

## Skin Aging

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### INTRODUCTION

- The Anatomy of Our Skin

Skin is the largest organ of the human body, weighing approximately 10 pounds and covering an area of about 16 square feet. We generally take skin for granted and tend not to take very good care of it. Our skin is responsible for protecting our internal organs from the toxic external world. Our skin protects us from heat, cold, and physical injuries. It also provides us with sensory information about the nature of the external world and is our first defense against invasion by bacteria, viruses, and other toxic elements. The skin is also an excretory organ, removing toxins from the body via perspiration.

Although there are many diseases that can affect the skin, the most common problems that we all have are the effects of our exposure to ultraviolet (UV) radiation from the sun over time. Having a healthy tan has, in the past, been a sign of good health. In the last 10 years, with the changes in the ozone layer in the upper atmosphere, it is clear that the effects of UV radiation from the sun are much more dangerous than originally thought. There are many causes for the accumulated cellular damage in the skin that we call aging. Among these are the oxidative processes and related free radical damage that result from UV sunlight, smog, toxins, cigarette smoke, X-rays, drugs, and other stressors. Young skin is also exposed to these potentially damaging changes, but when we are young, there is sufficient cellular energy (ATP) for DNA repair and cell renewal. Enzymes that provide antioxidant activity such as SOD and catalase are readily available. As we age, there is increased wear and tear, while at the same time the energy for cell repair and renewal is diminished and the antioxidant enzymes are less available.

Specific diseases that affect the skin will not be covered in this protocol, but will rather be listed under the disease category itself (e.g., Acne). This protocol will primarily deal with the effects of aging on the skin.

Health-conscious Americans are concerned about the damage that sunlight inflicts on the skin. Protecting against the effects of ultraviolet radiation is a multi-million dollar industry. Creams, lotions, cosmetic products, and protectants are to be found everywhere, resulting in confusion for the consumer regarding what products are really helpful. Cosmetic companies may seize upon an idea, put that ingredient into a cream or lotion without much research, and then advertise it to an unsuspecting public. This protocol will only use evidence from peer-reviewed journals.

#### The Anatomy of Our Skin

Our skin consists of two main layers: the dermis and epidermis. The dermis is the inner layer of skin that contains nerve fibers, fat cells, blood vessels, sweat and oil glands, and hair follicles. The dermis also contains collagen and elastin, two proteins that are responsible for the structure and elasticity of the skin itself. These proteins are subject to the process of aging. The sweat and oil glands in the dermis protect the outer layer of skin with a thin coating of oil and perspiration.

The epidermis is the outermost layer of our skin. New cells generated by the dermis continually replace this layer. Removal of the epidermis, as in a scrape or burn, reveals an unprotected sensitive dermis underneath. The epidermis also contains melanocytes or pigment cells. These cells produce melanin, which determines the shade of your skin (a heritable factor).

### SKIN AND FREE RADICALS

- Other Factors

Scientists now believe that the free radical theory of disease also applies to the aging of the skin. Free radicals are unstable small molecules generated by an oxygen environment which require stabilization by the body's antioxidant system. Free radicals occur throughout every cell in our body simply by virtue of the fact that oxygen is our principal metabolic fuel. Strong sunlight readily

generates free radicals in the skin. Our hands, face, neck, and arms are the areas usually chronically exposed to light. These parts of the body, particularly the face, are where aging of the skin shows up.

The skin protein collagen is particularly susceptible to free radical damage, and when this damage occurs, it causes the collagen protein molecules to break down and then link back up again in a different way; this is known as cross-linking. Collagen cross-linking causes the normally mobile collagen to become stiff and less mobile. Sunlight also causes the messenger molecules present in skin cells to become active and create inflammatory products. Fisher et al. (1977) have shown that the multiple small exposures to ultraviolet irradiation lead to sustained elevations of enzymes that degrade skin collagen and contribute to photo-aging.

Skin cancer typically occurs in skin that is photo-aged. Wrinkles, laxity, uneven pigmentation, brown spots, and a leathery appearance characterize photo-aged skin. In contrast, chronologically aged skin that has been protected from the sun is thin and has reduced elasticity, but is otherwise smooth and unblemished.

The following factors can accelerate skin aging:

- sun exposure
- first- or secondhand cigarette smoke
- environmental toxins
- poor diet
- excess alcohol consumption
- stress
- harsh soaps or detergent-based moisturizers
- sleep deprivation

One way of mitigating the effects of these skin-damaging foes is to increase levels of protective antioxidants through a diet rich in fruits and vegetables or by direct topical application.

Critics used to claim there was no evidence that topically based products affected skin aging. Over the years, a remarkable number of published studies have proven these skeptics wrong! Science clearly substantiates the role that free radicals play in causing skin aging and the fact that topically applied antioxidants confer significant protection and can even partially reverse some aspects of skin aging. Indeed, various animal and human studies have proven that low molecular weight antioxidants, especially vitamins C and E, as well as alpha-lipoic acid exert protective effects against free radical damage (oxidative stress) (Podda et al. 2001).

