SUNLIGHTAND SKIN: NOT ONLY AGING

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The skin has many endogenous chromophores that can absorb UV and visible radiation: nucleic acids, aromaticaminoacids (such as tyrosine, tryptophan, and histidine), peptide bonds and keratin, lipoproteins, melanin, heme derivates.

Several exceedingly interesting data are now known on the biological effects of sunlight irradiation on human skin, concerning UVB, UVA and also visible light.

UVA can be absorbed by several chromophores within the epidermis and dermis while for UVB the most important cromophores are in the epidermis: nucleic acids and proteins. Radiations from 350 to 1200 nm are absorbed by melanin, the main chromophore in the epidermis.

UVA radiation, absorbed by skin chromophores essential for cell life such as NADH or flavin, causes oxidative stress leading to damage lipids, proteins and DNA and inducing alterations of many cell functions.

Experimental evidence for UVA oxidative stress has been given:

1) lipid peroxidation is induced, and is more evident in normal human fibroblasts than in keratinocytes.

2) UVA lipid peroxidation in cultured human fibroblasts is dose related, and cell membranes damage is inhibited by vitamin E.

3) lipid peroxidation by UVB is 10 to 100 times more efficient than UVA (in contrast with the generally higher biological efficiency of UVA versus UVB). But, due to the greater amount of UVA in the sun radiation, UVA is equally or more effective in this respect than UVB, under the normal conditions of sun exposure.

A significant protection of human fibroblasts against UVA peroxidation is played by glutathione and to a lesser degree by catalase, as UVA decreases the cellular content of catalase up to 85% and only glutathione to 15%.

The extent of lipid peroxidation appears inversely correlated with SOD content.

Low doses of UVA are able to decrease the release epidermal growth factor.

UVA efficiently inhibits antigen presentation by Langerhans cells in allogenic situations. This effect is inhibited by Vitamin E.

UV and longer wavelenghts of sunlight have a relevant effect on Langerhans cells and on urocanic acid in the epidermis, playing an intriguing role in skin immunomodulation and alterating normal skin immunoresponse.

UVB, UVA (and also PUVA treatments), as shown in several animal and human studies, are able to deplete surface markers of Langerhans cells and inhibit their function. The effects of VIS radiation on these cells are less known.

It has been shown (by our group)that VIS radiation depletes also, with a dose-dependent effect, Langerhans cells membrane markers in mice.

The ultraviolet-absorbing component of the stratum corneum urocanic acid is a deamination product of histidine. The trans form undergoes - under UV-light 290 to 340 nm - cis isomerization, which accumulates in the stratum corneum and diffuses into deeper epidermal layer or is eliminated with sweat and differentiated keratinocites.

Cis-UCA is considered to play an important role in the mechanism at immunosuppression; experimental data evidentiated alteration of Langerhans cells and suppression of contact hypersensitivity (mediated by epidermal TNF-α).

Since the wavelenght dependence for cis-UCA production in mammalian skin is reported to extend to higher wavelenghts, broadband UV sunscreens are necessari against cis-UCA production.

Together with the direct or indirect mentioned actions on the skinimmune system, UVA rays can induce complex photosensitization reactions. Some dermatoses can be caused by exposure to sunlight.

Photodermatoses include a group of diseases in which unidentified endogenous substances interact with specific UV or VIS radiation to produce a clinico-pathological entity.

Some of these occur frequently in this Country, such as mild cases of Polimorhous Light Eruption (PMLE) and Solar Urticaria; other more episodic forms include chronic actinic dermatitis (photosensitive eczema, chronic photosensitivity dermatitis, persistent light reaction, actinic reticuloid) more severe variants of PMLE, actinic prurigo and others. UVA rays are strongly implicated in the aetiology of these group of dermatoses, either alone or in synergy with UVB.

<u>Solar urticaria</u>

This disorder is characterized by pruritic erythema and wheals after sun exposure, manifestations that sometimes restrict normal daily life in summer.

In our Department 57 cases of this photodermatose were studied. The skin type was:21% s.t. II, 68% s.t. III and 11% s.t. IV. Eliciting wavebands were: 67% VIS, 28% UVA, sunlightradiations for the few others. Time between onset and complete disappearance was from 2 to more than 6 yrs. In this series solar urticaria resulted a longlasting disease affecting both sexes frequently under thirty of age. In about one fourth of cases it was associated with dermographic urticaria or with a history of atopic dermatitis. Eliciting radiation were mainly VIS blu to green (400-500 nm) or UVA (While studies in North Europe and USA show a major role played by UVA).

Polimorphous light eruption

Otherwise healthy persons develop a pruritic eruption appearing on exposed areas, few hours or days after sunlight exposure. Half of the patients show an action spectrum of the disease in the UVA range, one fourth react to both UVA and UVB and others react primarily to UVB.

PMLE appears to be a manifestation of a delayed hypersensitivity reaction, and actived lymphocytes predominate in skin infiltrate. An inherit trait may be considered (autosomal dominance with reduced penetrance in some cases).

Benign Light Eruption

Benign Light Eruption (LEB) is considered a distinct entity by our group, in agreement with Thomas and other French authors; some of these cases might have been published in English literature as mild cases of PMLE.

