

Review Article

Skin changes in “screen dermatitis” versus classical UV- and ionizing irradiation-related damage – similarities and differences

Two neuroscientists’ speculative review

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Abstract: An increasing number of persons say that they get cutaneous problems as well as symptoms from certain internal organs, such as the central nervous system (CNS) and the heart, when being close to electric equipment. A major group of these patients are the users of video display terminals (VDTs), who claim to have subjective and objective skin- and mucosa-related symptoms, such as pain, itch, heat sensation, erythema, papules, and pustules. The CNS symptoms are, e.g. dizziness, tiredness, and headache. Erythema, itch, heat sensation, edema and pain are also common symptoms of sunburn (UV dermatitis). Alterations have been observed in cell populations of the skin of patients suffering from so-called “screen dermatitis” similar to those observed in the skin damaged due to ultraviolet (UV) light or ionizing radiation. In “screen dermatitis” patients a much higher number of mast cells have been observed. It is known that UVB irradiation induces mast cell degranulation and release of $\text{TNF-}\alpha$. The high number of mast cells present in the “screen dermatitis” patients and the possible release of specific substances, such as histamine, may explain their clinical symptoms of itch, pain, edema and erythema. The most remarkable change among cutaneous cells, after exposure with the above-mentioned irradiation sources, is the disappearance of the Langerhans’ cells. This change has also been observed in “screen dermatitis” patients, again pointing to a common cellular and molecular basis. The results of this literature study demonstrate that highly similar changes exist in the skin of “screen dermatitis” patients, as regards the clinical manifestations as well as alterations in the cell populations, and in skin damaged by UV light or ionizing radiation.

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Key words: “screen dermatitis” – “electrosensitivity” – visual display terminal (VDT) – ultraviolet (UV) light – grenz rays – ionizing irradiation – antigen-presenting cells – mast cells – dendritic cells – human skin

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Introduction

Today’s public discussion about the health effects of electromagnetic fields (EMFs) deals with certain major issues, such as the relationship between EMF and different cancer forms, e.g. leukemia (especially children’s leukemia), brain tumours, pituitary tumours and male breast cancer, neurological diseases, e.g. Alzheimer’s senile dementia, Parkinson’s disease and multiple sclerosis, asthma and allergy, affections of EMFs on fertility, pregnancy

and foetal development, and the phenomenon “electrosensitivity” or “screen dermatitis”.

The first public reports of skin complaints in people exposed to VDTs came from Norway and USA in the late seventies and in the beginning of the eighties. Since then the phenomenon has increased and it has been described in several countries (1). Patients claim to have subjective and objective skin- and mucosa-related symptoms, such as pain, itch, heat sensation, erythema, papules, pustules, etc. (2). Even symptoms from internal or-

gan systems, such as the heart and the central nervous system, have been reported (3). Hypersensitivity, allergy, Pavlovian-type conditioning, phobias and "techno-stress" are terms circulating in the discussion around so-called "screen dermatitis" or "electrosensitivity". Hypersensitivity may be a better term to explain this phenomenon, including a large number of symptoms that cannot be explained in the same way as allergy, but which increases strongly these days in our society. Clinical dermatologists often describe these patients as suffering from earlier acknowledged skin diseases and they have regarded the symptoms to be mostly of a rosacea or rosacea-like dermatitis nature (2). So far, however, very little is known about the cause of these health complaints and further investigations are needed.

It is well known that extensive radiation from ultraviolet (UV) light and ionizing irradiation, including X-rays, can be extremely harmful and induce severe skin damages. The role of UV light in skin cancer induction in humans was recognized already in the late 1800s (4), and the role of UV radiation in causing sunburn and premature aging of the skin is now well established. It is also known that ionizing irradiation at sufficiently high doses causes skin cancers in humans. The major source of risk factors for the induction of skin cancers by ionizing radiation comes from the experience of those therapeutically exposed to X-rays for the treatment of tinea capitis (5, 6).

Björn Lagerholm, a Swedish dermatologist previously at the Karolinska Hospital in Stockholm, early described cutaneous changes in "screen dermatitis" patients which he indicated to be similar to skin changes seen after UV light and/or ionizing irradiation. However, his data have never been fully published or acknowledged.