In a double-blind study, a topical vitamin C complex was applied to one half of the face and a placebo gel to the opposite side. Clinical evaluation of wrinkling, pigmentation, inflammation, and hydration was performed prior to the study at weeks 4, 8, and 12. The results showed a statistically significant improvement of the vitamin C-treated side, with decreased photoaging scores of the cheeks and the perioral area. The peri-orbital area improved in both the vitamin C and placebo-gel group, probably indicating improved hydration. The overall facial improvement of the vitamin C side was statistically significant. Biopsies showed increased collagen formation in the vitamin C group. This study showed that topically applied vitamin C results in clinically visible and statistically significant improvement in wrinkling when used for 12 weeks. This clinical improvement correlated with biopsy evidence of new collagen formation (Fitzpatrick et al. 2002).

In response, cosmetic companies have increased the percentages of active ingredients with the goal of replicating the antiaging effects revealed in the published studies. The problem of increasing the level of active ingredients is that the wrong layers of the skin can be overly saturated resulting in irritation and reduced efficacy.

The first step in resolving this problem is to encase the active ingredients so that they can be absorbed through the top layer into the lower layers of the skin where they are most active. The second step is to design a delayed release system so that the active ingredients can be released over an extended amount of time.

### **Other Factors**

In spite of the effect of sunlight on the skin, there are other factors that affect skin health that occur regardless of our exposure to sun rays. Dryness, loss of tone and fullness, diminished immune responses, and reduced ability to repair damage are all factors that contribute to the aging process.

There are many types of skin tones and qualities. Men tend to have thicker skin than women due to the dominant hormone testosterone. However, in later years, the lack of estrogen in women and testosterone in men tend to cause changes in both genders.

Each individual will have a different skin, with different oil production, color, and texture. Clearly, people with dry, white skin should use only mild cleansers and never use grainy cleansing products. Moisturizers and oil-based make-ups will also be required. On the other hand, those with an oily, darker skin can use mild liquid cleansers and an oil-blotting foundation. Generally, the use of sunscreens is reasonable as long as it does not create a false sense of security. Do not go out for longer periods of time in the sun just because you're wearing a sunscreen.

Skin damage occurs when the membrane covering of the skin cell is damaged by free radicals. Free radicals make the membrane more permeable, allowing the cells to dehydrate (lose water). The membrane of the cell is what is called a lipid bilayer: two layers of fat end-on-end. Enzymes are activated when the skin is traumatized or exposed to sun. Enzymes break down the lipid bilayer and cause inflammation. Thus, any antioxidants must be fat-soluble to protect this layer.

Chronic inflammation is an underlying cause of common degenerative diseases. One study found that pro-oxidative factors that accelerate skin aging might activate a self-maintained micro-inflammatory process that interferes with skin elasticity and thickness. This study stated that topical antioxidants decrease this inflammatory cascade and thus afford protection to the skin structures (Giacomoni et al. 2000).

The effect of exposure to even ambient UV irradiation increases the risk for long-term, detrimental effects characterized by wrinkles and loss of skin tone and resilience. Photo-aged skin displays prominent alterations in the cellular component and the extracellular matrix of the connective tissue. UV exposure results in an accumulation of disorganized elastin and a severe loss of collagens, the major structural proteins of the dermal connective tissue. The unifying pathogenic agents for these changes are UV-generated free radicals. As well as causing permanent gene mutations, free radicals activate signal transduction pathways that are related to growth, differentiation, senescence, and connective tissue degradation (Scharfetter-kochanek et al. 2000).

## WHAT IS GOOD FOR YOUR SKIN?

- Outside Story
- Antioxidants
- Beyond Antioxidants
- Keeping Skin Moist
- Botox
- Inside Story
- Vitamin D
- Thyroid Function
- Hormones And Skin

When most people think about good things that they can do for their skin, they usually think about things they will put on their skin rather than what they will put inside themselves to make their skin healthier. Although topical application of certain products is essential, equally important is the nourishment of the skin from the inside. Everything from essential fatty acids, antioxidants, and other supplements to the food that we eat is critical in maintaining healthy skin that ages slowly.

### The Outside Story

The first preventive measure you can take is to reduce the amount of UV light that you are exposed to. This can be done either by avoiding the sun completely or more practically by wearing at least an SPF15 sunblock. One danger with using a sun block is that it tends to make people feel like they can go out in the sun more! So they end up with the same amount of UV radiation because they are simply out in the sun longer. For areas that are more exposed, such as the nose and cheekbones, a sun-blocking titanium oxide would probably be best.

Considerable interest has been generated about combining antioxidants with sunscreens to provide enhanced protection against UV rays. Two of the best-known antioxidants are vitamins C and E, both of which have been shown to be effective in different models of photodamage. In a study done on swine skin, vitamin C provided additive protection against acute UVB damage (sunburn cell formation) when combined with a UVB sunscreen. When a combination of vitamins E and C were used, very good protection from a UVB insult occurred. Vitamin C, however, was significantly better than vitamin E at protecting against a UVA-mediated phototoxic insult in this animal model (Darr et al. 1996).

When it comes to makeup and skin care products, people with oily skin should clearly avoid products that have oil in their formula. Those with dry skin need products that have essential oils combined in the formula. Cleansing the skin by washing once daily without astringent products is probably a good idea as well. Facial masks can help hydrate skin, but can be harmful if they cause irritation. They should never be used more than once a week.

## ***Antioxidants***

Although antioxidants are well-known for their beneficial effects inside the body when taken orally, in the case of skin, there are a number of antioxidants that are helpful when applied topically (Podda et al. 2001).

