HEALTH AND STRESS

The Newsletter of
The American Institute of Stress

Number 1 January 2009

SURPRISING EFFECTS OF SUN & STRESS ON SKIN & HEALTH

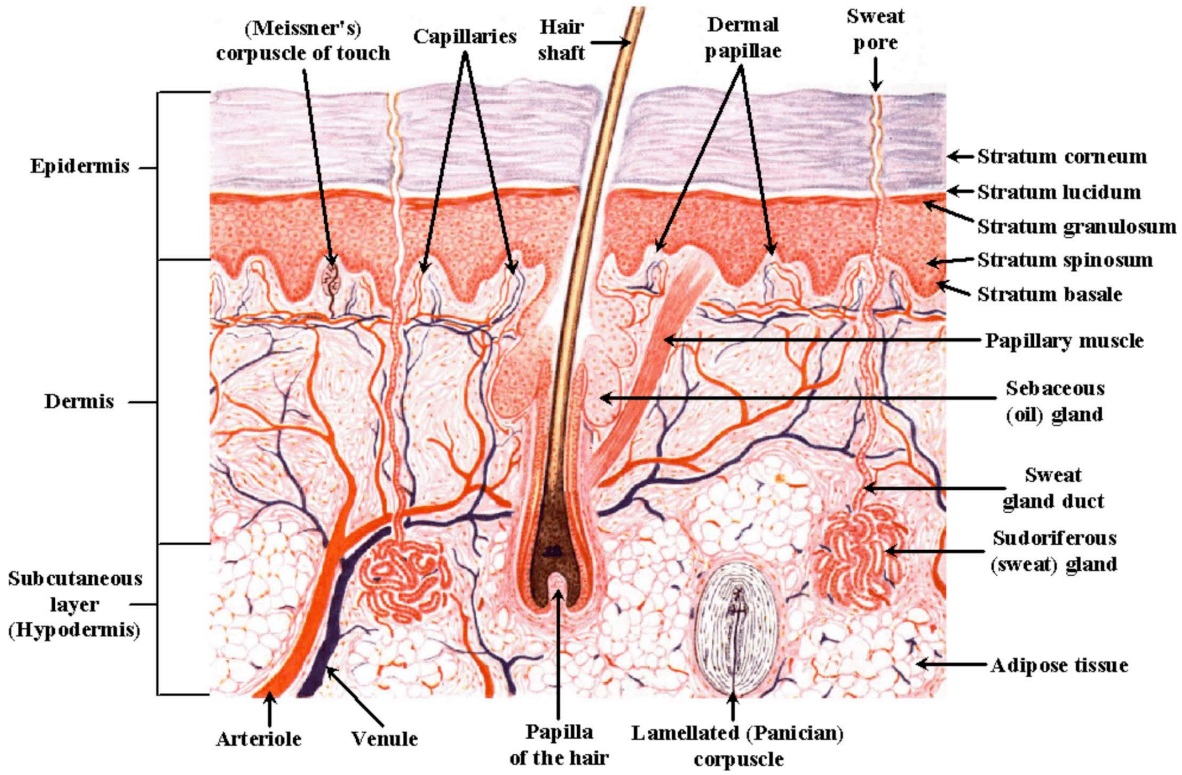
KEYWORDS: Cellulite, UVA, UVB and UVC radiation, cod liver oil, 25-hydroxyvitamin D or 25(OH)D, Vitamin D fortified foods, sunscreen products, sunlight and cancer, statins and vitamin D, antimicrobial peptides, cathelicidin, heart attacks associated with psoriasis and periodontal disease, Selye's General Adaptation Syndrome

The skin is by far the largest organ in the body, and can react to stress in different ways for each us. Some people blush, but others grow pale, perspire profusely, develop rashes, hives, itching, severe neurodermatitis, or hair loss. Stress can also have hormonal and immune system effects that contribute to lupus, psoriasis and other diseases that affect the skin. In addition to providing a protective barrier that shields us from environmental challenges, skin has many other important and frequently unappreciated functions that can have significant effects on health and the quality of life.