The aim of the present literature study was to compare classical skin damages due to UV-light and ionizing radiation, including X-rays, with the cutaneous manifestations seen in so-called "screen dermatitis" in order to elucidate possible similarities and/or differences. Special emphasis has been put on mast cells and dendritic cells. Our text should be regarded as being a speculative attempt to review a new and highly interesting field of the public health panorama.

Material and methods

Literature from 1955 until 1996 concerning damages due to UV-light, ionizing radiation (including X-rays), as well as cutaneous manifestations seen in "screen dermatitis" or "electrosensitivity" was selected and studied. All literature studied is found in the reference list.

Results & Discussion

Screen dermatitis

Berg (2) investigated whether skin diseases were more common in people exposed to VDTs than among non-exposed controls. He observed that the exposed individuals significantly more frequently had non-specific skin symptoms with or without mild skin lesions than the non-exposed control population, but he claimed that they had not a higher frequency of visible skin signs. Thus, an increase in subjective sensations in the skin of people working with VDTs was registered.

A descriptive investigation was done 1989 in Sweden by Arbetsmiljöinstitutet (7) on a group of patients suffering from "electrosensitivity". Ninety-seven percent (31/32) showed symptoms from the skin such as erythema (75%), heat sensation (69%) and itch/smarting/pain (63%). Other main symptoms, such as dizziness, could be classified to belong to the central nervous system (CNS). The skin and the CNS were also sites of the body where the symptoms first appeared. But also other internal organs, such as the heart, seem to be affected (3).

In an open-field provocation (8), one "electrosensitive" patient responded with skin redness already after 10–15 min in front of an ordinary household TV set. This redness was further aggravated until the patient stopped the provocation (after 60 min). The skin was at that moment swollen and gave an impression of general edema. The patient was also sweating somewhat, and reported sensations of tingling in the body parts facing the TV screen. At the end of the provocation, the patient complained of dizziness and gave incomplete and inadequate answers to the interviewer's questions. Her speech was also slurred. The patient was, after a couple of weeks, provoked once more, showing the same objective and subjective symptoms as before. At inspection of the same patient 24 h after the end of the provocation, a large number of papules and pustles was seen in the skin of the face. Another patient did not react with any acute symptoms, however, both patients in the study reported feelings of subjective illness 24 h (and onwards) after the provocation.

In a study on persons with skin symptoms associated with VDTs, Oftedal et al. (9) demonstrated that the subjectively registered facial skin symptoms were reduced by decreasing the static and the low-frequency EMFs produced by the VDTs, by mounting electric-conducting screen filters in front of the VDTs. Two kind of filters were used: active and inactive. The inactive ones had the ground cable cut. They observed that most of the subjective symptoms were less pronounced when active filters were used. They also observed that at

days when the persons worked within 2 meters from the VDTs for a long period of time, the symptoms were more pronounced than at days they worked near the VDTs for a short period of time. Ofstedal et al. (9) suggested that the relation between the symptoms and the amount of time near the VDT may be due to different physical stress factors related to the VDT or the computer, and that electric and magnetic fields are possibly among these factors. They further suggested that electric fields are the only factors, among all the physical or psychosocial factors registered, that can explain why less pronounced symptoms were observed in the period with the active filter than in the period with the inactive filter.

Mast cells

Dermal mast cells synthesize and secrete an array of substances that have a potential effect on the immunobiology of the skin. Numerous studies indicate that mast cell products are essential for eliciting contact hypersensitivity (CHS) reactions (10, 11) and the pathogenesis of certain skin diseases (12–14).

In the open-field provocation mentioned before (8), an increased number of mast cells in the upper dermis in the "screen dermatitis" patients, as compared to normal healthy skin, was observed before and after the provocation. In another study (3), it was also found that the normally empty zone between the dermo-epidermal junction and mid-to-upper dermis was not present in the patient group and, instead, this zone had a high density of mast cell infiltration. Furthermore, in the patient group, the cytoplasmic granules were more densely distributed and more strongly stained than in the control group. Also the size of the infiltrating mast cells was found to be larger in the patient group. The high number of mast cells present in the patient groups may very well, due to histamine effects, explain the clinical symptoms of itch, pain, edema and erythema.

