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CONTROVERSIES IN DERMATOLOGY

Climatic Change and Skin: Diagnostic and Therapeutic Challenges

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Abstract
Many scientists have reported on the current trend toward global warming and decreased precipitation. The magnitude and cause of these changes and their impact on human activity are matters of debate. Higher temperatures could increase the prevalence of some skin diseases. More people would suffer from sensitive skin and dry skin due to the reduction of relative humidity. An impaired skin barrier function would increase the severity and prevalence of atopic dermatitis. The greater percentage of UV-B radiation reaching the earth's surface, combined with the increased popularity of sunbathing, may lead to greater rates of skin cancer and photoaging if effective sunscreens are not used. Furthermore, the habitats of various vectors of infectious disease are changing. Such changes, should they occur, will be a challenge for dermatologists who will face the important task of prevention and early diagnosis and treatment of these diseases.

PALABRAS CLAVE
Cambio climático;
Dermatosis de baja humedad;
Cáncer cutáneo;
Calentamiento global;
Enfermedades trasmitidas por vectores

Cambio climático y piel: retos diagnósticos y terapéuticos

Resumen
Numerosos científicos informan de una tendencia actual al calentamiento global y a la disminución de las precipitaciones. Su cuantía, sus causas y la influencia de la actividad humana son motivo de controversia. Un aumento de la temperatura podría incrementar la prevalencia de algunas patologías cutáneas; más personas padecerían piel sensible y una mayor xerosis cutánea por disminución de la humedad relativa. Las alteraciones de la función de la barrera cutánea aumentarían la gravedad y prevalencia de la dermatitis atópica. La mayor proporción de radiación UVB que alcanza la superficie terrestre, unida a hábitos poblacionales de aumento de fotoexposición, junto con una fotoprotección incorrecta, hacen esperables mayores tasas de cáncer cutáneo y de fotoenvejecimiento. Además, los hábitats de diversos vectores de patologías infecciosas están cambiando. Afrontar estos problemas, en caso de que se produjesen, será un reto para el dermatólogo, que tendrá una importante labor de prevención, diagnóstico y tratamiento precoz de estas patologías.

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Many articles have been written based on observations and various predictive models of how climate change could affect social, economic and health systems, but few studies focus on how change may affect our skin.

Climate Change: Truth and Fiction

Before discussing the effects of climate change on skin, it would be useful to provide a brief outline of current knowledge on climate change itself.

The Intergovernmental Panel on Climate Change of 2007 estimated that temperature would increase between 1.1ºC and 6.4ºC between 1990 and 2100,[1] underlining the significance of these data by referring to the summer of 2003, which was the warmest in the last 500 years.[2] The role of human activity is a hotly debated topic; those who consider it a determining factor argue that the increase in temperature is proportional to greenhouse gas emissions (mainly carbon dioxide, methane, chlorofluorocarbons [CFCs] and nitrous oxide)[3]; in contrast, others argue that air temperature also depends on factors such as solar activity and thermoregulation by oceans and other water masses, or that the relationships among the various factors remains unknown.[4,5] A global rise in extreme climatic events (heat waves, extreme cold, cyclones, etc) has also been predicted, although the type and intensity may well vary relative to the environmental characteristics of the different countries and continents.[6]

Little is known concerning the accuracy of predictive meteorological models, particularly for long-term forecasting.[7] Furthermore, reliable climate measurements are not available at the global scale and do not go back more than a century.[8] Thus, it is easy to find information in high-impact journals that runs counter to what is commonly presented by the mass media on the state of glaciers[9] or the economic consequences of extreme climatic events such as El Niño.[10] An example of this is provided by recent news on the use of nitrogen trifluoride, a potent greenhouse gas,[11] in the manufacture of solar panels, among other products.

Attempting to clarifying to what extent there is an actual global warming effect caused by human activity, or to what extent such events are due to normal climatic variations goes beyond the scope of this article and would probably require many improvements in climate prediction systems and detailed analysis.

In regard to environmental humidity, it is assumed that the increased temperature and changes in plant biomass, secondary to increased carbon dioxide (CO_2), will change precipitation patterns and lead to a greater number of extreme climatic events, including droughts and more intense flooding.[6] Precipitation patterns are much more influenced by local conditions than by temperature,[12] and global estimates based on them are even less reliable.