Also Included In This Issue

Some are so crucial, that if more than fifty percent of skin is lost or severely damaged due to burns or trauma, your chances for survival are slim. Death becomes almost inevitable when it is no longer possible to control excessive loss of fluids. maintain body temperature within normal limits, or prevent lethal infections from a variety of virulent microorganisms.

Although skin is often viewed as a single organ, it actually consists of three distinct layers with different functions. The translucent epidermal top layer allows light to partially pass through because it has no vascular or other interfering structures. Its nourishment comes from capillaries that project up from the underlying dermis layer that contains arteries and veins, as well as nerves, hair roots and sweat glands. Beneath this, there is a subcutaneous layer with larger blood vessels nerves, as well as fat that is loosely attached to underlying muscles and bones by connective tissue, as illustrated below.



This flexible attachment allows skin to move fairly freely when it is pushed or pinched. However, when this layer fills up with excess fat, the resultant expansion makes the attachment below more rigid and an upward bulge often produces a hard, orange peel appearance called cellulite. What causes cellulite is not clear, but it is much more common in women, especially in the thighs and lower abdomen. In addition to estrogen, stress related hormones like adrenaline and noradrenaline have also been implicated.

As shown above, the epidermis itself has five layers or strata, the top one being the stratum corneum, which is composed mainly of dead cells that have migrated up from the stratum granulosum. As dead stratum corneum cells slough off, they are continually replaced by new cells from the stratum basale below. These cells contain keratin, a protein that helps keep the skin hydrated by preventing evaporation of water. Keratin rich cells can also absorb liquid, which further promotes hydration, and causes the wrinkling seen in fingers and toes that have been immersed in water for prolonged periods of time. This lowest layer of the epidermis is also responsible for the skin's "spring back" and stretching properties.

The sun's light and heat are essential to maintain life on earth, but it also bombards us with invisible ultraviolet rays that can be a mixed blessing. UVA, UVB and UVC rays all have different effects on our skin and health.

UVB radiation is only strong enough to reach the epidermis, where it stimulates the production of vitamin D as well as melanin, a pigment that gives skin its color. UVB is strongest in the summer when the sun is closest to the earth, which explains why it is more difficult to get a suntan in the winter. UVA rays are the same strength every day, regardless of how far away the sun is. Like x-rays, they can penetrate light clothing and windows, and go through the epidermis to the dermis layer, where their dissipation can cause damage due to the production of high-energy free radicals that injure healthy cells. Similarly, if you expose a colored bound book or furniture to the light from a sunny window, the color will start to fade after a few months, or other signs of aging may surface due to UVA exposure. UVC rays have the shortest wavelengths and usually do not reach the earth because they are absorbed by the ozone layer. However, if the ozone layer is depleted or has "holes" in it, even a brief exposure can cause a sunburn.

When UVB radiation strikes the skin, it converts a substance called 7-dehydrocholesterol into vitamin D_3. Most of us make adequate amounts of vitamin D_3 after fairly brief exposure to the sun when the UV index is at least 3. People who are dark skinned, elderly or obese require longer periods of exposure. Abundant UVB radiation is usually received daily in the tropics and on most days during late spring and summer in temperate climates, but not at higher latitudes, and almost never within the arctic circles. When the UV index is 3.5 or above, sufficient amounts of vitamin D_3 can be made in the skin after only ten to fifteen minutes of exposure of the face or extremities twice a week, if no sunscreen is applied. It is impossible to overdose with vitamin D_3 from sunlight, since the supply of 7-dehydrocholesterol in the skin is limited, and takes time to build up again after it is exhausted. **Without any significant exposure to sunlight, most people require around 5,000 units of vitamin D daily.** Unless your consumption of cod liver oil, caviar or lard is high, or you eat oily fish several times a week, **you would need to drink 50 glasses of milk or take over a dozen multi-vitamin capsules daily to prevent vitamin D deficiency**. In contrast, the skin produces approximately 20,000 IU of vitamin D in response to 20–30 minutes of exposure to the summer sun. That's 100 times more than the US government's recommendation of 200 IU per day. Fish oil supplements have become popular because of the numerous health benefits of omega-3 polyunsaturated fatty acids that mimic the rewards of eating oily fish. However, these supplements do not provide the significant amounts of vitamin D that is found in cod liver oil, because vitamin D is concentrated in the liver and other fish oils are usually made from the rest of the fish.