Human studies have demonstrated pronounced protective effects of antioxidants when applied topically before UV radiation exposure. With respect to UVB-induced skin damage, the photoprotective effects of antioxidants are significant. Topical application of such combinations may result in a sustained antioxidant capacity of the skin, possibly due to antioxidant synergisms. Free radicals are culprits behind UVA-induced skin alterations, thus indicating a basis for topical antioxidant administration. In a human study, topical application of antioxidants resulted in diminished severity of UVA-induced sun damage. Thus, regular application of skin care products containing antioxidants may be of the utmost benefit in efficiently preparing skin against exogenous oxidative stressors occurring during daily life. Sunscreen agents may also benefit from combination with antioxidants resulting in increased safety and efficacy of such photoprotective products (Dreher et al. 2001).

*Vitamin C Esters.* Vitamin C ester is vitamin C with a fatty acid attached to it. It is fat-soluble and rapidly penetrates the skin, being much better absorbed than vitamin C alone. Products containing vitamin C ester, such as ascorbyl palmitate, will be helpful in reducing and preventing skin damage (Yamamoto et al. 2002).

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## Skin Aging

Vitamin C does more than inhibit skin-damaging free radical activity. It is also required for collagen synthesis, which declines markedly in aging skin. As humans age, they suffer diminished microcapillary circulation within the skin, thereby depriving skin cells of the supply of vitamin C it needs for youthful collagen synthesis. The topical application of vitamin C in a skin-penetrating medium can enhance the availability of vitamin C for collagen production. Vitamin C regenerates vitamin E in the skin. An antioxidant like vitamin E can only suppress a limited number of free radicals before it runs out of electrons to donate. Vitamin C regenerates vitamin E and enables vitamin E to provide sustained antioxidant protection in the skin's elastin fibers. Vitamin C also plays a vital role in skin repair. When skin is injured, its vitamin C content is used up rapidly in the scavenging of free radicals, and in synthesizing collagen to speed healing.

A randomized double-blind controlled study was conducted on human volunteers to determine the efficacy of topical vitamin C application in treating mild to moderate photodamage of facial skin. Methods of evaluating efficacy included an objective computer-assisted image analysis of skin surface topography, subjective clinical and photographic appearance and patient self-appraisal questionnaires. Topical vitamin C was applied to one side of each patient's face and a control vehicle on the other side for 3 months.

The results using the optical image analysis demonstrated that compared to the placebo-vehicle, the vitamin C-treated side of the face showed a statistically significant 71% combined score improvement. Clinical assessment parameters demonstrated significant improvement with vitamin C treatment compared to the placebo vehicle for fine wrinkling, tactile roughness, coarse rhytids, skin tone, sallowness, and overall features. Patient questionnaire results demonstrated statistically significant improvement overall, with the vitamin C treatment 84.2% greater than control. Photographic assessment demonstrated significant improvement with vitamin C treatment (57.9% greater than the improvement in the control group). This 3-month study using topical vitamin C provided objective and subjective assessment of the improvement in photodamaged facial skin (Traikovich et al. 1999).

*Alpha-Lipoic Acid.* Alpha-lipoic acid is an antioxidant that has been found to be extremely important in the management of Type II diabetes. It appears to be able to increase the beneficial effects of other antioxidants and is both water and fat-soluble. Alpha-lipoic acid is also found in the mitochondria, the powerhouses of the cell itself. Thus, it can augment the metabolic processes of the cells, and in addition, it turns off an inflammatory messenger known as nuclear factor kappa beta (NFKB), which turns on inflammation.

**Note:** *NFKB is a transcription factor. Transcription factors are messengers found inside the cell, which carry information from the cytoplasm to the nucleus. There they may activate or inhibit the production of certain proteins or enzymes, which then carry out a particular cell function. Such a function might be increased inflammatory factors.*

Another factor known as AP-1 may either damage or heal skin depending upon how it is activated. If it is activated by sunlight, it produces free radicals; but if it is activated by alpha lipoic acid, then it turns on enzymes that digest only the damaged collagen. As we age, proteins can become glycosylated. Glycation is a process where a glucose molecule is attached to the protein and is commonly measured in the body by estimating the blood levels of glycosylated hemoglobin (HbA1c). Alpha-lipoic acid can decrease glycation, decrease pore size, and activate AP-1. Often the result of this is a decrease in facial lines when applied topically.

A concern amongst dermatologists is whether agents that are proven effective in fighting skin aging can be consistently delivered to the specific layers of the skin where they are known to induce their biological effect. The advent of liposome delivery technology has enabled scientists to increase the efficacy of topical anti-aging agents by delivering them into the inner layers of the skin.

A patented liposome delivery system trademarked QuSomes  $\text{AE}$  (meaning "quick liposomes") was discovered in late 2000. This technology represents a substantial enhancement in conventional liposome vehicles. QuSomes not only delivers active skin-protecting ingredients faster into the lower layers of the skin, but these liposomes are also designed to protect the active ingredient from deterioration. With the unique QuSome delivery system, the solubility of the active anti-aging agents is preserved, thereby enabling them to reside longer in the areas of the skin where they exert their greatest biological effects. The availability of QuSomes enables nutrients like alpha lipoic acid to be reliably delivered to the inner layers of the skin. This makes alpha lipoic acid an exciting new weapon in the battle against the ravages of time.