Higher Temperatures and the Skin

The effects of temperature on the skin can be classified as direct (physical action, such as burns) and indirect (through changes in the distribution of various disease vectors, changes in relative environmental humidity, etc). Although global trends may come into play, local climatic conditions have a strong influence on temperature variations.

Global Warming and Vector-Mediated Disease

Variations have been recently observed in the geographical distribution of the vectors of some diseases (malaria, dengue fever, leishmaniasis, tick-borne diseases, etc) and their possible association with climate change has been suggested. One of the most well-known natural events linked to climatic variation is El Niño, also known as the Southern Oscillation; this phenomenon leads to a 30% increase in the number of cases of malaria in Venezuela and Colombia, and to the presence of malaria in places such as northern Pakistan.[13] "El Niño" also affects the incidence of Murray Valley encephalitis, Rift Valley fever and visceral leishmaniasis in different geographical zones.[13]

Temperature is a critical factor in the ability of a vector-borne disease to become epidemic, since vector density and the vector's ability to transmit the pathogen depend on temperature, which affects vector survival and the population growth rate, by modifying the vector's vulnerability to the pathogens, the incubation period of the pathogen inside the vector and its transmission pattern.[14] Thus, a temperature rise of almost 2ºC has increased the length of the breeding season of many mosquitoes and their ability to colonize higher latitudes, although vector viability decreases after a certain threshold. Mosquitoes of the genus *Anopheles* breed optimally between 20ºC and 27ºC, and *Plasmodium* species cannot be transmitted when temperatures are less than 15ºC or more than 38ºC, since schizogony is arrested outside that range.[14] In another example, the mean temperature increase in Sweden, along with the construction of rural housing (thus increasing contact between humans, vectors and disease reservoirs) and reductions in the number of deer predators, combine to form an acceptable explanation for the observed increase in cases of Lyme disease.[15] Because a rise in temperature affects several parameters at once, the change can increase the incidence of a vector-borne disease in some areas and decrease it in others.[8]

More precipitation leads to greater plant density, creating local wet microclimates that favor the spread of insects and increasing the food supply available to disease reservoirs, such as rodents and other herbivores.[14] On the other hand, droughts in wet areas also leave pools that increase the size of the breeding areas and the feeding requirements of fertile females, thus raising the number of bites.

Nevertheless, insect and arthropod life cycles are modified by many other factors such as land use, water availability, demographic shifts and changes in intermediate hosts or natural reservoirs, and thus it is to be expected that these changes will be modulated by such local factors.[16] By stimulating plant growth, CO_2 favors the spread of insects, and urban growth facilitates epidemics, especially in unhygienic conditions.[17] Other factors, such as

deforestation or the use of certain pesticides, have more variable effects.

Given the complex interrelationship between climatic and social factors and some arthropod and insect disease vectors outlined above, it is increasingly difficult to find robust scientific evidence that supports a relationship between climate change and disease, since the association between temperature and disease incidence is routinely simplified by the assumption that it is linear, without conducting a comprehensive statistical analysis which takes into account possible confounding factors (improved diagnostic methods of diseases, vector resistance to antibiotics, environmental humidity and demographic shifts, among others).[18,19]

In the context of Spain, there could be an increase in dengue fever, encephalitis and viral hemorrhagic fever, Boutonneuse fever, Lyme disease, and leishmaniasis. It is unlikely that malaria will reestablish itself in Spain,[14] however, since the only potential vector still present is *Anopheles atroparvus*, which is resistant to the tropical strains of *Plasmodium falciparum*. This is not the case for dengue fever, whose vector *Aedes albopictus* is also able to transmit some arboviruses and which was detected in Europe in 1979 and in Spain in 2004.

Nevertheless, regardless of the influence of climate and the facts outlined above, an increase in the incidence of these types of disease in Spain is expected due to the continuing increase in geographical mobility of populations.