There are different tests to determine if you need more Vitamin D, but as will be seen, the most accurate is measuring 25-hydroxyvitamin D or

25(OH)D blood levels. Although 20-50 ng/ml is considered normal, most authorities now believe that 50-65 ng/ml is optimal, concentrations should never be below 32 ng/ml, and anything under 20 ng/ml indicates a severe deficiency. Age adjusted blood levels of vitamin D are significantly lower now than they were a decade ago, possibly because of increased use of sunscreen products to prevent skin cancer and rising rates of obesity. Another factor is decreased intake of vitamin D fortified milk and dairy products because of the erroneous belief this will lower cholesterol and prevent heart attacks.

As a result, **most of us do not meet either dietary or UVB skin conversion needs for vitamin D. The late winter average in the U.S. for vitamin D is only 15-18 ng/ml and it is estimated that 85 percent of the public are deficient. This jumps to over 95 percent for senior citizens.** African Americans and other dark-skinned people, as well as those living in northern latitudes, make less vitamin D, and one study showed that almost half of African American women of childbearing age were vitamin D deficient. Another report on healthy adolescents revealed that one in four were vitamin D deficient and 42 percent had levels below normal. In a group of women with osteoporosis hospitalized for hip fractures, 50 percent were also vitamin D deficient. Daily supplements of 800 IU have been shown to reduce osteoporotic fractures in elderly people with low vitamin D levels. All that most physicians learned in medical school was that vitamin D deficiency caused rickets in children and osteomalacia in adults, which results in weak muscles as well as bones. However, we now know that vitamin D also has important hormonal effects that influence the nervous system, immune function, renin-angiotensin system, insulin secretion, skin function, regulation of cell growth and the activation of numerous genes. As will also be seen, recent research has implicated vitamin D deficiency in heart disease, stroke, hypertension, autoimmune diseases like rheumatoid arthritis and psoriasis, diabetes, depression, chronic pain, muscle weakness and atrophy, osteoarthritis, osteoporosis, birth defects, periodontal disease, and well over a dozen types of cancer. Most of these appear to be related to insufficient vitamin D_3 production in the skin due to less sun exposure and/or other factors previously noted that interfere with this conversion process.

Vitamin D's Unbelievable Ability To Prevent Disease And Preserve Health

In a recent *Archives of Internal Medicine* article, researchers measured vitamin D in over 13,000 people in their forties and followed them for nine years. They were separated into four groups based on their vitamin D levels. Those in the lowest quartile, whose vitamin D was less than 17.8 ng/ml were 26 percent more likely to die over this period from any cause, compared to those in the top quartile. There are well over two dozen diseases that have been linked with a lack of vitamin D or have been shown

to improve with appropriate vitamin D supplementation. A few of the most important, some of which may be surprising, include:

1. **Coronary Heart Disease** – several studies have now shown that **people with low vitamin D are twice as likely to have a heart attack or die from cardiovascular disease as those with normal values.** In addition, a clear correlation has been found with the degree of deficiency and the incidence of coronary events or deaths. In Europe, heart disease deaths are higher in northern compared to southern countries, and are lowest along the Mediterranean, where sun exposure tends to be the greatest. In the U.S, the higher the altitude of residence, and hence the higher the intensity of sunlight, the lower the risk of heart disease. Other studies have also shown spikes in heart disease-related deaths at higher latitudes and during the winter months when there is less daylight, with decreases in cardiac deaths at lower latitudes and during the summer. The only dietary change that consistently protects against this is a significant consumption of oily fish that contain large amounts of vitamin D. In the Netherlands, heart disease mortality was more than 50 percent lower in men who consumed at least 30 grams of fish daily. A similar result was reported in a 16-year study in U.S. women. Researchers believe that the cardioprotection of vitamin D_3 produced by sun exposure may be due to the inhibition of vascular smooth muscle growth, suppression of calcification in blood vessels and by increasing the immune system's anti-inflammatory responses.

