wax similar to that in human sebum. It is uniquely stable compared to most oils. Jojoba oil possesses antioxidant, <u>antimicrobial</u> and anti-inflammatory activities, and has been <u>used traditionally</u> by indigenous Americans for hair and skin care, particularly for acne.

# [H3] Coconut oil

Coconut (*Cocos nucifera*) oil and ingredients derived from it can support barrier health and aid barrier repair. In a controlled study, the topical use of virgin coconut oil significantly improved skin health in <u>preterm infants</u>, who have an immature skin barrier. In a second <u>controlled trial</u>, coconut oil was demonstrated to improve skin hydration in people with very dry skin.

And a specific form of coconut oil was <u>shown in one study</u> to significantly boost skin health and barrier function in children with atopic dermatitis. To make this product, virgin coconut oil was treated with enzymes to release fatty acids, resulting in a clear, colorless liquid. <u>A second study</u> tested a virgin coconut oil that was fermented with bacteria to release fatty acids. This product stimulated cultured human skin to make components of the skin barrier plus collagen.

Coconut oil contains fats that are broken down in the gut or on the skin to yield lauric acid (a fatty acid) and monolaurin (glyceryl monolaurate), both of which have antimicrobial properties. In particular, monolaurin can inhibit the growth of *S. aureus*, which is often associated with eczema and a damaged skin barrier. Clinical studies have shown that monolaurin can inhibit the growth of *S. aureus* in the vagina and in the nose, two places it tends to colonize.

# [H3] Macadamia Oil

<u>Macadamia</u> (*Macadamia integrifolia*) nut oil contains triglycerides made of monounsaturated and saturated fatty acids plus <u>bioactive compounds</u> such as <u>tocopherols</u>, <u>phytosterols</u>, squalene, and polyphenols.

#### [H3] Shea butter

<u>Shea butter</u> (*Vitellaria paradoxa*, formerly *Butyrospermum parkii*) contains triglycerides primarily composed of monounsaturated fatty acids. It is rich in triterpenes, tocopherol, phenols, and sterols that possess anti-inflammatory and antioxidant properties.

### [H3] Sunflower Seed Oil

Sunflower (*Helianthus annus*) seed oil contains tocopherols, phytosterols, and fatty acids, and possesses anti-inflammatory activity. It has been shown to <u>improve skin hydration</u> and to preserve skin barrier integrity in adults. Both almond oil and sunflower seed oil have been shown to <u>improve skin hydration</u> in preterm infants, who have an immature skin barrier. In a blinded, controlled study the oils were applied to the entire body except for the face four times daily. Both oils also improved scores of dryness and redness.

# [H3] Almond Oil

<u>Sweet almond</u> (Prunus Amygdalus Dulcis) oil has been used traditionally to improve skin texture, promote skin elasticity, and treat dry skin. It is used safely as an emollient, emulsifier, and occlusive agent in cosmetic products. Almond oil has been the subject of multiple research studies, a number of which have reported benefits for skin that is dry and itchy.

#### [H3] Skin-Similar Lipids

A lipid mixture, L-22, <u>was created that mimics the skin surface lipids</u> of healthy 22-year-old women, and when tested on dry or aged skin, it was found to significantly improve barrier health, skin hydration, and elasticity.

In order to assess the composition of healthy skin lipids, samples were collected from the 22-year-old women's foreheads. The samples were found to contain, from most to least, glycerides, free fatty acids, squalene, wax esters, cholesterol esters, and cholesterol. Jojoba oil, macadamia oil, squalene and phytosterols were used to formulate a mixture of similar composition. Plant sterols (phytosterols) were used in place of cholesterol.

Four separate experiments showed that treating skin with the skin-similar lipids improved skin barrier function and skin hydration in dry or aged skin. The skin-similar lipids were significantly more effective—immediately and over the long term—than olive oil or common moisturizer ingredients at increasing skin hydration and reducing water loss. And in aged skin, elasticity and firmness were significantly higher after one week's use of the skin-similar lipids.

#### [H3] Ceramides and Stratum Corneum-Mimicking Lipid Mixtures

Moisturizers <u>containing ceramides</u> have been shown to improve the integrity of the stratum corneum. Ceramides, cholesterol, and fatty acids are essential lipid components of the stratum corneum. They form an impermeable matrix surrounding cells, and when they are depleted, barrier function is reduced. In eczema, psoriasis, and aged skin, ceramide is depleted, lipid levels are low, and this is associated with a <u>dysfunctional skin barrier</u>. In addition to low ceramide content, reduced barrier function is also associated with <u>abnormal types of ceramides</u>.