Changes in Some Skin Characteristics

Some authors have considered "sensitive skin" to refer to the decreased tolerance of the skin to everyday cosmetics and toiletries,[20] although it could be defined in a broader sense as skin that gives rise to sensations of burning, tautness, or itching in response to various physical, chemical, or psychological stimuli. In this type of skin, transepidermal water loss is enhanced, altering the skin barrier and leading to increased contact with allergens. A neurocutaneous disorder has also been proposed as responsible for abnormal sensations.[21] The prevalence of this disorder may be as high as 40% in men and 60% in women, and it is more frequent in summer and in fair-skin phototypes.[22] Patients attribute their symptoms to numerous climatic trigger factors, such as environmental dryness, wind, cold, sun, abrupt changes in temperature, and air conditioning and environmental pollution[22]; subjects of Caucasian race are particularly prone to such beliefs.[23] Thus, the increased seasonal prevalence of sensitive skin that responds to heat, in addition to numerous physical factors, will predict a rise in visits to dermatology clinics in relation to this problem.

The colder external ambient temperature of winter is associated with a vasoconstrictor response that leads to a lower baseline skin temperature and delay in reaching any given temperature. This type of vasoconstriction, which is thought to be mediated mainly by cyclic guanosine monophosphate, is more pronounced in women and particularly in patients with primary Raynaud's disease. The result is impaired blood flow to the extremities.[24] An average temperature increase could reduce the number of cases of primary Raynaud's disease and improve blood flow to the extremities, although this may have limited clinical relevance if a greater number of extreme climatic events occur.

Sebum secretion is greater in the warmer months and in younger patients.[25] Furthermore, several studies have shown that between 30% and 50% of young people experience aggravated symptoms during summer due to increased sweating.[26,27] Thus, there may be an increase in the incidence of acne and, in particular, its symptoms, although it is difficult to make predictions in this setting.

Increased atmospheric CO_2 stimulates growth in most plants, including poison ivy, whose toxin (urushiol) produces acute irritant contact dermatitis in a high percentage of those exposed to it; the allergenic potency also increases.[28]

Global Warming and Skin Infection

Pyoderma is more prevalent in warmer areas, especially when there is high relative humidity.[29-31] Thus, in the marginated black population in the southern United States, the incidence of bacterial skin infection in the warm, humid months is reported to be as high as 50% in children aged from 2 years to 6 years, but the incidence decreases to 4% in winter.[32] Given that most of these infections are caused by normal skin flora, gram-positive bacteria predominate, including *Staphylococcus aureus* and *Streptococcus pyogenes*, which are the pathogens responsible for most of these infections.[33] Nevertheless, a warm, humid environment also encourages the colonization of the skin by gram-negative bacteria,[34] and extreme climatic events (floods and tsunamis) can also lead to skin infections caused by so-called atypical bacteria such as *Vibrio vulnificus*, *Vibrio parahaemolyticus*, *Burkholderia pseudomallei* and others, due to prolonged contact with contaminated water.[35]

Humidity and Skin

Dry Skin

Dry skin has impaired function and its stratum corneum has decreased water content, which should ideally range between 10% and 15%. Skin hydration is based on the interrelationship between corneocytes and intercellular lipids, although the molecular mechanism by which it is controlled is still not completely understood—as demonstrated by the problems involved in the hydration of cultured epidermis.[36] In simplified terms, there are 2 types of water content: static and dynamic. The static type, also known as bound water, is held in the corneocytes by the osmotic pressure of the natural humectant factors produced by the enzymatic degradation of filaggrin. In contrast, the dynamic type, or free water, is located between the intercellular lipid membranes. The amount present depends on the gradient between the water content of the Malpighian layer keratinocytes

and environmental relative humidity. As a result of flow at this level, evaporation occurs in the superficial layers of the epidermis, in a process known as transepidermal water loss.[37]

A study conducted in healthy volunteers verified that exposure to a low relative humidity of 10% for 6 hours led to a reduction in water levels in the stratum corneum, in transepidermal water loss, and in skin temperature.[38] In this context, fine wrinkles undergo rapid change, becoming more evident after 30 minutes of exposure to low relative humidity.[39]

To summarize, low environmental humidity (especially when this occurs abruptly), in combination with low temperatures, increases transepidermal water loss and decreases lipid and natural hydrating factor levels, leading to dry skin. Over time, a series of compensatory responses that partially prevent excessive dehydration occur; examples are the thickening of the stratum corneum and increased ceramide synthesis.[40]