*Alpha- and Beta-Hydroxy Acids (Glycolic Acid and Salicylic Acid).* Alpha-hydroxy acids have been around for about 20 years and make a marked improvement in skin quality by their exfoliative action. Exfoliation removes dead skin cells from the surface. In the late 1980s, the media reported on the age-reversal properties of glycolic acid, an alpha-hydroxy fruit acid that functioned to slough dead skin cells off the surface so that more youthful appearing fresh cells would be visible. The effect of the topical application of these fruit acids was the disappearance of fine lines and wrinkles and a fresher looking tone to the skin.

Importantly, several years before this announcement, a researcher named Carmen Fusco had added an alpha-hydroxy fruit acid (lactic acid) to a skin cream formula called Rejuvenex. This formula became the first anti aging cream in history to incorporate an alpha-hydroxy fruit acid as an active ingredient.

A physician, Dr. Benjamin S. Frank, first developed Rejuvenex in the 1970s. He believed that nutrition played a major role in preventing disease. Dr. Frank proposed that aging was partially a result of decreased energy production in the cell's mitochondria. He felt that in the presence of reduced mitochondrial function, cells become defective and lack the energy needed to effectively repair DNA. Published scientific studies have since validated Dr. Frank's theory about cell energy depletion and aging.

One of Dr. Frank's most famous hypotheses was that the topical application of RNA improved cell energy metabolism and therefore the health and appearance of the skin.

Much has been discovered about skin aging since Dr. Frank began experimenting with RNA-based face creams at his New York City medical office. His premature death did not deter the further development of his skin-saving cream. His assistant, Carmen Fusco, continued the research, producing a cream with the nutrients and antioxidants noted for their anti-aging properties.

Hydroxys are not just an exfoliant, but also a stimulator of collagen production and cell growth (Kim et al. 1998). In animals they have been found to reduce tumor incidence (Hong et al. 2001). Psoriasis, a common debilitating skin condition with increased epidermal production, also responds to hydroxy acids and even more so with topical steroid added, according to Kostarelou et al. (2000). The authors concluded from this double-blind study:

The present clinical study demonstrates for the first time that the effective and well tolerated therapeutic efficacy of glycolic acid scalp lotions is enhanced when used in conjunction with a 0.1% betamethasone scalp application against scalp psoriasis. This potential offers the practising dermatologist novel treatment modes against severe skin conditions by combining topical corticosteroid with exfoliative agent therapy.

*DMAE (Dimethylaminoethanol)*. One of the major problems of advanced aging is the sagging of tissues caused by the destruction of the skin's underlying support structure (primarily collagen and elastin). While much of this structural deterioration may be preventable by lifestyle changes and proper use of oral and topical agents, it is difficult to reverse this unsightly collapse of facial tissues. In a study published in *Skin Research Technologies*, DMAE was shown to produce a firming effect on the skin (Uhoda 2002). This mechanism may be due to the fact that DMAE functions as a cell membrane stabilizer. Based on clinical reports, DMAE may be the first topical agent that can help firm sagging skin.

*Other Antioxidants and Topical Treatments*. Tixier et al. (1984) found that the antioxidant pycnogenol (Pine Bark extract) can bind to elastin (one of the skin proteins) and prevent its degradation by elastase in a rabbit model. Another study indicates that oral supplementation of pycnogenol (PBE) reduces erythema in the skin (Saliou et al. 2001).

Vitamin A analogs such as tretinoin and tazarotene creams are also available for topical treatment of photo-damaged skin (Nyrady et al. 2001).

Vitamin A and its retinoid analogs stimulate skin cell renewal by increasing the rate of mitotic cell division (Ridge et al. 1988; Chapellier et al. 2002; Koussoulakos et al. 1990). One mechanism by which vitamin A induces this phenomenon is to act as a signaling agent to stimulate the binding of epidermal growth factor to skin cells (Chapellier et al. 2002).

A characteristic of sun-damaged skin is the degradation of the supporting structure of skin caused by reduced collagen synthesis. A study involving 72 individuals of varying age groups was done to see if the topical application of natural vitamin A could improve function in both natural aged, sun-protected, and photo-aged skin. In one of the study groups consisting of individuals 80+ years of age, topical application of vitamin A for 7 days increased fibroblast growth and collagen synthesis, while reducing levels of a collagen degrading skin enzyme (metalloproteinase).

The overall findings indicated that naturally aged, sun-protected and photo-aged skin share important molecular features including connective tissue damage, elevated metalloproteinase levels, and reduced collagen production. Topical vitamin A treatment reduced matrix metalloproteinase expression and stimulated collagen synthesis in naturally aged and sun-protected skin, as it does in photo-aged skin (Varani et al. 2000). Vitamin A drugs (Retin-A) have shown more profound acute effects in reversing both photo damaged and naturally aged skin, but some people find it irritating to the skin (Varani et al. 1998).

Studies show that the upper layer of the skin (epidermis) can be easily loaded with natural vitamin A by topical application. Besides being a precursor for retinoic acid, vitamin A also has a free-radical scavenging potential. Vitamin A absorbs ultraviolet light to help protect the most delicate areas of the skin against damaging free-radical attack (Sorg et al. 2001). Natural vitamin A thus functions via several pathways to guard against normal and sun-induced skin aging.

Other studies indicated that natural vitamin A (retinyl palmitate), had some of the cell renewal properties that were once attributed solely to retinoic acid drugs.