According to our study of 200 cases of these forms, LEB can be differentiated according to: distribution of clinical lesions, time elapsing for their manifestation, and phototests.

Sunlight tolerance increases as exposure is continued. The fact that the face is frequently spared is probably an expression of the “hardening” effect due to UV radiation, the face being very frequently exposed to sunlight.

Chronic actinic dermatitis

This term encompasses photodermatoses presenting several common aspects and an abnormal sensitivity to UVB. Common features of this spectrum of forms, previously individually described as photosensitive eczema, chronic photosensitivity dermatitis, persistent light reaction, actinic reticuloid, are: 1) incidence prevalent in men older than 50 years of age; 2) longlasting pruritic dermatitis of sun exposed areas with eczema and lichenification; 3) persistence through the entire year; 4) variable result of phototesting: abnormal minimal erithema dose (MED) to UVB, with or without abnormal MED to UVA and sensitivity to VIS; 5) photopatch tests positive in patients with persistent ligh reaction; 6) patch tests positive to plant antigens (Compositae). It has been postulated that in these forms the chronic inflammatory process may be induced by transformation of a skin chromophore into an endogenous photoreactive persistent antigen.

Exogenous photosensitizations include phototoxic and photoallergic mechanisms of reaction, that may be differentiated according to sensitizing substance and other aspects. The most susceptible areas of the body, as for other photodermatoses, are those exposed to sun with prevalence: ears, nose, cheeks, nape, lateraland lower regions of the neck, arms and the hands.

Phototoxic reactions occur more frequently and manifest like intense sunburn. The great majority of potential phototoxins (psoralens, porphyrins, cyclin antibiotics, certain non-

steriod antinfiammatory substances, benzoylperoxide, tars and others) and photoallergens (certain perfumes, allergens of vegetable origin, some antibiotics, some non steroid anti-inflammatory substances, and some neuroleptics) are activated by UVA.
Most phototoxic photosensitivity reactions are oxygen dependent (photodynamic action). The photosensitizer is converted in a compound participating with high probability in photobiologic reactions; or in presence of oxygen absorption of UVA rays by some molecules leads to the formation of radical states and singlet oxygen, toxic to cells (e.g. haematoporphyrins used in photodynamic phototherapy). Other molecules can be transformed without oxygen into toxic products under UVA irradiation, and the photoproducts react with other endogenus molecules (e.g. binding of psoralens to DNA).
Phototoxic reactions mediators include histamine, proteases and prostaglandine, complement, and others.

Potentially photoallergenic conpounds form photoproducts capable of attachingto a protein. The antigen, presented to the Langerhans cells, via the activation of T lymphocytes initiate the chain of events involved in delayed contact hypersensitivity. The active radiation is in the Visible range, UVA and also UVB spectra. The action spectrum of the disease indicates the spectrum of irradiation required by the photosensitizing chemical to produce skin manifestation and, for most chemicals, is similar to the absorption spectrum of the photosensitizer. Not all drugs absorbing radiation produce a photochemical reaction in the skin: this depending also on variables such as percutaneous absorption, metabolic alteration, combination with a substrate, stability and solubility. The mechanism involved depends on topical applications or systemic ingestion of the drug (e.g. systemic photoallergic reactions are much less frequent than topical ones).
Some drugs are able to induce both a photoallergic and/or a phototoxic reaction; and others may increase the subject photosensitivity to non ionizing EM radiation with a mechanism that probably involves neither a phototoxicnor a photoallergic reaction.
Most photoallergic reaction are mediated by rare topical agents. Only few drugs (such as phenotiazimes, chloropromazine, sulfa-derived products and NSAIDs) are systemic photoallergens.

The number of drugs photosensitizers is not exceedingly large: probably about 50 groups. Here can be mentioned only few more common drugs.
<u>NSAIDs. Piroxicam</u>
This compound and its photodecarboxylated product induced by UVA produce damage to cell membranes, particularly to mast cells and leukocytes. Beside this photoxic mechanism it has been suggested generation of haptens and a photoallergic reactions.

Quinolone -derived antimicrobial agents (chloroquinolones) induce phototoxic effects in the UVA range: sunburn erythema, eczematous and edemato-bollous reactions. (The most potent is considered perfloxacin).

Tetracicline group

Among the compounds of this group a lower index of phototoxicity is assigned to tetracicline (parent compound) and to minocycline compared to doxycicline and DMCT. Their phototoxicity reaction is in the UVA range; dependent on oxygen and complement; and damages cell membranes and DNA.

Phenotiazines

These are phototoxic agents that can also produce photoallergic reactions. In this group chloropromazine induces a complex with melanin and clinically hyperpigmentation. Its is interstingthat the multiple metabolites of this drug have each one a different action spectrum within the UVA range.

Amiodarone

The photoreaction is due to the photoproduct desethylamiodarone and to direct cell membrane injury. The process produces clinically hyperpigmentations.

Tars and their constituent cyclic hydrocarbons. If the skin is exposed to UVA can produce intense smarting but no evident inflammation.

(Sunlight Cosm. Derm.)

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