Despite the unquestionable relationship between relative humidity and the degree of skin hydration, other factors also participate. Thus, many products lead to dry skin. One such is soap, especially those which include anionic detergents such as sodium lauryl sulfate, which has the capacity to change skin pH. Others are drugs that decrease sebum secretion and alter its lipid composition; examples are clofazimine, retinoids, hypolipidemic agents, cimetidine, or lithium carbonate.[40]

Age also influences skin hydration and sensations of dryness. Those over 60 years of age are more affected by relative humidity (skin and eye dryness can be sensed at 30% relative humidity and at 10% relative humidity there is also dryness of the nasal mucous membrane with impairment of ciliary function), but subjectively they need more time to perceive it and take any measures necessary.[41] In postmenopausal women, hormone replacement therapy improves skin hydration by decreasing transepidermal water loss.[42]

Low-Humidity Dermatosis and Sick Building Syndrome

The optimal relative humidity range lies between 40% and 60%, and lower levels are known to cause skin disorders. Low-humidity dermatoses, described in 1980,[43] are a group consisting of pruritus, erythema, and dry skin. These disorders occur particularly in exposed areas, worsen on working days, and improve on weekends and holidays. Occupations that bring workers into low-humidity environments to avoid corrosion or the proliferation of biological agents (eg, hospital medicine, computer product manufacturing, or librarianship and information science) put workers at risk for these dermatoses.[44] Recently, Chou et al[45] studied the results of blood and urine analyses and information on symptoms obtained from questionnaires covering 3 years from 12 men who worked in an ultra-low relative humidity environment (1.5%), comparing them to results for age-matched controls. They observed a greater incidence of skin pruritus and disorders on the legs that were diagnosed as contact dermatitis.

Sick building syndrome is a related phenomenon. It encompasses a group of nonspecific problems such as headaches, dizziness, nausea, and skin and eye pruritus. A proposed multifactorial origin for this entity includes the following components: environmental contaminants (dust, smoke, smells, irritants), suboptimal air-conditioning (low relative humidity, high ventilation flow, excessive temperature), and psychological traits (as the prevalence is higher in women in unskilled jobs and people under physical or psychological stress).[46] It is frequently difficult to isolate a specific cause and environmental improvements do not mitigate the problem, thus, some consider it a compensation neurosis.[47] These disorders are estimated to reduce productivity and increase absenteeism by 20% to 40% among exposed workers.

Finally, it is worth noting that these types of problems have been identified in other environments in which both contaminants and low-humidity conditions are present; for example, aircrew dermatitis has been recently described.[48]

Influence on Some Chronic Dermatoses

Flare-ups of various dermatoses, such as atopic dermatitis and other types, are related to environmental factors. Climate has a strong impact on the number of flare-ups of atopic dermatitis and the intensity of symptoms, and therefore on the ensuing social effects. Thus, marked improvements are found in warm, humid climates.[49] The worsening of this dermatosis owes as much to low relative humidity (which aggravates changes in the skin barrier[50]) as to low temperatures.[51] Regardless of the influence of climate change, most authors consider that its prevalence will continue to rise.

The Skin Barrier and Skin Sensitivity

Low environmental humidity increases skin permeability,[52] thickens the epidermis as a defense mechanism, and stimulates the generation of inflammatory mediators.[53] Furthermore, mast cells and histamine in the dermis of mice and scratching behavior have been shown to increase under conditions of low relative humidity; these effects can be prevented by applying pure vaseline.[54]

These changes are also observed in patients with chronic inflammatory dermatoses such as psoriasis, atopic dermatitis, and senile xerosis, in which pruritus is more intense in cold dry climates.

Experimental studies in which a cutaneous immune reaction has been induced in mice under controlled relative humidity conditions show that the intensity of the induction and elicitation phases of the reaction is greater in individuals housed under low relative humidity, with an observed increase in the number of Langerhans cells in the epidermis as well as increased migration of the antigen to the regional lymph nodes.[55]

Similarly, low temperatures and low relative humidity have been shown to lead to an increase in irritant reactions in humans, as well as to weakly positive reactions to

various substances used for patch testing with the German Standard Series. Thus, the German Contact Allergy Group recommends repeating these tests in warmer weather conditions and using the repeated open application test in case of weakly positive reactions of unknown significance.[56] The allergens that caused a positive reaction and that appeared to be more influenced by weather conditions in studies by that group were fragrance mix, formaldehyde, and paraben mix.