## Going Beyond Antioxidants

While free radicals have been implicated in much of the damage that occurs to aging skin, there are other injurious factors that result in unsightly structural and functional deterioration.

For instance, aging skin cells suffer from metabolic imbalances that preclude them from performing youthful repair functions. The groundbreaking work of Benjamin S. Frank, M.D., showed that RNA improved cellular energy and the ability of the skin's cells to use oxygen. This improved metabolism enhances the movement of young cells to the surface of the skin where they replace old cells.

Another benefit from topically applied RNA is to repair early skin cell damage. Clinical trials by Dr. S.J. Jellinek in the 1970s demonstrated how creams containing RNA/DNA caused a visible lifting and tightening of the skin, with the wrinkles appearing to be less visible in a three-week period. Although this was a small-scale study, it was nonetheless a double blind test. Very few commercial products provide the potency of RNA and DNA used in these studies.

## Keeping the Skin Moist

Replacing moisture lost to aging is a prime reason why women use face creams. Most commercial face creams are oil-based and work by blocking the release of water from the skin. As people grow older, however, they cannot rely on oil-based preparations to block the release of moisture. That is because aged skin loses the ability to attract moisture in the first place and fundamentally becomes dehydrated. At this point, aged skin needs to be replenished with its natural moisturizer complex in order to attract and retain water.

The most advanced moisturizer is Ceraphyl GA-D, which functions by reducing the excessive drying in the upper layers of the skin. Drs. Stig Friberg and David W. Osborne showed that Ceraphyl GA-D inhibits transepidermal water loss by preventing the lipids (fats) from crystallizing. This mechanism is central to preventing dry, thin, leathery, dull, wrinkled skin. Ceraphyl GA-D also seems to increase the effectiveness of sunscreens and enhance the receptiveness of skin cells to antioxidants such as vitamins A, C, and E.

Hyaluronic acid helps the skin retain its youthful moisture via a different mechanism than Ceraphyl GA-D. Hyaluronic acid maintains the integrity of the connective tissue because it is a source of manganese and glucosamine. Injectable hyaluronic acid may one day replace injectable collagen, but this important skin-preserving nutrient is available without a prescription today in over-the-counter skin creams.

The ability of skin to hold moisture is directly related to its sodium pyrrolidone carboxylic acid (NaPCA) content. NaPCA is one of the skin's most important natural moisturizers. Old skin, however, contains only about half the NaPCA as young skin. NaPCA facilitates the moistening by pulling water into the skin from the air. Optimal protection against age-accelerating dehydration is best obtained by the topical application of NaPCA, hyaluronic acid, lactic acid, urea, Ceraphyl GA-D and squalene every day.

## Botox (Botulinum Toxin)

Botox is quite literally a very dilute solution of the botulinum toxin Type A produced by the botulism species of bacteria. For about 10 years now, very dilute preparations of this toxin have been injected into humans to improve facial appearance (Becker-Wegerich et al. 2001). Botox partially blocks the nerve to the injected muscle. It usually takes about 3-5 days to notice the effects of Botox, and the effect lasts 4-6 months. Botox injections are best done on the upper third of the face. Forehead lines, furrows between the eyebrows, and lines around the eyes ("crow's feet") respond favorably to Botox. Frown lines (below the mouth) and chin creases may also be improved with a Botox injection, but the response varies. The cost of a Botox injection is about \$400 and includes up to 35 units of Botox. If Botox migrates to the wrong muscle, side effects such as drooping of the eyelid or unevenness of the eyebrows may develop. Botox is purely cosmetic and has no actual healing effect on the skin itself.

## The Inside Story

Nourishing the skin with topical ingredients is important, but in addition it is essential that you feed your skin nourishing food and drink. The effects of aging can be seen directly by looking at skin, not something possible for most organs in the body, which are hidden from view. The following are general considerations for nutritional optimization of skin function:

1. As much as possible, remove all processed foods from your diet. There are two reasons for this. First, processed foods tend to contain high levels of sodium, sugar, fat, and other undesirables, such as color and preservatives. Second, processed foods usually contain less nutrition than whole foods. Strange as it may seem, "enriched bread" has had 60% of its minerals removed along with most of the fiber. Some nutrients have been added back, but only some. The nutrient density of processed foods is very low and leaves much to be desired.
2. Eat foods that are natural and whole, such as whole grains, fresh or frozen vegetables, fruits, nuts and seeds, and so forth. Your plate should contain mainly fruits, vegetables, and grains with a small amount of protein, such as fish or poultry, added.
3. Drink plenty of water: 8 glasses a day are recommended. (Some of our water requirements can come from fruits and

vegetables.)

4. Do not fry foods or barbecue them for long periods of time.
5. Use alcohol only in moderation: one drink a day, for example.
6. Eat foods that are high in antioxidants. These foods are highly colored, such as cantaloupe, spinach, berries, and cruciferous vegetables (cauliflower, cabbage, and sprouts).
7. Remove sugar and saturated fats. Use a sweetener if you like.
8. Take a good multivitamin with an added antioxidant formula, particularly mixed carotenes, vitamin C, vitamin E, selenium, and zinc. Add some vitamin A, the "skin vitamin," together with supplements of RNA and B vitamins (for coenzymes) and the minerals zinc, copper, and manganese. These provide even more intensive protection against damaging free radicals. The increased cellular energy helps the skin repair, renew, and revitalize itself.