Ceramides, cholesterol, and fatty acids have been used singly or in mixtures to treat skin with a damaged barrier. Much of this research has been done in eczema, but the hope is that therapies to support barrier health will be useful in multiple skin conditions.

Ceramides are large molecules and generally sit on the surface of skin, although with ingredients that enhance permeation <u>some ceramide</u> may enter the stratum corneum, especially in dry skin. Short saturated fatty acids are somewhat smaller and <u>may</u> <u>provide substrate</u> for the skin to produce the longer fatty acids it needs.

Mixtures of these three lipids at ratios of 1:1:1 (one molecule of each) and 3:1:1 (ceramide-enriched) have been referred to as physiological lipids. Used topically, a mixture of ceramides, cholesterol, and fatty acids in a ratio of 3:1:1 has been reported to be helpful for skin therapy. In children with atopic dermatitis, a moisturizer containing physiological lipids enriched in ceramide was shown to improve the integrity and hydration of the stratum corneum and reduce water loss. Additional studies have found that physiological lipids reduce symptoms in people with atopic dermatitis, but further research is needed to verify and understand possible benefits for skin barrier function.

#### [H3] Topical Niacinamide

Niacinamide is a form of the B vitamin niacin. Consuming enough of this vitamin is important for skin health as discussed below, but niacinamide is also used topically to promote skin health.

<u>One clinical study</u> reported that a cream containing 2 percent niacinamide improved skin barrier function and hydration in people with rosacea. <u>Another clinical study</u> in women 35 to 60 found that a lotion containing a chemically modified niacinamide (myristoyl nicotinate) improved barrier function in photoaged skin. Water loss was reduced and the thickness of the stratum corneum was significantly increased. And several <u>studies of face creams</u> containing 4 to 5 percent niacinamide have demonstrated improved appearance after 12 weeks of use, including reductions in wrinkles and roughness.

In cultured skin cells, niacinamide supports <u>the formation of barrier components</u> including ceramides, fatty acids, cholesterol, and the proteins filaggrin and involucrin.

# [H3] Colloidal Oatmeal

Oats (*Avena sativa*) have been <u>used topically for centuries</u> to treat dry skin, itching, irritation, and rashes. So, it is not surprising that research has revealed <u>barrier-boosting</u> <u>properties</u>. Most research has been carried out on colloidal oatmeal, which is made by very finely grinding whole oats.

In 2003 the FDA approved colloidal oatmeal as an OTC ingredient that is safe and effective as a skin protectant, to "temporarily protect and helps relieve minor skin irritation and itching due to rashes, eczema, poison ivy, oak, or sumac, and insect bites."

The OTC ingredient must pass a number of quality control tests and is soothing, cleansing, moisturizing, and anti-inflammatory. It contains starches and beta-glucans that swell and hold water. Saponins provide cleansing properties, and phenols provide antioxidant and anti-inflammatory activities.

To elucidate how colloidal oatmeal may be working, skin cells grown outside of the body were treated with it, and barrier-building processes were monitored. It was shown to promote production of proteins used in barrier formation, and to help retain barrier function in the face of inflammation.

In addition, just as oat fiber is a prebiotic food for gut bacteria, colloidal oatmeal appears to be a prebiotic that may support the growth of skin bacteria and their production of lactic acid. Lactic acid is a component of NMF that supports hydration and a desirable skin acidity, and it is made by skin cells and bacteria. A lotion containing colloidal oatmeal was found to increase the amount of lactic acid on skin. By contributing to an acidic pH, colloidal oatmeal will boost multiple aspects of barrier function.

# [H3] Peptides

Bioactive peptides may be derived from proteins including rice bran protein. The peptides— short chains of amino acids—have properties unique to the type of protein and to the way the peptides are produced and purified. Some rice peptides have antioxidant activities, and preliminary research suggests that some are able to <u>inhibit</u> <u>enzymes</u> associated with aging skin: enzymes that break down hyaluronic acid in skin and that cause skin pigmentation. And <u>preliminary research</u> suggests that rice peptides can increase the production of hyaluronic acid by keratinocytes.