Dendritic cells

Johansson et al. (8) also found a high-to-very-high number of somatostatin immunoreactive dendritic cells in skin biopsies from patients with "screen dermatitis" before the provocation in front of an ordinary household TV set. Interestingly, the somatostatin-positive cells had seemingly disappeared after the provocation. Johansson et al. (8) suggested that the cells still remained in the tissue, but, for some unknown reason they were no longer immunoreactive towards the somatostatin antibodies used. But also direct cytotoxic effects have to be

taken into consideration as well as migration of the cells from the skin to other organs, such as the lymphoid system.

UV-light irradiation

Sunburn or UV dermatitis is a photosensitive skin reaction, due to acute UV exposure, that causes cutaneous inflammation. The inflammation produces symptoms such as erythema, pustles, papules, heat sensation, pain, itch, etc., followed by tanning and epidermal thickening. Chronic UV exposure can lead to skin ageing and carcinogenesis (15). The dose of light needed to produce erythema is dependent on the wavelength of light responsible for erythema production (16–18). For example, both UVA and UVB produce erythema at lower exposure doses than UVC. This difference in the intensity of the inflammatory response to various wavelengths of light may be due in part to differences in their penetration of the skin. UVC wavelengths are believed to be absorbed completely by the epidermis, UVB wavelengths penetrate the epidermis, and UVA penetrates to the deep dermis (19). The clinical pattern of erythema produced after UVB exposure may be biphasic with a transient immediate phase beginning in seconds and lasting only a few minutes. A prolonged delayed phase begins afterwards, which generally has its onset in 3 to 5 h, is maximal between 12 to 24 h, and fades over 72 h (20). This time course may be different with different exposure doses: small doses produce short-lived erythema, whereas larger doses produce erythema that is faster in onset, more intense, and persistent (21).

Mast cells

In humans, mast cells have been shown to degranulate and release histamine after exposure to UV light (20, 22). Cytokines, such as interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF)- α , are the most important mediators of UV dermatitis (23). In a study by Walsh (24), it was demonstrated that UVB irradiation induces mast cell degranulation and release of TNF- α , which leads to activation of dermal blood vessels and alteration of the traffic of the Langerhans' cells. In summary, the effects of TNF- α on dermal blood vessels and the known effects of histamine explains the common symptoms of sunburn, i.e. erythema, edema, itch and pain.

Dendritic cells

Langerhans' cells (LCs), normally found in the suprabasal epidermis, are dendritic cells that play a key role in the epidermal immunological system.

LCs constitute a morphologically well characterized subpopulation (3–8%) of bone marrow-derived epidermal cells that bear immunoglobulin Fc and C3b receptors, express class II antigens, and function as antigen-presenting cells (APCs). The majority of the APC capacity of normal skin is believed to reside within the LC population (25). Langerhans' cells recognize, process, and present antigens to immune T lymphocytes (26).

Several studies have been done on epidermal LCs irradiated with different radiation sources, e.g. UVA, UVB, 8-methoxypsoralen+UVA (PUVA), grenz rays, X-rays, etc. (27–32). Stingl et al. (26) showed that LCs' immunologic functions are impaired by UV irradiation. A well-studied, local immunological effect of UV irradiation is the inhibition of the CHS response, which occurs after application of a contact sensitizer to UV-irradiated skin of certain strains of mice (33). The CHS response is thought to be initiated mainly by LCs (34). Bacci et al. (35) proposed that UV radiation prevents CHS induction in susceptible mice by disrupting the cytoskeleton of LCs thereby preventing them from carrying out their role as APCs.

In an ultrastructural study of human epidermal LCs irradiated with grenz rays (ultra-soft X-rays or Bucky rays) and UVA (36), it was found that the number of LCs was reduced after grenz ray irradiation and high (erythematous) doses of UVA. It has been reported by Toews et al. (37) that exposing the skin to suberythematous doses of UV radiation altered the appearance and decreased the number of LCs in mouse skin. These morphological changes were associated with altered immune function with a decreased CHS response (37), and antibody responses (38), caused by altered antigen presentation in LCs.