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## Skin Aging

Foods rich in nucleic acids (RNA), such as sardines, salmon, tuna, shellfish, lentils, and beans, help improve cell energy through a "salvage pathway" (see *Life Extension Magazine August 1997, 5-8*).

Foods rich in antioxidants and other phytochemicals, such as fruits, vegetables, and green tea, help protect against oxidative damage and free radical attack of all body cells including the skin.

Aging causes a progressive decline in our ability to internally synthesize the essential fatty acids (EFAs) required by the skin to maintain a youthful, moist appearance. The most important oils to supplement are the omega-3s that can make the skin smoother, softer, and more radiant-looking. When skin is properly nourished, it shows less of the effects of aging. The oral ingestion of fish, flax, or perilla oil provides abundant quantities of the omega-3 fatty acids that are so beneficial to the health and appearance of the skin. Also, if there is a tendency to develop eczema (a common skin condition), oil of Evening Primrose or borage oil are essential nutrients to be supplemented.

Avoidance of more than modest exposure to the sun's UV light is critically important to protect the skin against the oxidizing effects of solar radiation. UV rays are categorized by wavelengths: UVA, UVB, and UVC.

The ozone layer filters out the UVC and many of the UVB rays, but the ozone layer is not the same as it used to be and seems to have little or no effect on UVA rays which make up 90% or more of the sun's radiation that reaches the earth. Indeed, it is exposure to UVA that causes most of the photo-aging damage: the premature wrinkles, loss of elasticity, hyperpigmentation, and a dry, dull, leathery texture.

UVB, which is most intense from 10 a.m.-2 p.m., can cause sunburns and basal-cell cancers of the skin as well as increase the risk of melanomas. Yet sunscreens, which are geared to filter out UVB, seem to have no effect on the incidence of melanoma. Of interest are studies showing that people who are continuously exposed to the sun--farmers and fisherman, for example--seem to be less at risk for melanoma than a vacationer, especially a fair-skinned sunbather who exposes his or her skin to intense sun for a few days or a week.

### A Word about Vitamin D

Recent publications regarding the adequacy of vitamin D in the general population have been alarming. It appears as though not only are people not getting enough of this vitamin, but that even in the summer months the amount is suboptimal in some population groups in the northern latitudes (i.e., above the 35th parallel) ( Viethl et al 2001). Most of our vitamin D comes from sunlight, specifically the UVB fraction. Lack of sun exposure will, in time, inevitably lead to suboptimal levels of vitamin D ( Tangpricha et al. 2002). The supplemented form of vitamin D found in milk is insufficient to bring levels to normal ( Trang et al. 1998). Milk is fortified with vitamin D2,, not vitamin D3, which is the active component. Vitamin D2 is also the form of vitamin D that is likely to lead to toxicity if taken in large quantities. What is the answer? First, if you live above the 35th parallel, make sure you obtain at least 400 IU a day of vitamin D3 in supplement form. Some doctors are advising much higher amounts of vitamin D3 to protect against cancer. Because this is such an inexpensive vitamin, doses up to 1400 IU daily should be considered without the need for blood tests to guard against vitamin D toxicity. Some research indicates that much higher amounts of supplemental vitamin D3 are safe and desirable.

### Thyroid Function

Like most hormones in our body, as we age, less and less thyroid hormone is available. Glands, which produce these hormones, become sluggish or irregular. The thyroid gland is no exception. Often physicians will see patients who are not only overweight, but who also have dry, flaky, sluggish skin. A thyroid profile in the blood will often show a low or borderline-low thyroid function. Nutrients and foods which support the thyroid such as sea vegetables, seafood, fish, and iodized sea salt, or prescription thyroid preparations such as Armour or Cytomel, when necessary, can reverse this form of skin aging.

### Hormones and Skin

- DHEA And Melatonin
- DHEA Saves Skin
- Melatonin Protects
- Prevention Of Skin Aging And Cancer
- Vitamin A And Skin Tumors

## **DHEA and Melatonin**

The sleep hormone (melatonin) and the anti-stress hormone (DHEA) are both found in human skin. Both are converted to other entities with important jobs to do. DHEA is converted into estrogen- and androgen-type metabolites found only in skin (Labrie et al. 2000). Melatonin is synthesized in skin. In low concentrations it can stimulate cell growth. This type of on-site, organ-specific production of hormones is called *intracrine biosynthesis*. Intracrine biosynthesis allows different organs to manufacture the substances they need without flooding the entire body with growth factors.

Estrogen's skin-enhancing effects are well-known (Dunn et al. 1997; Shah et al. 2001). It provokes collagen and a moisture factor known as *hyaluronic acid*. Aging decreases both estrogen and collagen. Enzymes that convert DHEA to estrogen also decline. Not surprisingly, women who take synthetic estrogen have scientifically proven thicker skin. Women who take both estrogen and testosterone have really thick skin (48% thicker than women who don't take either hormone) (Brincaat et al. 1983). DHEA is converted to both estrogen and testosterone, providing the benefits of both hormones.

Although the exact roles of DHEA and melatonin in human skin are still under scrutiny, researchers have identified several mechanisms through which these hormones protect against aging, maintain the health of skin, and affect how sunlight reacts with skin cells.