2. **Hypertension and Stroke–** some of these observations may also explain the correlation between vitamin D deficiency and hypertension, a leading cause of stroke. The further one moves from the equator, the greater the likelihood of high blood pressure and lower vitamin D levels. Some studies show that exposure to ultraviolet rays can increase endorphins, which lower elevated blood pressure and provide pain relief and a sense of euphoria. Decreased vitamin D also stimulates the production of parathyroid hormone, which elevates blood pressure. In addition, vitamin D inhibits renin-angiotensin-aldosterone mechanisms known to cause hypertension.

3. **Cancer** – living farther away from the equator also increases your risk of dying from cancer. The risk of breast cancer and colon cancer is much higher in northwest Europe than for Mediterranean countries. More people in the north of the UK die from or do not live as long after being diagnosed with cancer of the stomach, bladder or colon compared to the south. On the other side of the pond, cancer death rates in the U.S. and Canada were two and a half times higher among

residents of the most northern cities compared to those in the most southern. An extensive study of 5000 U.S. cities found that cancer rates were lowest where ultraviolet exposure is greatest and that bladder, breast, colon, kidney, esophageal, ovarian, prostate, rectal, stomach and uterine cancers, as well as non-Hodgkin lymphoma were associated with low exposure to UVB radiation. The incidence of prostate cancer in the U.S. increases with distance from the equator, and is greater in the eastern states compared to western states that have a higher altitude, which also supports the protective effect of sunlight. In Iceland, the cancer incidence is 90 per 100,000 people/year, compared to only 25 per 100,000 for those living in the tropics. According to Dr. William Grant, an internationally recognized vitamin D authority, **about 30 percent of cancer deaths (2 million worldwide) could be prevented each year with higher levels of vitamin D_3**. With respect to the U.S., there would be up to 200,000 fewer cancer deaths annually, since the majority are due to vitamin D sensitive malignancies. Other researchers estimate that 250,000 cases of colorectal cancer and 350,000 cases of breast cancer could be prevented each year by increasing intake of vitamin D3, particularly in countries north of the equator. In one study of U.S. postmenopausal women who started taking vitamin D and calcium daily to prevent osteoporosis, the risk of developing cancer was reduced by 60 percent compared with a placebo over the next four years.

Another intriguing observation is that patients live longer when their cancer is diagnosed and treated in the summer, compared to the winter, whether it be cancer of the breast, colon, prostate, lung, or a lymphoma. That this is related to greater vitamin D production is supported by a Harvard study to determine whether high vitamin D from sunlight and diet improved survival in early stage lung cancer. The survival rate was 29% in those who took no vitamin D supplements and had treatment in the winter, compared with 72% in those who did take vitamin D supplements and were treated in the summer. In another study, malignant melanoma patients who experienced continued sun exposure, were 60 percent less likely to die, compared to controls that avoided the sun. US prostate cancer rates increase with distance from the equator, and are greater in eastern states compared to western states that have a higher altitude and are closer to the sun. An interventional trial also showed that vitamin D reduced PSA levels in patients with cancer of the prostate. **More importantly, just increasing baseline vitamin D levels from 29 ng/ml to 38 ng/ml with 1,100 units daily resulted in a 60-percent reduction in all internal cancers**. It appears likely that higher doses or other approaches to increase vitamin D blood levels

could achieve an even greater reduction. A link has been reported between vitamin D and seventeen different malignancies either with respect to deficiency as a cause, or the beneficial effects of supplementation. Vitamin D is believed to protect against cancer through various mechanisms, including:

- increasing the self-destruction of mutated cells, which if allowed to replicate, could result in cancer
- reducing the reproduction and spread of cancer cells
- causing cells to become more differentiated as opposed to malignant cells that lack differentiation
- reducing the growth of new blood vessels that are required to supply nutrition to rapidly growing malignancies. This is a crucial step in the transition from dormant precancerous cells to active cancer.