Furthermore, Nordlund et al. (39) and Okamoto & Horio (40) demonstrated that LCs are sensitive to UV light and easily lose their surface markers. Several studies by other investigators showed the same results (29, 37, 41). Toews et al. (37) also suggested that the altered induction of CHS is preceded by a decrease in the number of LCs in UV-irradiated skin, which is thought to result from the migration of these cells to the draining lymph nodes (DLNs); when antigens are introduced through UV-exposed skin depleted of LC, there is a marked depression in the eliciting of CHS. Ikai et al. (42) demonstrated that exposure to UVB irradiation results in both a reduction in the number of LCs and a decrease in activity of prostaglandin D synthetase, an enzyme localized in the LCs. If similar changes occur in LCs/dendritic cells in "screen dermatitis" patients due to VDTs, this could confirm the suggestion by Johansson et al. (8) that the disappearance of som-

atostatin immunoreactive dendritic cells after provocation in "screen dermatitis" patients either depends on the disappearance of immunoreactivity towards the somatostatin antibodies or on a genuine migration of the LCs/dendritic cells from the skin. However, further investigations are needed to fully confirm this hypothesis.

Ionizing radiation/EMFs

An early clinical symptom of ionizing irradiation connected directly with high irradiation doses (10 Gy) given at low dose rate (2 Gy h⁻¹) is erythema, which seems to be associated with an injury to blood vessels (43) or an immediate vascular dilatation caused by released histamine or serotonin (44). It persists for about 2 to 3 days as the result of a continued, but decreasing, output of the vasoactive amines. A delayed erythema (the main erythema) then develops at about the 8th to 10th day postirradiation and continues for about 7 to 8 days. This second type of erythema is due to the release of proteolytic enzymes (lysozymes) from damaged epithelial cells (44). It is well known that both UV and grenz rays have a labilizing effect on lysosomal membranes. The affected skin may then thicken and the epidermal ridges flatten. There may be loss of hair, and severe pain. Histologically marked hyperkeratosis, a disorderly progression and nuclear atopy is seen. The collagen bundles are swollen and often show irregular staining. The blood vessels lying most superficially in the dermis are widely dilated. Also appendages, such as sebaceous glands and hair follicles, are entirely absent (44). This type of radiodermatitis, i.e. chronic radiodermatitis as a consequence of occupational over-exposure, was reported early in the use of ionizing radiation, and has frequently been seen in dentists, veterinarians, workers in industry, and physicians, especially dermatologists (44).

Other symptoms seen after high dose irradiation are, e.g. nausea, fever, headache and dryness of mouth. However, there is still a lack of knowledge whether low irradiation doses will induce the same symptoms, or not.

Henshaw et al. (45) have recently reported, in their very interesting study, the attraction of radon (²²²Rn) daughter nuclei, a known carcinogen, in normal domestic room air to every-day sources of power frequency EMFs. The observations showed that EMFs could concentrate in their vicinity a "cocktail" of radon daughter nuclei and presumably other potentially harmful agents. These phenomena may be understood in terms of standard aerosol physics. They result from the oscillation of charged aerosols, among others radon

daughter aerosols, and their drift due to the induced polarization of all the aerosols (45). A clear implication of the experimental results is that a person situated near a source of EMFs would receive a higher skin dose from radon daughters (46), and that the dose to internal organs also rises from inhalation of radon daughters.

Radon, an inert gas, rapidly diffuses across the alveolar membrane of the lung, and is transported by the blood to all parts of the body, where, by diffusion, it is taken up by the organs (47). The link between exposure to EMFs and radon daughter nuclei is of special interest in view of the carcinogenic potential of α -particles, being delivered mainly by the radon daughter nuclides ^{218}Po and ^{214}Po . Even at natural exposure levels α -particles are unique in their efficiency in inducing DNA double-strand breaks, and their ability to engender genetic instability in human bone marrow stem cells has recently been demonstrated (48). This is of even greater interest in view of the recent findings of DNA breaks in rodent CNS nerve cells seen after radiofrequency electromagnetic microwave irradiation (49), potentially leading to a highly frightening panorama for humans.