Skin is such a specialized organ that it has its own immune system. It has been proposed that faulty skin immunity affects the entire immune system. Sunlight can penetrate deep into skin and alter immunity directly, or it can cause changes in dermis and epidermis that provoke immune changes. Sunlight affects hormones. It decreases melatonin, norepinephrine, and acetylcholine, and increases cortisol, serotonin, GABA, and dopamine.

Studies show that both DHEA and melatonin are absorbed by skin when applied topically. A study from CHUL Research Center (in Canada) shows that the activity of DHEA applied topically is 85-90% greater than when taken orally (at least in rodents). No special carriers are needed to get DHEA and melatonin into skin. A properly formulated topical preparation of melatonin and DHEA will contain just enough hormone to benefit skin without providing enough to escape into circulation. It makes sense to apply the hormones directly to the skin if skin protection is the goal, since ingested hormones may end up everywhere but the skin (Labrie et al. 2000).

## **DHEA Saves Skin**

DHEA has beneficial effects beyond its conversion to skin-friendly hormones. DHEA itself has powerful skin protective effects. A study in the *Journal of Surgical Research* demonstrates the extraordinary ability of topically applied DHEA to protect skin's delicate blood vessels. Researchers found that if DHEA was applied after a serious burn, the blood vessels underlying the burned area are protected (Araneo et al. 1995). Protecting the blood vessels saves the skin. Skin and blood vessels that would otherwise die and peel off can be saved by DHEA. No one knows for sure how DHEA saves skin this way, but its anti-inflammatory action no doubt has something to do with it. DHEA prevents destructive white blood cells and their biochemical cousins from gearing up. In particular, DHEA affects a blood vessel killer known as "tumor necrosis factor."

DHEA has action against everyday insults as well. By maintaining skin immunity, DHEA preserves the ability of skin to react to cancer-causing, skin-destroying pollutants in air, food, and water. DHEA also has antioxidant action against peroxy and superoxide free radicals.

Free radical defense may have a lot to do with DHEA's ability to prevent skin cancer and papillomas (benign tumors). According to several studies in mice, topically applied DHEA keeps oxidant-loving enzymes at bay. Chemicals with carcinogenic potential depend on oxidases for transformation. DHEA's antioxidant action stops them (Schwartz et al. 1986a; Schwartz et al. 1986b; Hastings et al. 1988). DHEA has another important defense: It keeps chemical carcinogens from binding to DNA (Pashko et al. 1985; Pashko et al. 1991).

## **Melatonin Protects**

Melatonin is an antioxidant hormone that protects against UV radiation (Fischer et al. 1999). A group at the University of Zurich has shown that topical melatonin gives excellent protection against sunburn if applied before sun exposure (Bangha et al. 1997). Melatonin also appears to have a role in repairing burned skin. In a study in *Brain Research Bulletin*, melatonin levels rose 6 hours after burn injury, then fell to normal (Scott et al. 1986).

In small amounts, melatonin causes skin cells to proliferate. (In large amounts, it stops proliferation.) People with psoriasis and atopic eczema do not have normal melatonin secretion. Instead of peaks, they have valleys. With psoriasis, melatonin peaks in the day when it shouldn't, and patients have little at night. It is surprising that a hormone connected to sleep has a lot to do with skin health, but maybe not to those researchers who consider the pineal gland another endocrine gland. Melatonin is secreted by the pineal gland.

## **Prevention of Skin Aging and Cancer**

It seems reasonable to avoid midday sun when possible and avoid tanning salons. Use protective clothing, hats, and umbrellas during prolonged sun exposure. Apply and reapply sunscreen or use preparations that contain micronized zinc oxide or titanium oxide for more complete protection.

Published research indicates that both children and adults are still spending considerable time in the sun during peak UV exposure periods (Kozarev 1998). A survey conducted on 51 physician volunteers of various specialties showed that 33% spent more than 2 peak UV hours outdoors every day and another 33.33% are regularly sun exposed for at least 5 hours. Only 39% of the survey group regularly used sunscreen and those that did used an inadequate amount for full body protection. A majority of the respondents did not believe that sunscreens protected against skin cancer, but they did believe that sunscreens could slow the aging process. Common reasons for not using sunscreen were the amount of time involved in application and the relative high cost. The researcher concluded that participants lacked well-formed sun protection habits and that there continues to be a poor understanding of the need for sun protection despite worldwide campaigns warning of the dangers.

Use a good sun protection formula containing antioxidant vitamins and sun protection factor (SPF) 15. Vitamins A, C, and E, contained in some formulas, protect skin cells from free radical damage caused by UV light exposure. The formula should be moisture-proof, sweat-resistant, and should be able to be worn under makeup.

Also use a body lotion containing some titanium oxide, glycolic acid (alpha- and beta-hydroxys), vitamin C, and melatonin, which protects against photo-aging of the skin epidermis.

Some products contain minimal sunscreen protection (SPF-12), but contain ingredients such as vitamin C complex, vitamin E, Ceraphyl GA-D, vitamin A, and RNA. These do more to prevent and repair DNA damage than even the strongest sunscreen.

Anti aging creams that contain all the anti aging ingredients (including DHEA and melatonin) to help the skin to repair, renew, and revitalize itself are available. These creams must contain the precise DHEA amounts and melatonin, together with associated factors, that work specifically in the epidermis of the skin, not transdermally. These creams may be used at night or during the day with a sunscreen.