4. **Depression** – Seasonal Affective Disorder, appropriately known as SAD syndrome, refers to the depression often seen during the winter months when there is less sunlight. Exposure to bright light therapy for an hour after waking up relieves or significantly reduces symptoms in SAD syndrome, as well as other types of depression, such as that seen in pregnancy. Research reports reveal links between low vitamin D and depression in older adults that improves after administering vitamin D supplements. A study of overweight people, who tend to have low vitamin D levels, similarly found that taking vitamin D supplements for a year significantly improved their mood.

5. **Autoimmune Diseases** – multiple sclerosis, Type 1 diabetes, rheumatoid arthritis, psoriasis and other autoimmune diseases are more prevalent in patients with lower levels of vitamin D. Vitamin D supplements have been shown to benefit many of these patients. Multiple sclerosis is almost nonexistent at the equator and increases with the latitude gradient in both hemispheres, with the world's highest incidence being reported in Scotland. According to one report, regular vitamin D supplementation may reduce the risk of developing multiple sclerosis by at least a third. Rheumatoid arthritis, another autoimmune disease, can show dramatic responses to vitamin D. **In one study of 19 patients who received such supplements, nine reported a complete remission of symptoms and eight had a satisfactory response.** There was also a reduction in disease activity and markers of inflammation, with a 43 percent fall in the sedimentation rate and a 52 percent drop in C-reactive protein. In another study of women with rheumatoid arthritis, 16 percent had low vitamin D levels compared to controls. However, during the winter, 73

percent were below seasonally adjusted levels, and the lowest levels were in those with the most active disease.

6. **Infections** – one of the genes that vitamin D stimulates is responsible for producing over 200 antimicrobial peptides made in the body that fight infections. A recent review presented evidence that flu epidemics, and perhaps even the common cold, are brought on by winter deficiencies in antimicrobial peptides like cathelicidin, that is found in white cells and phagocytes. Vitamin D increases the production of cathelicidin, and low levels of both may explain why colds and influenza are much more common during winter months when there is less sunlight. Support for such a relationship comes from a study showing that **2,000 IU of vitamin D/day for one year virtually eliminated self-reported incidence of colds and influenza**.

7. **Osteoporosis and Fractures** – these are particular problems in the elderly, especially those in northern climates who are housebound or confined in convalescent or nursing homes. Vitamin D deficiency also weakens muscles, which makes falls more likely in older people. Studies in senior citizens show that vitamin D and calcium increase bone density and reduce the likelihood of falls and fractures.

8. **Diabetes** - the international incidence of Type 1 diabetes in children also increases with distance from the equator, again suggesting the protective effect of sunlight and vitamin D production. Children of women who took cod liver oil during pregnancy had lower rates of Type 1 diabetes compared to controls who did not. A retrospective Finnish study of 821 children born in 1966 found that **the incidence of diabetes in adulthood was almost ten times lower in those who took vitamin D supplements in childhood** than those who did not. A large Norwegian study showed that taking cod liver oil regularly during the first year of life greatly lowered the risk of Type 1 diabetes.