Sunlight and the Skin

Sunlight can lead to a variety of problems: acute sunburn and photosensitivity reactions and, in the long term, chronic photodermatitis, photoaging, local or systemic immunosuppression and photocarcinogenesis. We focus on photocarcinogenesis and the immune changes it gives rise to.

The Ozone Layer and Its Influence on UV Radiation

The amount of UV-B radiation that reaches the Earth's surface is modified by several factors: the hour of the day (50% of UV radiation reaches the surface between noon and 3 PM); season (tilt in relation to the planet's orbit around the sun produces variations in the percentage of sunlight that reaches the Earth; in the northern hemisphere, for example, the greatest levels occur in summer); latitude; altitude (with each 300 m increase in altitude UV radiation rises by 4%[57]); the ozone layer; cloud cover; and relative humidity (as relative humidity decreases, UV radiation increases). In addition, it should be taken into account that specific surfaces, such as sand and snow, can reflect between 25% and 90% of the rays they receive.[58]

The mean ozone loss since the 1990s at mid-latitudes in the northern hemisphere has fluctuated between 3% (in summer) and 6% (in spring and winter) each decade.[59] Nevertheless, the current rate of stratospheric ozone loss is slowing down.[60]

The increases in UV-B radiation predicted by the United Nations Environment Programme[61] (an increase of 1%-5% per decade in relation to latitude) differ from predictions of up to 12% by some authors using ground-based measurements, possibly because of the multiplicity of factors that affect the amount of UV-B radiation reaching the Earth's surface. Nonetheless, UV-B radiation is expected to rise. Given the latency of the chronic effects of UV-B exposure and slow change in peoples' behavior, however, it will be difficult to estimate what proportion of adverse effects will be due to a real change in the radiation spectrum caused by changes in the ozone layer.[59]

In regard to the relationship between photocarcinogenesis (discussed in more detail below) and changes in the ozone layer, it is worth noting that the estimates are based on modeling the increased incidence of skin cancer due to the destruction of the ozone layer while assuming that the other factors remain unchanged. Models predict values ranging between an increased incidence of 9% in 2050 (if the release of all compounds that damage the ozone layer cease immediately) and 300% in the worst-case scenario.[62] These models were produced by extrapolating carcinogenic doses in hairless mouse models, adjusting the data by the known epidermal differences between the 2 species and introducing the expected increase due to UV-B radiation as the "biological amplification factor."[63] It is estimated that for each 1% reduction in the thickness of the ozone layer the incidence of melanoma will increase between 1% and 2%.[64] The same percentage reduction in thickness will increase risk for squamous cell carcinoma between 3% and 4.6% and risk for basal cell carcinoma between 1.7% and 2.7%.[65,66]

Thus, the annual age-adjusted incidence rate of melanoma tripled between 1975 and 2004, increasing from 6.8 cases to 18.5 cases per 100 000 population.[67] It has been estimated that the incidence of nonmelanoma skin cancer in the Netherlands will double between 2000 and 2015, partly due to a large increase in population aging, but also to increased UV radiation.[68]

Immunosuppression

Numerous animal models have confirmed that UV (especially UV-B) radiation is able to inhibit the immune response activated by an antigen coming into contact with the skin, by acting on the afferent and efferent phases.[69] The effect is caused by DNA mutations and changes in the isomerization of urocanic acid and in lipid membranes. Thus, in mice, irradiation can lead to contact sensitivity inhibition and delayed hypersensitivity reactions. However, immunosuppression does not occur similarly in all mice models or in all humans, since the process is dose-dependent (occurring locally at low doses and systemically at high doses) and a specific genetic substrate is required, as shown by the discovery that certain tumor necrosis factor-α polymorphisms confer greater susceptibility to UV-B-induced immunosuppression in humans.[70]