Some epidemiological studies have suggested an association between α -particle exposure via radon and the occurrence of leukemia, brain tumours, and kidney cancer, especially in children (50–53). Eatough & Henshaw (54) could show, in their study, that in the order of 2% (range 1–10%) of non-melanoma skin cancers, composed predominantly of basal cell carcinoma and squamous cell carcinoma, in the UK may be associated with radon exposure. They suggested that target cells for radiation-induced skin cancer lie in the basal layer of the epidermis which over most areas of the body is situated 50 μm below the surface. This is well within range of α -particles from radon and thoron daughters which may plate out on the skin surface. In this context, it may be noted that the epidermal innervation is as close as 20–40 μm from the living skin surface (55), which means that the α -particles could interact with these nerve fibers perhaps leading to the symptoms, such as itch and smarting, described previously. Most recently, it has also been proposed that there is an intimate association between such epidermal nerve fibers and Langerhans' cells (56), which may be a cellular "route" for spreading of the effects of α -irradiation. Furthermore, irradiation of the dermis may not even be necessary for skin cancer induction. Their study (54) also demonstrated that the radon-related dose to skin covered in clothing, is much less than that to uncovered regions, such as the skin of the face and neck. In addition, the dose to the hands is negligible due to the thickness of the epidermis.

Again, it may be remembered that often the "screen dermatitis" patients complain about rashes, etc., on their face and neck region, but not as often on their hands. Using risk factors from one study of X-ray irradiated tinea capitis patients, Harley et al. (57) have estimated that in the USA 20% of basal cell carcinoma may be linked to background radiation, principally due to radon-associated α -irradiation of the face and neck. It is of great interest to mention that in a follow-up study of patients who had received irradiation to the scalp for the treatment of tinea capitis a greater incidence of conformed mental illness was found compared to control subjects. The mental illness was both of the neurotic and psychotic categories (44).

However, further investigations are needed to explore the ability of EMFs to affect the movement of radon daughter nuclei and other aerosol particles and, further, the role of EMFs in carcinogenesis.

The fact that endogenous opioids can affect central cholinergic activity is well established (58–62). A series of experiments have demonstrated that magnetic fields have effects on the function of the endogenous opioid system (63–68). Changes in central cholinergic activity after exposure to magnetic fields could have important implications on the physiology and behaviour of an animal, since central cholinergic systems are involved in many such functions (69). In humans, changes in cholinergic activity of the brain can lead to various neurological and psychiatric disorders, such as Alzheimer's disease (70, 71), anxiety, and depression (72, 73). Recently, it has been reported that pulsed-magnetic fields can affect spatial memory functions, caused by the effect of the field on cholinergic systems, as measured in a radial arm maze, which is a spatial memory test for rodents (74, 75).

A question remains on where in the brain, and through which neural pathways, endogenous opioids mediate the effect of magnetic fields on central cholinergic activity, and how magnetic fields affect the function of the nervous system. The discovery of ferromagnetic materials in the special organs of some animal species, and, more recently, in the human cerebellum and cerebral cortex, suggests a possible biophysical mechanism of interaction of magnetic fields in living organisms (76–78). Furthermore, cells sensitive to magnetic fields have been reported in the pineal gland (79, 80).

Lai et al. (62) reported that microwaves, another form of non-ionizing radiation, decreases the cholinergic activity in the frontal cortex and hippocampus of the rat. Apparently, magnetic fields and microwaves alter the activity of the frontal cor-

tical cholinergic system via different neuronal mechanisms (81). Lai et al. (82) also showed that a single exposure to the microwave field causes a rapid increase in the concentration of benzodiazepine receptors in the cerebral cortex of the rat. Because benzodiazepine receptors in the brain are responsive to anxiety and stress, this supports the hypothesis that low-intensity microwave irradiation can be a source of stress (82). Most recently, a Canadian research team (83) has presented epidemiological data pointing to a connection between EMFs and depression as well as suicide!

Lai & Singh (84) studied the effect of acute exposure to low-intensity microwaves on DNA damage in brain cells of the rat and found that acute microwave exposure increases DNA single-strand breaks in brain cells of the rat. Previous studies have also suggested damages of chromosomal DNA in cells after microwave exposure (85, 86). Recently, Lai & Singh (49) measured single- and double-strand DNA breaks in individual brain cells after acute exposure to radiofrequency electromagnetic radiation (RER). They observed an increase in both types of DNA strand breaks after exposure to RER. Lai & Singh (49) speculated that these effects could result from a direct effect of RER on DNA molecules and/or impairment of DNA damage repair mechanisms in brain cells. DNA strand breaks could lead to disruption of cell functions, carcinogenesis, and cell death. Since cumulative DNA damage in cells in the central nervous system could be the cause of accelerated ageing and neurodegenerative disorders, it is imperative that the effects of RER on DNA in brain cells will be further studied and understood.