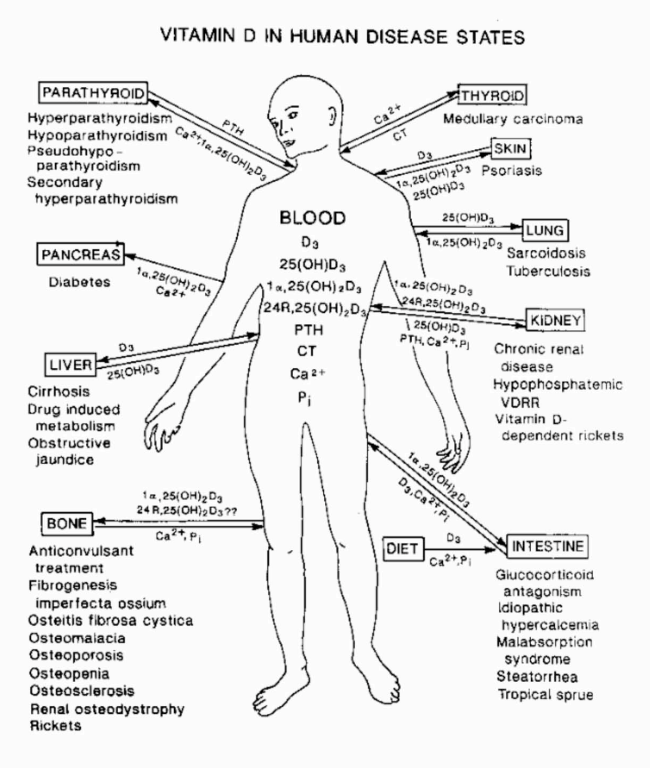
Many also believe that vitamin D deficiency may be responsible for the epidemics of autism, asthma, and Type 1 diabetes now being seen in children and adolescents. All of these growing problems started to surface after medical advice to avoid the sun and/or to use sunscreen during pregnancy and early childhood. In addition to the above, low vitamin D has been linked to inflammatory bowel disease, ulcerative colitis, osteoporosis, periodontal disease, cavities, myopia, macular degeneration, insomnia, cystic fibrosis, migraine, schizophrenia, muscle weakness, chronic pain, and Alzheimer's disease. These claims for such a wide variety of diseases may seem incredible. However, they are quite plausible when one considers that vitamin D provides the substrate for numerous diverse repair functions, and

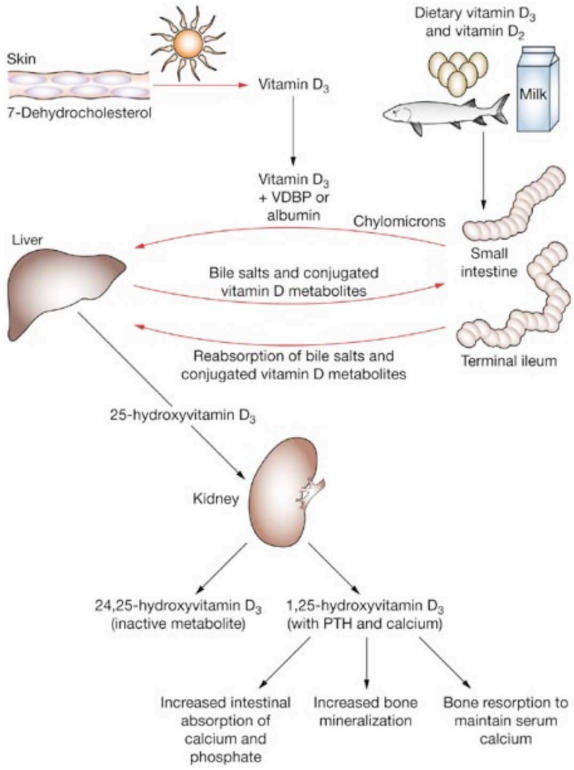
also affects several hundred genes with different actions. Whether these are cause and effect relationships or simply statistical associations remains to be proved. This will necessitate demonstrating that vitamin D supplementation that boosts blood concentration to optimal levels for each of these diseases can prevent or significantly improve them.

How Much Vitamin D Should You Take And What Blood Level Is Optimal?