The immunosuppressive properties of UV radiation are also implicated in photocarcinogenesis, since the tumors induced are highly immunogenic and sunlight-induced immunosuppression has been shown to be strongly associated with their proliferation.[71] UV radiation-induced regulatory CD4+ and CD25+ T lymphocytes, which are kept in circulation by costimulation received through CD80 and CD86 signaling, prevent incipient skin tumors from being detected. In addition, UV-B radiation, through the production of cyclobutane-pyrimidine dimers, alters the pattern of the cytokines produced by the keratinocytes, and stimulates the secretion of interleukin-10, which has a key role in the development of CD4+ and CD25+ T lymphocyte-induced immunosuppression, although the exact mechanism is still not fully understood.[71]

Furthermore, the immunosuppressive properties of UV radiation are widely used in dermatology to treat certain diseases such as psoriasis, atopic dermatitis, or fungoid mycosis. In addition, experiments have shown that single-dose UV-B increases the minimum erythemogenic dose 4-fold and inhibits the respiratory tract response to egg

albumin in asthmatic mice, which opens the possibility of expanding its therapeutic range in humans.[72]Sunlight exposure induces flare-ups of herpes labialis through these immunosuppressive mechanisms[73] and may also influence the incidence of papillomavirus. Sunlight can also lead to a worsening of various bacterial skin infections or pyoderma.[74]

Skin Cancer

Photocarcinogenesis

That sunlight can cause skin tumors has been known for many years.[75] UV radiation can cause skin tumors through a direct mechanism (by inducing mutations) and an indirect mechanism (through immunosuppression, as outlined above).

From a cellular and molecular point of view, and in very simple terms, UV radiation may lead to several changes that induce mutations and promote and sustain the conditions under which they are responsible for skin tumors. Through the direct route, UVB rays penetrate the epidermis and interact with DNA, the principal chromophore, to produce mutations[76] (particularly pyrimidine dimers) and reactive oxygen species that damage DNA, proteins or lipid membranes. UV-A, although a weak producer of DNA-derived photoproducts, produces a range of mutations similar to those caused by UV-B.[77] UV-A also produces cyclobutane-pyrimidine dimers and inhibits the response to actin-based damage, with decreased production of p53 (which when increased stimulates the cell's repair system),[78] and lower apoptosis rates.[79] As a consequence of these effects, the risk of photocarcinogenesis rises. Nevertheless, the main mutagenic effect of UV-A light occurs indirectly, by means of production of reactive oxygen species through interactions with other intracellular chromophors.[80]

Gandini et al[81] conducted a meta-analysis of risk factors for melanoma, analyzing 57 studies published before 2002 to demonstrate the following predictors of risk: intermittent sunlight exposure (relative risk [RR], 1.61; confidence interval [CI], 1.31-1.99) and sunburn during childhood (RR, 2.03; CI, 1.73-2.37).

Many years ago, murine experiments demonstrated that temperature mediated an increase in the tumorigenic effect of UV radiation.[82] These experiments showed increases ranging from 3% to 7% in the induction efficacy of UV radiation for each increase of 1°C. Assuming an estimated 5% increase in induction efficacy per degree, it has been calculated that a 2°C global increase would lead to a 9% to 11% excess in the incidence of tumors by 2050, in relation to the increase in UVB.[62] Clearly, the assumed induction efficacy of UVB light does not take into account the different thermoregulation systems of mice and humans, and should be regarded as a working hypothesis that requires further study in human models.

New Sunbathing Trends

The perception that a suntan indicates greater social status, in combination with rising temperatures, encourages longer exposures with fewer clothes and may be significantly increasing UV radiation exposure regardless of any changes in the spectrum of light reaching the Earth's surface.[59] This is a possible confounding factor that should be taken into account when studying the causes of the current increase in skin cancer.