# [H3] Allantoin and Urea

Allantoin and <u>urea provide humectant, osmolyte, moisturizing, and healing support</u> for the skin barrier. Under dry conditions, urea and allantoin can help take the place of water inside cells, protecting them from osmotic stress. Topically applied urea reduces water loss and improves water retention by the skin, and <u>preliminary evidence</u> suggests that the same is true for allantoin. Urea may <u>reduce skin sensitivity</u> to certain irritating compounds and stimulate keratinocytes to produce antimicrobial peptides and lipids. However, urea at levels of 5 percent or more may cause <u>stinging and irritation</u>, especially in sensitive skin, and may break down and release compounds with an unpleasant odor. Allantoin is less irritating than urea and may be a better option for sensitive skin. <u>Allantoin</u> is valued for its moisturizing, smoothing, and healing properties and may be used as a skin conditioning agent and protectant.

Moisturizers containing urea have been shown to be helpful in improving barrier health and reducing symptoms in skin with atopic dermatitis and psoriasis. And high concentrations of urea have been shown to boost barrier function in <u>very dry skin</u> (xerosis) and psoriasis. In controlled clinical trials, urea-based creams have been shown to improve hydration and reduce flaking, roughness, and redness in <u>ichthyosis vulgaris</u>, which is caused by mutations in the barrier protein, filaggrin.

# [H2] NUTRITION FOR THE SKIN

#### [H3] Water Intake and Hydration

Hydration is crucial for healthy skin, but there's more to it than maintaining plumpness and smoothness. Water is needed to <u>moisturize the proteins in the stratum corneum</u>, keeping them elastic and resistant to breakage so that the barrier is intact and skin doesn't crack. Water is needed to keep enzymes working to produce proteins and lipids that form the barrier.

And there's a positive feedback loop: Hydration keeps skin healthy, and able to perform one of its most important functions which is to prevent potentially dangerous loss of water. When sizable areas of the skin barrier are destroyed, such as in people who have large areas of burned skin, water loss is extensive and dangerous, and hydration is a crucial part of therapy. But don't get carried away—like most things nutritional, moderation is best. Both overhydration and underhydration can be fatal. There is no evidence <u>that we need to</u> <u>drink eight glasses of water</u> daily, and the claim that coffee and other beverages (including beer in moderation) don't count toward water intake have been disproven. The Food & Nutrition Board of the National Academies of Science say that for most people it works to drink water with meals and otherwise<u>let thirst be the guide</u>. <u>Healthy</u> <u>women consume</u> around 72 ounces (9 cups) of beverages including juices and coffee per day, and <u>get another 18 ounces from foods</u>.

# [H3] Essential Fatty Acids (EFAs)

Polyunsaturated fatty acids are essential in our diets for every cell and tissue in the body including skin. Classic <u>symptoms of essential fatty acid deficiency</u> are a dry scaly rash and hair loss. The two essential fatty acids are found in many foods and deficiencies are uncommon, but deficiency can occur when fat absorption is compromised, such as in cystic fibrosis or celiac disease, or after bariatric surgery.

Since the value of omega-3 fats has been extensively publicized, it is may not be surprising to hear that one of the EFAs is an omega-3. The essential fatty acid ALA, alpha-linolenic acid, is found in nuts, seeds, and soy and canola oil.

The second EFA is an omega-6 fat, linoleic acid, which is found in most vegetable oils and animal products. Both EFAs support skin health and are <u>associated with good heart</u> <u>health</u>. Linoleic acid is an important component of the stratum corneum lipids.

# [H3] Vitamins and Minerals

Like other tissues, <u>skin requires all of the essential vitamins</u>, minerals, fats, and amino acids. A deficiency of the <u>B vitamin niacin</u> causes the disease called pellagra, with a dark red rash. <u>Women need about 14 milligrams</u> per day to avoid deficiency. A <u>vitamin B2 (riboflavin) deficiency</u> causes scaly patches on the head, and a <u>B6 (pyridoxine)</u> <u>deficiency</u> causes a red, scaly rash. Less than two milligrams daily of these vitamins will prevent a deficiency.

<u>Vitamin C provides</u> antioxidant support for the skin to help protect against UV light, photoaging, and damage to collagen and DNA, and it is necessary for collagen production. Without it the skin is fragile and wounds do not heal. The RDA for vitamin C is about 75 milligrams for women, and <u>supplements of 100 milligrams</u> or more have been used to boost free-radical-scavenging activity in the skin.

Whereas vitamin C is water soluble, vitamin E is found in the fatty membranes in cells, <u>where it protects lipids</u>, especially unsaturated fatty acids, from free radical damage. The RDA for women is around 23 international units (IU) (15 milligrams) and <u>it's best to</u> <u>limit</u> supplements, typically alpha-tocopherol, to less than 150 IU.