These are tough questions, since nobody really knows all the answers. It is likely that Vitamin D requirements vary with different diseases, age, race, and other factors. Strong support for a causal relationship comes from a meta-analysis of 18 randomized controlled trials, which found that **vitamin D supplementation significantly reduced mortality from all causes**. This discovery is remarkable, since despite the low average 528 IU dose of vitamin D and the short duration of these trials, mortality was reduced by seven percent. It has recently been discovered that statins can mimic certain vitamin D effects and/or increase vitamin D blood levels. This raises the possibility that many statin benefits may be mediated via such activities, especially for diseases in which lowering cholesterol or LDL is obviously irrelevant. However, cholesterol is essential for making vitamin D, which illustrates how complex and confusing tracing these interactions can be.

Most authorities agree that the recommended daily allowance of 200 IU of vitamin D for most people established well over a half century ago need to be increased based on the low blood levels that are so prevalent. This is a particular problem in older individuals even though it is now recommended that they take twice as much or more. The best way to determine if you need vitamin D is to determine the blood levels of 25(OH)D (25-hydroxyvitamin D). As previously noted, although 20-50 ng/l is considered normal, this also needs to be upgraded based on recent research. Values below 50 are now considered insufficient, 50-65 is optimal and cancer patients should probably be in the 65-90 range. Concentrations over 100ng/L are excessive and could be toxic. There are numerous diseases that have been linked to low vitamin D or have been shown to improve with appropriate vitamin D supplementation as illustrated below. Vitamin D requirements vary with these different disorders, age, and other factors. More is not always necessarily better and it is important to distinguish between physiologic and pharmacologic effects. The physiologic amount of vitamin C needed to prevent scurvy is less than 60 mg/day, but more is required in smokers and pregnant women, and because of its antioxidant and other benefits, some advocate taking hundreds and thousands times more than this. Although such megadoses do not appear harmful, this is not true for vitamin D, and excess supplementation could lead to vitamin D toxicity, which can have serious consequences if not detected early.





Vitamin D therapy is further complicated because there are different types of supplements and various forms of vitamin D in blood and tissues. Vitamin D metabolism is also affected by the liver, kidney, bone, parathyroid, thyroid and other organ activities, as well as absorption in the small intestine, as illustrated above. Most 25(OH)D in the blood is bound to protein and only small amounts are "free" to enter tissues. In addition, the half life of 25(OH)D in the circulation is about 2-3 weeks, as compared to 12-14 hours for 1,25(OH_2)D (calcitrol), the most active form of vitamin D, which works with parathyroid hormone to maintain calcium balance. That is why 25(OH)D is the best indicator of nutritional vitamin D status as well as a red flag to warn of possible toxicity. Excess doses of vitamin C are not likely to be toxic since its half life is only 30 seconds. The dangers of vitamin D toxicity are due to increased blood calcium, but you would have to take over 30,000 IU daily for several weeks because of compensatory mechanisms that prevent this. Vitamin D_3 is the preferred supplement and 10,000 IU daily appears to be perfectly safe.

Psychodermatology, Stress, Psoriasis, Pustular Acne And Rosacea

In addition to sun, wind, temperature, humidity, repetitive trauma and other physical stressors, emotional and mental factors can affect the skin in different ways. Conversely, some skin diseases and complaints are significant sources of stress. As a result, there has been growing interest in the emerging field of Psychodermatology, which focuses on these diverse mind and skin interrelationships. Most psychodermatologic disorders fall under one or more of the following four categories:

1. Psychophysiologic disorders, in which skin diseases like acne, eczema, hives and psoriasis are triggered or worsened by emotional stress.
2. Primary psychiatric disorders, in which there is no primary skin disease but rather a psychological problem. Such lesions are usually self-induced, as in trichotillomania, (compulsive plucking of hair from the scalp or face and often eating it), or delusions of parasitic infestations.
3. Secondary psychiatric disorders, where patients develop emotional problems as a result of having a skin disease where disfiguring lesions are very visible and cannot be concealed. This is not uncommon in severe psoriasis and widespread vitiligo that involves the face.
4. Cutaneous sensory disorders, in which the patient presents with a purely sensory complaint, such as a burning sensation in the groin, but there is no evidence of any dermatologic disease or underlying medical disorder.