Barnothy & Sümegi (87) reported that magnetic fields evoke significant changes in the organs of mice. They observed, among other things, changes in the zona fasciculata of the adrenal cortex. They suggested that some hormone imbalance was created during the exposure to magnetic fields leading to the observed changes. Furthermore, they observed abnormalities in the spleens and livers of the exposed mice which could best be described as resulting from a general stimulation of the reticuloendothelial system, which, in turn, might be a manifestation of the defense mechanism of the organism against the stimulus of the magnetic environment.

Biological effects of low-frequency magnetic fields on Ca^{2+} oscillations in human leukemic T cells (88) as well as rat pituitary cells (89) have also recently been demonstrated. These highly interesting studies may provide further understanding regarding the molecular mechanisms behind EMF-induced cellular effects.

Mast cells

In a study on effects of exposure to electromagnetic radiation on a mast cell analogue, Donnellan et al. (90) observed that the rate of DNA synthesis and cell replication increased, that actin distribution and cell morphology became altered, and the amount of β -hexosaminidase (a marker of granule secretion) released to a calcium ionophore was significantly enhanced, in exposed cultures as compared to unexposed.

Langerhans' cells

Grenz rays have been used for more than 60 years in the treatment of cutaneous diseases, such as allergic contact dermatitis (ACD), psoriasis and chronic lichenified eczema. X-rays of various qualities are known to reduce the number of epidermal LCs, including human skin (27, 28, 31, 32), and thus may reduce their immunological function. Such an alteration may partly explain why the ACD is so well suppressed by grenz rays. Furthermore, Lindelöf et al. (32) suggested that the reduction of the LCs probably was due to both a physical absence of LCs and a modulation of surface markers. The reduction of LCs due to loss of surface markers may be seen a short time after irradiation, whereas the reduction may be due to the physical absence of LCs later on (32). Lindelöf & Forslind (91) also studied the effects of grenz rays on LCs at electron microscopic resolution in humans and reported that the reduction in the number of LCs after grenz ray therapy, seen in their previous study, was not due to a depletion of the surface markers, but to an actual loss of the LCs themselves. However, the fate of the disappearing LCs persists as an enigma and so far no answers have been obtained as to what happens to LCs after exposure to grenz rays.

Conclusion

The results of this literature study demonstrate that highly similar changes exist in the skin of "screen dermatitis" patients, as regards the clinical manifestations as well as alterations in the cell populations, and skin damaged by UV light or ionizing radiation.

One very intriguing issue that needs to be clarified is if, e.g. ordinary TV screens and computer terminal screens leak high-frequency electric or magnetic fields that affect our cells in such a way that the effects mimic the effects seen after, e.g. UV light or weak X-ray irradiation. Also a possible UV leakage cannot be ruled out, and so cannot the attraction of radon (^{222}Rn) daughter nuclei

with a secondary α -particle radiation damage to the superficial skin (and maybe even the deeper tissues).

At the cellular level it is very important to investigate the exact fate of mast cells, LCs and other cell types after microwave irradiation, radiofrequency electric and/or magnetic fields, radar, etc. Special emphasis must also be put on non-thermal effects, since the knowledge there seems very scarce. Perhaps again we will learn that the effects seen after, e.g. grenz rays on LCs will be mimicked by these different kinds of fields, and also at levels commonly used in the society, both in our homes as well as in our occupational milieu.

So, in conclusion, it is evident that biological changes are present in the patients claiming to suffer from "screen dermatitis" and EMF exposure. In view of the recent epidemiological studies pointing to a correlation between long-term exposures from magnetic fields and cancer (92, 93), the obtained results from the presently reviewed studies have to be taken most seriously.

It may be that our cells, having developed over 3.5 billions of years, are not capable of withstanding today's modern low- and high-frequency EMFs. The tissues in our body have developed protections against the harmful effects of heat, light and UV-light; however, since most of the other EMFs commonly now around, are the inventions of the very last decades, perhaps we entirely lack cellular and molecular protective strategies, other than the simple "alarm" set off: erythema, itch and pain. It will be a very fascinating investigative task for future scientists to throw light onto these questions!

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