Vitamin A, zinc, and selenium are necessary for <u>keratinocytes</u>, and <u>copper supports</u> <u>collagen and elastin</u> production for skin firmness and elasticity. Recommended daily

intakes for adults for vitamins and minerals are summarized on the <u>Harvard School of</u> <u>Public Health's website</u>, and more detailed recommendations for different age groups can be found on the NIH's <u>Office of Dietary Supplement's website</u>.

A diet containing a wide variety of unrefined whole foods provides these nutrients. However, many of us get a substantial portion of our calories from refined foods depleted of nutrients. And it is extremely common for people—because of sunscreen, lack of time outside, or clothing—to miss out on the little bit of sun needed to catalyze vitamin D production by the skin.

Preliminary research suggests that <u>vitamin D supplements</u> (2000 to 4000 IU daily) may help support ceramide production in the body. And a large body of research has demonstrated that niacinamide supplements support healthy skin.

#### [H3] Niacinamide—The Skin Vitamin

Niacin is a B vitamin—used to make the cofactor NAD— that is essential for all cells to grow, replicate, produce lipids and proteins, and much more, but it is particularly important for skin health. In the form of niacinamide, this vitamin is used both topically and orally to promote skin health in amounts far greater than we would consume in a healthy diet.

Niacinamide supplements have been demonstrated to help protect the skin from photodamage. Most vitamins are best consumed in amounts similar to what would be obtained from a healthy whole-foods diet, amounts that are considered physiological. Niacin appears to be an exception to this rule. High doses of niacinamide (500 to 1000 milligrams per day) have been shown to <u>significantly protect skin from sun damage</u>, reducing actinic keratoses and nonmelanoma skin cancers, and this has been demonstrated in several large double-blind, placebo-controlled clinical trials. Niacin keeps cells healthy by promoting repair of DNA, and it also promotes immune surveillance in the skin to remove damaged cells.

#### [H2] PROTECTING THE SKIN FROM EXCESSIVE SUNLIGHT

Using sunscreen and protective clothing is the first line of defense against UV damage to the skin barrier. The stratum corneum is our body's first line of defense against UV light, absorbing much of the UVB radiation we are exposed to. However, the stratum corneum pays a significant price for protecting deeper layers of skin from solar radiation.

Some ways in which excessive sunlight damages the skin are obvious: dryness, redness, cracking, and inflammation. Less obvious is what UV radiation is doing to the structures and functions of the skin barrier. <u>UVB radiation makes the barrier more permeable</u>, increases water loss, and disrupts the carefully structured layers of lipids. Cells in the stratum corneum must link together tightly to be waterproof, and these links are weakened by UV light.

Look for sunscreen with zinc oxide or titanium dioxide, which physically block radiation. A damaged skin barrier may allow sunscreen ingredients to <u>permeate more deeply</u> into the skin, so keeping the barrier healthy may help the sunscreen stay on the surface of the skin and perform better.

Similar to air pollution, UV light damages the skin by generating free radicals, so it's a good idea to maintain healthy antioxidant levels in the skin with nutrition and skin care. There's more <u>on antioxidants here</u>.

# [H1] Here's How We Fit In: Skin Barrier Products.

Skinfix products are specifically formulated to achieve and maintain a well-functioning skin barrier, resulting in skin that feels and looks smooth and healthy. In clinical trials, Skinfix products have been demonstrated to enhance skin barrier function as well as skin comfort and appearance.

The Skinfix approach is three-fold: including barrier-supporting ingredients, excluding potentially irritating ones, and providing a skin-friendly slightly acidic pH.

Barrier-boosting ingredients include colloidal oatmeal, glycerol, ceramides, cholesterol, fatty acids, and niacinamide. Further skin protection comes from the skin-lipid-mimetic combination of squalene, jojoba oil with its liquid waxes, and macadamia oil, and from sunflower and sweet almond oils, shea butter, hyaluronic acid, and aloe.

In addition, plant extracts are added for their antioxidant and anti-inflammatory bioactive components. And all products are free from the following ingredients that may cause skin irritation: fragrance, silicone/dimethicone, parabens, sulfates, essential oils, formaldehyde, phthalates, lanolin, propylene glycol, and PEGs.

