SKIN DISORDERS

What is the largest organ in the body? Most people think it's the liver on even the intestine, but in fact it's the skin. Besides providing a protective barrier against the environment, the skin performs a large number of important functions, endocrinological, thermoregulatory, immunological, toxicological and circulatory.

The skin can host a huge variety of diseases and disorders and about one third of North Americas will experience some sort of skin problem. Skin disorders also affect patients differently, especially in their psychological reaction to the disease. Firstly, the fact that they can actually see the problem makes it hard to forget; secondly they are often nervous about the actual or perceived reaction of others, and the social or interpersonal consequences.

GSH AND SKIN DISEASE

Given the number of functions served by the skin, it is no surprise that glutathione is involved in many skin problems. The role of GSH in detoxification and prevention of radiation damage in other tissues is well-known. It plays just as vital a role here. Low levels of GSH have been documented in many types of skin disease, including:

Psoriasis
Eczema
Vasculitis
Mycosis fungoides
Polymyositis
Scleroderma
SLE (lupus)
Atopic dermatitis
Seborrheic dermatitis
Contact dermatitis
Dermatitis herpetiformis
Pemphigoid
Acne conglobata
Acne vulgaris

In this chapter we will focus on psoriasis, dermatitis and ultra-violet radiation damage.

PSORIASIS

Psoriasis is a common, chronic recurrent skin condition characterized by scaly white or red patches of skin on the legs, knees, arms, elbows, ears, scalp or back. The rash may consist of one or two inconspicuous small patches or cover the whole body. This can affect the joints and occasionally even lead to disabling arthritis. However, such extreme cases are rare and general health for most psoriatic patients is good. Lesions are typified by an overgrowth of skin cells which multiply up to ten times faster than normal skin cells. This overgrowth continues and leads to the classic raised, silvery, flaky appearance of the condition.

The actual cause of psoriasis remains unknown. It may be triggered by different factors in different people. Fair-skinned individuals in particular may have a genetic predisposition to it. It certainly has something to do with the immune response itself. Attacks or flare-ups can be triggered by emotional or physical stress, illness, injury, infection, drug and alcohol abuse, obesity, and many different chemicals. The other chapters of this book describe the critical role of glutathione in many of these processes.

One source of relief for psoriatic patients is travel to a healing environment. The Dead Sea in Israel is particularly popular. A medical facility – The Dead-Sea Psoriasis Treatment Center – has been set up specifically for this purpose. Researchers have tried to understand why this particular area seems to help. High levels of sunlight seem to affect psoriasis positively. Most interestingly, the drinking water in the area is very high in selenium. A local research team explains that the best indicator of selenium bioactivity is patients' glutathione peroxidase levels. Compared to a control group and to their own initial GSH levels, patients spending weeks in this treatment center increased GSH peroxidase levels, often as much as 50%.

Psoriasis patients suffer from abnormal glutathione enzyme activities, and researchers have inked the disease to high levels of free radicals. Lowered GSH activity results in greater damage. The clinical results of raising GSH in this disease are promising and more studies are underway.

CASE STUDY

Roland is a 44 year-old energetic and sociable business entrepreneur who suffered from psoriasis for ten years. Itchy, scaly eruptions often covered his entire body, and aggressive scratching led to bleeding and scabbing. His dermatologist tried many different treatments including strong topical corticosteroids and methotrexate tablets, which he had to discontinue due to side-effects. Ultraviolet light therapy was suggested, but having the financial means, Roland preferred frequent trips to Mexico and the Caribbean to sitting in artificial light. Having done significant homework on his condition, he concluded that the psoriasis was caused by an immune dysfunction. He started taking 40 grams/day of Immunocal to raise his glutathione levels. Within two weeks he was free of bleeding and scabs and described his scaling as 75% improved.

DERMATITIS

Dermatitis is a general term meaning inflammation of the skin. It is caused by a wide range of different ailments. Toxins or irritants can lead to contact dermatitis. Allergies can lead to allergic or atopic dermatitis. Many intestinal or immunological diseases can lead to such forms as dermatitis herpetiformis. Overproduction of oils in the skin can lead to Seborrheic dermatitis. Dermatitis can be triggered by stress or illness. Overly hot, dry, cold or wet environments also promote dermatitis. All are characterized by red itchy skin and in extreme cases blistering, crusty or oozing lesions. Almost all of these conditions have been linked to abnormal glutathione activity.

In both irritant contact dermatitis and allergic contact dermatitis, glutathione levels fall both in the skin and the whole body. A group of Japanese dermatologists inhibited GSH production with BSO. They found that both allergic and irritant contact dermatitis rashes were subsequently more severe. They link this both to the detoxification abilities of GSH, and to the effect of GSH on the immune system.

Several research teams have shown that GSH-precursors help the immune system respond to contact sensitivity. A Swedish team using the GSH enhancing drugs NAC

and DiNAC demonstrated significant results with contact and delayed-hypersensitivity reactions. G. Senaldi of the University of Geneva successfully used both topical and oral NAC to experimentally treat contact and irritant dermatitis. His team suggested that a similar approach may benefit cancer patients suffering from skin inflammation secondary to TNF-alpha (tumor necrosis factor-alpha), an inflammatory side-effect of cancer.

Contact dermatitis often arises from the use of cosmetics, including make-up, skin creams, eyeliners and other products. One particular culprit is a group of preservatives/sanitizers known as MCI-MI (methyl-chloro-isothiazolinone/methyl-isothiolinone). A group of Swedish occupational and environmental dermatologists found that the addition of as little as 2% GSH to these emollients deactivates the MCI/MI.