Among sunbathing trends, the use of sunbeds is increasingly widespread: they are widely accepted but are not strictly regulated at present. The intensity of UV-A radiation emitted by these appliances can be 10 times to 15 times greater than that received in a country like Spain at noon.[83] A meta-analysis[84] carried out in 2005 examined studies of risk for melanoma and nonmelanoma skin cancers. Nineteen studies (18 of which were case-control studies) published between 1981 and 2005 included 7355 cases of melanoma. The use of sunbeds was associated with a RR of 1.15 (CI, 1.00-1.31). When only patients under 35 years of age were taken into consideration, the RR increased to 1.75 (CI, 1.35-2.26). Nevertheless, when the 8 studies which took into account confounding factors like photosensitivity and sunlight exposure were analyzed, the results were no longer significant (RR, 1.19; CI, 0.33-4.30). Neither was a dose-response relationship found.[84] Thus, it may be prudent to consider the use of these appliances to be a possible risk factor for melanoma, especially in the case of early exposure, but this possibility awaits confirmation. The meta-analysis also included 5 studies on the development of basal cell carcinoma and squamous cell carcinoma among sunbed users and found an RR of 2.25 (CI, 1.08-4.70) in the case of squamous cell carcinoma, although the results did not reach statistical significance in the case of basal cell carcinoma.[84]

Environmental Contaminants, Suspended Particles and the Skin

First, we provide a brief description of the skin disorders induced by environmental pollution and suspended particles, as well as those directly associated with modernization and urbanization.

Although radiation emitted by many domestic electric appliances is also thought to lead to skin disorders, UV radiation is the more significant factor. Irritative and allergic contact dermatitis, atopic dermatitis, chloracne (particularly associated with halogenated products), chemical skin lightening, scleroderma-like diseases, nonmelanoma skin cancer, mycosis fungoides[85] (associated with halogenated hydrocarbons) and a long list of diseases can be induced or aggravated by various substances in our environment.[86]

How to Manage These Problems From the Viewpoint of the Dermatologist

Skin Hydration

This article does not provide an in-depth review of the different chemical compounds that can be used as topical emollients (agents to increase stratum corneum hydration

by forming a film that limits water evaporation) or moisturizers (substances that increase the ability of the stratum corneum to capture water by other mechanisms).[87] Emollients are considered very safe, since they have a low rate of adverse effects, although various diseases such as irritative dermatitis, allergic contact dermatitis, folliculitis and pigmentary disorders, etc, have been associated with their use.[88]

As alternatives to classic drugs or as adjunctive agents, we highlight the topical application of products such as the following: a) mixtures of ceramide, cholesterol, and fatty acids in proportions similar to those of the lipid barrier; b) serine-protease inhibitors similar to trypsin; or c) peroxisome proliferator-activated receptor (PPAR) modulators, such as farnesyl, that activate PPARα and that can stimulate the normal epidermal regeneration systems and increase the speed at which the skin barrier is restored.[89]

Special emphasis should be placed on behavioral measures that prevent major changes in the skin barrier, such as bathing in warm water using non-aggressive gels, avoiding intense friction and using emollients afterwards, avoiding washing the hands and face too frequently, or using breathable loose-fitting clothing.[90]

Environmental Humidification

As described above, the optimal relative humidity to maintain correct skin hydration ranges between 40% and 60%. Home-made humidification methods can be employed; examples are placing containers of water on radiators or using top-range air conditioners, which can regulate both humidity and temperature to obtain optimal levels of each. What is important is to come as close as possible to these relative humidity values.

Airflow directed toward the user should be avoided in the case of air conditioning or acclimatizers, and dwellings should be appropriately ventilated.

Photoprotection

Studies of racial pigmentation indicate that the degree of dermal melaninization is the result of a trade-off between the advantages and disadvantages of having low quantities of the pigment. The main advantage of low pigmentation is appropriate vitamin D synthesis. Among the disadvantages is increased photocatalysis of folates and decreased UV radiation protection.[91] Although it is difficult to define the minimum UV radiation needed to achieve appropriate vitamin D synthesis, it appears that exposing the face, arms and hands from 5 minutes to 10 minutes 3 times per week may be sufficient.[92]

Although our skin has a set of natural defense mechanisms, such as thickening of the epidermis, melanin synthesis and enzymatic DNA repair and detoxification systems, these may be insufficient, especially in people with a fair-skin phototype.

Thus, when patients come for consultation, we should offer advice on certain precautions they can take in daily life to prevent photoinduced damage as much as possible. In this regard, educating children and young people is especially important, since they belong to the age group that engages in more outdoor activities and that has a longer life expectancy, and so any adverse effects may be more intense.