# [H2] THE BARRIER+ TRIPLE LIPID CLINICAL STUDY

The Barrier+ <u>Triple Lipid product line</u> provides all the types of lipids found on the skin: both the lipids coming from sebum—squalene, triglycerides, free fatty acids, and waxes—plus those found in the stratum corneum— ceramides and cholesterol. Glycerol is added to help bolster the skin's NMF content, and plant extracts provide multiple bioactive components.

Skinfix carried out a <u>groundbreaking study</u> on a regimen of Barrier+ Triple Lipid products that revealed more than superficial or temporary benefits for the skin barrier. The regimen was assessed in women with facial fine lines, wrinkles, and hyperpigmentation. They used the <u>Foaming Oil Cleanser</u>, the <u>Triple Lipid-Hyaluronate</u> <u>Serum</u>, and the <u>Triple Lipid Boost 360 Eye</u> twice daily, plus the <u>Triple Lipid Peptide</u> <u>Lotion</u> in the morning, and the <u>Triple Lipid Peptide Cream</u> at night.

Moisture content of the stratum corneum was increased by this regimen, and scores for overall health of skin, wrinkles, firmness, smoothness, and roughness were significantly improved.

What was particularly unique about this study was that levels of total lipids, fatty acids, and ceramides were significantly increased after four weeks of the regimen. In addition to providing squalene, waxes, triglycerides, and ceramides that coat the surface of the skin with smoothing and occlusive benefits, the effects of this regimen went deeper, stimulating the skin's own production of lipids.

How could skin care products help keratinocytes to produce lipids? It could be due to improved hydration contributing to keratinocyte health. Ceramide, squalene, and other occlusive lipids sit on the surface of the skin, preventing water loss. And glycerol boosts the skin's NMF content, attracting water to the stratum corneum.

Keratinocyte functions including lipid synthesis are also likely promoted by the slightly acidic pH of the products. And bioactive components from plant extracts contribute anti-inflammatory and antioxidant activities that support keratinocytes and barrier stability.

In a second clinical study, Skinfix <u>911 Ointment</u> was also shown to promote skin barrier health. In this <u>clinical study of healthy women the ointment</u> significantly reduced water loss through the stratum corneum, which is the most widely accepted measure of skin barrier function. This product contains <u>allantoin at a clinical level</u> for temporary protection of the skin after minor cuts and sunburns, along with barrier-supporting petrolatum, sunflower seed oil, shea butter, and aloe.

Other important ingredients we use for skin support include PCA, niacinamide, allantoin, coconut oil, and shea butter. Our Barrier+ <u>Skin Barrier Restoring Gel Cream</u> contains niacinamide for skin cell health and protection, squalene and allantoin for smoothing and healing, plus PCA to replenish the skin's NMF. The Resurface+ <u>AHA/BHA</u> <u>Renewing Cream</u> contains healing coconut oil and shea butter, plus NMF-replenishing glycerol.

#### [H2] THE GENE EXPRESSION STUDY

In most clinical studies on skin care products, the readouts are skin appearance and properties like hydration and elasticity. We can gain a deeper understanding of what is going on inside skin cells by measuring gene expression. Measuring which genes are turned on and off provides a better picture of short and long-term consequences for the skin.

What does it mean when a gene is turned on, or expressed? It means that the cell will use that gene as a template and produce the encoded protein. The proteins might be structural, such as filaggrin, or enzymes that synthesize lipids.

By looking at gene expression in a 3D model of skin, we've discovered numerous ways in which our patent-pending BL-3 complex—a combination of squalene, jojoba and macadamia seed oil esters, plus growth factors and an algal extract—promotes healthy skin. In skin cells, the complex:

- Significantly reduced the expression of genes that contribute to inflammation.
- Reduced the expression of a matrix metalloproteinase enzyme that breaks down collagen.
- Boosted the expression of enzymes that form ceramides and fatty acids.

In general, processes associated with barrier repair were upregulated, and processes associated with unhealthy skin were down-regulated.

# [H1] Additional Resources (TOC)

- We've provided a succinct overview of the skin barrier in our <u>Skin Barrier 101</u> page.
- The <u>American Academy of Dermatology</u> offers tips on skincare, as well as information on skin conditions and diseases.
- <u>Medline Plus</u> from the National Library of Medicine provides comprehensive links to reputable sources of information about skin conditions including diagnosis of rashes and job-related conditions.
- The <u>National Institute of Arthritis and Musculoskeletal and Skin Diseases</u> provides information on causes, symptoms, and treatments of skin conditions, and provides links to ongoing clinical trials that may be recruiting participants.
- The <u>University of New Mexico</u> has published a photo gallery for dermatological conditions.

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