Thimerosol is another popular preservative used in toiletries, including contact lens solutions. It is known to cause skin and eye reactions, probably because of its organomercury content. At Rome's Dermatological Institute, B. Santucci showed that adding I-cysteine or glutathione to solutions containing Thimerosol reduced or prevented reactions to this chemical.

AIDS patients are more prone to skin disease than others. These conditions include Karposi's sarcoma, Seborrheic dermatitis and others. As we discussed in chapter 12, most AIDS patients are glutathione-deficient, a factor that contributes to these skin conditions. S. Passi and A. Morrone in Italy and other teams have shown a deficiency of glutathione peroxidase activity both in HIV-positive patients and in otherwise healthy individuals with Seborrheic dermatitis.

An interesting experiment was carried out at the Welsh School of Pharmacy. They examined the dermatitis-inducing chemicals of plants such as poison ivy and poison oak and found that most inflammation was due to free radicals. Using the GSH-precursor OTZ they were able to reduce the irritation and sensitizing effect of these noxious compounds.

SUN AND ULTRAVIOLET RADIATION SKIN DAMAGE

By far the most common cause of abnormal aging, wrinkling and cancer of the skin is sun exposure and ultraviolet radiation. We may pay later in life for the 'healthy' bronzed glow of our youth. The skin-aging consequences of tanning lead many people to plastic surgery. But most facelifts would be unnecessary if these patients had avoided tanning when they were younger. Many skin cancers that appear in adult life may actually be initiated by severe sunburn as a child.

The well-known ozone layer in the atmosphere blunts the damaging effects of ultraviolet. A and B radiation found in sunlight. The ozone depletion which has so concerned scientists in recent years has already increased the number of skin cancer patients. We may yet witness an even more dramatic increase in the years to come. Physicians are treating sunburn in more and more patients who claim they have never before been so dramatically affected by sun exposure.

Radiation releases high levels of hydroxyl-radicals in the skin. These are the most toxic free radicals known to man. Such radiation comes from sunlight UV-A and UV-B, sun lamps, radiotherapy treatment and X-rays. The damaging radicals are normally neutralized by glutathione, but overexposure overwhelms this protective system and GSH levels can fall, resulting in even more damage. For this reason, doctors have considered using antioxidant supplementation to protect the skin. Studies using various antioxidants have had mixed results. Research into elevated GSH levels has been much more encouraging.

P. Baas and his team at The Netherlands Cancer Institute used halogen lamps to sensitize their patients to light, and showed that sensitivity decreased when the patients were pretreated with NAC to raise glutathione levels. Another Dutch team at the Department of Medicinal Photochemistry, Leiden University looked at various oral and topical products and their capacity to decrease UV skin damage. They found that NAC, whether ingested or applied to the skin was a practical means of protecting from UV-B radiation damage.

French researchers at Joseph Fourier University in Grenoble examined how effectively various GSH precursors could limit UV-A radiation damage. These products included NAC, OTZ, CIT, and selenium. Most are described in detail in chapter 4. To various degrees, all GSH-enhancing substances inhibited the deleterious effects of UV-A radiation. The researchers conclude that elevated GSH levels protect against UV-A damage.

Similar studies at Harvard University and Hirosaki University in Japan investigated the way UV-B radiation causes sunburn. Using animal subjects they first showed that glutathione depletion resulted in significantly greater sunburn damage. Further studies with orally administered esterified glutathione raised GSH levels and resulted in less damage. Other Japanese experiments using higher doses of UV-radiation on their animals showed that pre-treatment with glutathione esters could actually decrease the number of skin tumors that developed much later on.

A German team at the University of Berlin studied the effect of UV-B damage on people with an inherited defect in a glutathione enzyme called GSH S-transferase. The GSH-impaired group suffered significantly more intense damage than the control group, so it seems that inherited GSH-transferase deficiencies determine how sensitive an individual is to sunlight.

UV-B exposure not only damages skin, at high doses it can affect the immune system itself by suppressing the local and general functioning of T-cell lymphocytes. Substances that deplete GSH levels decrease this response even more, and substances that elevate glutathione levels protect it. D.P. Steenvoorden and his team at the Amsterdam Center for Drug Research used BSO to lower glutathione levels and NAC or GSH-esters to raise them, demonstrating that elevated GSH levels provide protection against UV-B immunosuppression.

CASE STUDY

The 61 year-old Canadian Charles loved boating. His dream was to retire and spend most of his time on the water, traveling the coasts. Tall, handsome and fair-skinned, he was unfortunately prone to sunburn. Despite sunscreens and hats, being on the water often left him unprotected and his complexion grew ruddy and inflamed. His physician was worried about the possible development of pre-cancerous sun-induced lesions on his face. Charles had already started taking Immunocal for a potential prostate problem. After several weeks he noticed that his tendency to burn was significantly decreased, despite some "accidental" exposures. In two months his in-the-sun complexion was no longer so different from his winter complexion.

CONCLUSION

Low glutathione levels characterize many skin diseases. Practical applications with GSH-raising substances have been studied in the treatment of several diseases. There has been success in some but not all cases of psoriasis. This may reflect the multiple and various causes of this disease. Many of the diseases that fall under the very general definition of dermatitis may be positively affected by raised glutathione levels. GSH is of extreme imp9ortance as a protective agent against ultraviolet radiation of the sun.

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