Psoriasis is a very fertile field for psychodermatologists, since the majority of patients report that attacks are precipitated and/or aggravated by emotional disturbances, usually within a few days. Conversely, psoriasis can also be a source of severe stress when ugly lesions affect appearance or become extremely itchy, which can lead to a vicious itch➞scratch➞itch➞scratch self-repeating cycle. The word "psoriasis" is actually derived from *psor*, which is Greek for itching. Many patients become frustrated and depressed because there is no cure for either itching or psoriasis. What causes itching is not clear, but there is some evidence to support the belief that it involves an inappropriate response of the immune system that may be activated or exaggerated by stress. Since the skin is often the first line of defense against infections, it can be a battleground where white blood cells attack invading bacteria and viruses. When immune cells that join the fray overreact, there is an increased inflammatory response that can lead to psoriasis and other dermatologic diseases.

Some researchers suspect that stress makes things worse by increasing the number of immune cells in the skin. To test this theory, they subjected mice to stress and confirmed that more immune system white blood cells started to appear in the skin. As they also reported in the November issue of the *American Journal of Pathology*, when they blocked the function of two proteins called LFA-1 and ICAM-1 that attract these cells to the skin, there was no increased inflammation or white cell production in response to stress. As previously noted, the stratum corneum continuously sloughs off and must be regenerated from cells in lower epidermal layers that are constantly proliferating to form a new outer layer. Emotional stress accelerates this process, and the piling up of these excess cells is responsible for the scaling and inflammation that results in the unsightly lesions seen in psoriasis.

Researchers have shown that this piling up is due to the stress hormone cortisol, by demonstrating that it does not occur if either cortisol production or its activities are blocked. They are now investigating whether stress reduces the skin's production of antimicrobial peptides, which might help to explain the beneficial effects of vitamin D3, sunlight, exposure to ultraviolet light and stress reduction in psoriasis. Others suggest that stress contributes to psoriasis, pustular acne and rosacea by interfering with the permeability barrier of skin, which increases inflammation. Stress induced cortisol makes sebaceous glands produce more oil that blocks the pores. That is why stress causes flare-ups in acne that result in inflamed, pus filled papules, rather than simple whiteheads or blackheads. Rosacea is a disease characterized by excessive redness and bumps on the face, and 95 percent of episodes in women are triggered by some emotional disturbance. Pustular acne and rosacea have also been linked to vitamin D deficiency and although sunlight can cause rosacea flare-ups, vitamin D_3 supplements have been shown to provide significant benefits in both of these skin diseases.

These observations raise intriguing questions about stress, vitamin D, skin and health. If stress causes the inflammation and itching of psoriasis and neurodermatitis by increasing the production of cortisol, then why are cortisol creams and systemic steroids effective in treating these complaints? Patients with psoriasis are at greater risk for heart attacks, especially those who are younger and/or have more severe disease. Patients under 50 have an increased risk comparable to diabetics. Psoriatic arthritis is another common complication. Periodontal disease is also linked with a significantly increased risk of heart disease. Could inflammation due to vitamin D deficiency explain all these associations? Increased inflammation has been cited as the cause of heart attacks, arthritis and other stress related disorders, despite the fact that cortisol has powerful anti-inflammatory effects. Is this paradox explained by Selye's General Adaptation Syndrome? For some answers to this and other puzzling questions, — stay tuned!!

Paul J. Rosch, MD, FACP
Editor-in-Chief

Health and Stress
The Newsletter of
The American Institute of Stress
124 Park Avenue Yonkers, NY 10703

ANNUAL SUBSCRIPTION RATE:

E-Mail……$25.00

ISSN#108-148X

PAUL J. ROSCH, M.D., F.A.C.P.
EDITOR-IN-CHIEF
www.stress.org
e-mail: stress124@optonline.net