## ***Vitamin A and Skin Tumors***

One of the most disfiguring skin diseases is the appearance of cancer. A study was done to compare the effects of dietary administration of a vitamin A drug (13-cis-retinoic acid) to the natural form of vitamin A (retinyl palmitate). Female mice were administered a chemical carcinogen to evaluate the incidence and severity on mouse skin tumor promotion. The results showed that retinyl palmitate inhibited the number and weight of tumors, whereas 13-cis-retinoic acid resulted in a decrease in weight, but not in number of tumors promoted (Gensler et al. 1987).

In another study, tumors were chemically induced in a group of Swiss mice over a 23-week period. The topical application of 13-cis-retinoic acid was compared to natural vitamin A (retinyl palmitate). This study showed that both retinyl palmitate and 13-cis-retinoic acid inhibited the development of skin papillomas and also had a marked effect on skin cancers (Abdel-Galil et al. 1984). Vitamin A may be one of the better-documented vitamins to protect against several types of human cancers. One of its mechanisms is to induce healthy differentiation and apoptosis of aged cells. The value of vitamin A in protecting the skin is to help facilitate cell renewal and possibly prevent skin cancers.

## **SUMMARY**

Not only is skin the largest organ in the human body, it is arguably one of the most important as well. The age-accelerating effect of UV rays has been documented to the point where protecting the skin against sun exposure is mandatory.

Diet and lifestyle changes can have a potent effect on the appearance and health of the skin. In fact, published findings indicate that one may have more control over the rate at which their skin ages than any other organ of the body. To slow skin aging and partially reverse it, an individual must take a comprehensive approach to gain control over all of the factors that have been identified in the skin degeneration process. Scientific evidence now indicates that, in addition to proper nutrition and health care, the daily application of a variety of agents plays an important role in the preservation and rejuvenation of skin.

Rejuvenex is one such agent. Its scientifically backed ingredients have been shown to limit or reverse the effects of aging or damaged skin. Rejuvenex has been continually upgraded as new findings appear in the scientific literature. With the advent of the QuSome delivery system, it is now possible to concentrate potent doses of alpha lipoic acid, DMAE, RNA, vitamins A, C, E, natural moisturizing factors, and other active agents into the deeper layers of the skin.

By encasing the active ingredients using QuSome technology, Rejuvenex is now able to provide more alpha hydroxy acid to the skin's surface to slough off older unsightly cells, while simultaneously nourishing and protecting living cells in the dermis and lower epidermis.

What follows are different approaches that can help prevent and reverse the effects of aging on the skin:

**Diet:**

1. RNA-rich foods such as sardines, salmon, tuna, shellfish, lentils, and beans help improve cell energy through a "salvage pathway."
2. Antioxidant- and phytochemical-rich foods such as fruits, vegetables, and green tea help protect against oxidative damage and free radical attack of all body cells including the skin.
3. Avoid processed foods whenever possible.



## Skin Aging

### Oral Supplements:

1. Antioxidants such as vitamins A, C, and E; bioflavonoids; and the minerals selenium, zinc, and manganese provide protection against damaging free radicals and help to repair, renew, and revitalize skin. A convenient way of obtaining all of these nutrients is to take 3 tablets 3 times a day of the Life Extension Mix multinutrient formula.
2. Essential fatty acids are required by the skin to maintain a moist youthful appearance. One or more of the following EFAs may be considered:
  - Super GLA/DHA containing high potency gamma linolenic acid (GLA) from borage oil and DHA and EPA from marine lipid extract, three 1000-mg softgels twice daily.
  - Borage oil, one or two 1300-mg softgels daily.
  - Perilla oil, six 1000-mg softgels daily.
  - Flaxseed oil, six 1000-mg softgels daily.

### Topical Agents:

Several antioxidants are beneficial when applied topically to the skin. Look for formulas containing one or more of the following ingredients:

1. Rejuvenex contains ascorbyl palmitate, alpha lipoic acid, DMAE, alpha hydroxy acid, vitamin E, Ceraphyl GA-D, vitamin A, RNA, hylauronic acid, NaPCA, and other active agents. These ingredients are more effective than the strongest sunscreen in prevention and repair of DNA damage. Suggested use is as a day cream.
2. Dream Cream contains the hormones DHEA and melatonin and is most often used as a night cream. The ingredients in Dream Cream work specifically in the epidermis of the skin, not transdermally.
3. Rejuvenex Body Lotion, containing titanium oxide, glycolic acid, vitamin C, and melatonin, protects against photo-aging of the epidermis.
4. Apply and reapply sunscreen or use preparations that contain micronized zinc oxide or titanium oxide for more complete protection. (Use protective clothing, hats, and umbrellas during prolonged sun exposure.)

### Prescription Agents:

1. If skin is dry and flaky, consider a thyroid blood profile to determine if the thyroid gland is producing an adequate amount of hormone.
2. Consider retinoic acid drugs such as Retin-A (tretinoin) and tazarotene to reverse sunlight damage.

### PRODUCT AVAILABILITY

Rejuvenex, Dream Cream, Rejuvenex Body Lotion, Life Extension Mix, Super GLA/DHA, borage oil, flaxseed oil, or perilla oil can be ordered by calling (800) 544-4440 or by ordering online. Retin A, Botox, and tazarotene are prescription drugs.

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