Sun exposure should be avoided as far as possible (especially in the middle of the day). Recommendations should include the use of clothes, hats (especially with peaks or broad brims), and sunglasses, which offer basic photoprotection. The ability of clothes to protect us from the sun depends on their thickness, weight, the type of fabric and fiber density, among other factors, and fashion has an enormous influence. Furthermore, in order for sunglasses to effectively protect the eyes, the lenses must only allow less than 0.001% of rays in wavelengths between 200 nm and 320 nm to pass through them, and less than 0.01% of rays of wavelengths between 320 nm and 400 nm.[93]

Various substances can provide some systemic photoprotection thanks to antioxidant properties. Examples are genistein or the polyphenols found in green tea that are ingested to enhance general skin protection. Many substances have been used for topical photoprotection against both UV-A and UV-B radiation[94] (Table), usually in combination to achieve optimal protection. These substances also seem to prevent photoaging.[95] Thus, their use should be recommended on skin areas that are not physically covered. It is advisable to apply a generous and even amount of sunscreen with a factor higher than 15 (since protection indexes are measured at applications of 2 mg/cm^2, which rarely occurs in practice), between 15 minutes and 30 minutes before initial exposure and with frequent reapplications (at least every 2-3 hours if exposure is prolonged).[64] Of interest, a study is investigating the topical application of small molecules that activate p53, inhibiting the murine double minute 2 protein (implicated in the biochemical cascade of melanogenesis) with the aim of achieving an "artificial tan" without UV radiation.[96] In addition, studies have demonstrated the efficacy of substances that decrease actin-based damage response and increase DNA repair through various enzymatic mechanisms. Examples of this approach are the use of photolyase or T4 endonuclease (which is being used in patients with xeroderma pigmentosum[93,97]), or the topical application of DNA oligonucleotides, caffeine, and topical creatinine.[93]

Although most of these measures appear simple to put into practice, people tend not to do so. For example, a third of US residents surveyed report having at least 1 sunburn per year.[68] Furthermore, surveys on photoprotection use have not found an association between the respondents' phototype and their use of protection. Many patients cite high temperatures and sweating, as well as the desire to be tanned, as factors that make them reluctant to take appropriate measures.[98] In countries with lower UV radiation levels than those in Spain, on the other hand, the benefit of daily photoprotection use may not outweigh its drawbacks (cost and sensitivity problems, among others) in the months with less sunlight, as Diffey[99] proposed after a study conducted in the United Kingdom. However,

Table Some Substances Used in Topical Photoprotection

	Type of Substance	Name
Antioxidants	Carotenoids	Lycopene, B-carotene, astaxanthin
	Phenolic compounds	*Polypodium leucotomos* extract, green tea polyphenols, resveratrol, vitamins C and E, Seresis® (Ginsana, Bioggio, Switzerland)
	Antioxidant mixtures	Genistein, silymarin, red clover isoflavonoids (equol), quercetin, apigenin
	Flavonoids	
	Other	Ferulic acid derivatives, Pycnogenol (Horphag, Guernsey, UK), piperidine nitroxide, etc
Topical sunscreens	UV-B filters	PABA and its derivatives, salicylates, cinnamates, octocrylene, ensulizole
	UV-A filters	Benzophenones, anthralins, Eusolex 6300 (Merck, Darmstadt, Germany), Mexoryl SX® (La Roche-Posay, Vichy, France)
	Wide spectrum	Mexoryl XL® (La Roche-Posay), Tinosorb M® (Ciba, Basel, Switzerland), Tinosorb S® (Ciba)
	Inorganic filters	Titanium dioxide, zinc oxide

Abbreviation: PABA, para-aminobenzoic acid.

a moderate benefit of daily use has been demonstrated in places with high UV radiation levels, such as Texas, Australia, and Queensland.[100]

In relation to managing the demonstrated risks involved in sunbed use, Spain led the changes to the European Standard EN 60335-2-27 to limit the maximum erythemogenic effective irradiance of the lamps to 0.3 W/m^2 and to prohibit their emission of UVC rays.[101] Nevertheless, surveys of sunbed users show that establishments that offer this service tend not to inform users of the risks, a large percentage of users do not use eye protection and many clients exceed the duration and number of sessions recommended.[84] Thus, the important task of informing and educating consumers remains ahead of us.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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