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Local and Systemic Effect of Ultraviolet Irradiation (UVB and UVA) on Human Allergic Contact Dermatitis

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In subjects hypersensitive to nickel we have investigated local and systemic effect of whole body exposure of cumulative suberythema UVB doses as well as solarium-UVA exposure. UVB possesses both locally and systemically a suppressive effect on human allergic contact dermatitis, but UVA has no such effect. The systemic suppressive effect of UVB might be of therapeutic importance in patients with severe chronic dermatitis of the hands when adding this effect to a local suppressive effect. Also, patch testing should not be performed during UVB and/or overt sun exposure. (Received October 29, 1985.)

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The effect of UVB on induction and elicitation of allergic contact dermatitis (ACD) has attracted attention during the last few years (1–11, 17). Also the effect of UVA alone (12), but mostly in combination with psoralen (13–15) is a topic of great interest in photoimmunology. Restricting our interest to the effect of ultraviolet radiation (UVR) to the, from a clinical view, important efferent phase of ACD, it has been shown that UVB irradiation before elicitation decreases the intensity of experimental ACD in the guinea pig and the mouse (4, 6, 17). Contradictory results on the effects of applying a single dose of UVB on human allergic patch test reactions are reported, one showing suppression (7), the other no suppression of ACD (16). To our knowledge it is not yet documented if human ACD will respond to cumulative whole body UVB treatment, which is an effective treatment of psoriasis and endogenous eczemas (atopic-nummular eczema).

Several reports on experiments with mice (2, 3, 10, 11) have established a systemic suppressive effect of UVR in the afferent phase of ACD. Two contradictory reports in regard to systemic suppression of elicitation of ACD in experimental animals have been published (5, 6), but it is not investigated if such an effect exists in humans.

We wanted to investigate if repeated whole-body suberythema doses of UVB or/and solarium UVA exposure can decrease the intensity of human ACD either locally or systemically.

MATERIAL AND METHODS

Design of the study

The study was divided into two separate parts investigating the effect of UVB and UVA, respectively. The UVB-part of the study was performed from February–April and the UVA-part approximately 9 months later to avoid the influence of overt sun-exposure.

Subjects

Ten female subjects (mean age 34, range 22–44 years) hypersensitive to nickel as proved by earlier patch testing were enrolled in the study. Seven subjects participated in both parts of the investigation, two subjects only in the UVB-part and one subject only in the UVA-part (Tables I and II).

Patch testing before UVR

To determine the degree of individual hypersensitivity the left side of the upper back in each individual was patch tested, with a serial dilution of $NiSO_4$ ($6H_2O$) in distilled water with the following concentrations: 2.4%, 0.6%, 0.125% and 0.0375%. 20 µl of each concentration was micropipetted to filter paper discs in Finn Chambers® (Epitest Ltd, Finland) on Scanpor®, then immediately put on the back and applied for 48 hours, read 24 hours later and scored in the following way: 0 = no reaction, 1 = erythema and infiltration, 2 = erythema, infiltration and papules, 3 = erythema, infiltration, papules and vesicles/exudation. The 7 subjects particpating in both studies were tested before entering the UVB as well as the UVA part of the investigation.

Irradiation with UVB

After primary hypersensitivity screening 9 subjects started whole-body UVB irradiation. The light source was 26 Sylvania F 75/85W/UV21 fluorescent bulbs mounted in a Waldmann UV 1000 cabine emitting a spectrum of 230–365 nm with maximum at approximately 310–315 nm. The irradiance was 1.8 mW/cm^2 at a distance of 20 cm as determined with a UV-meter, Herbert Waldmann, Werk für Lichttechnik, Schwenningen, FRG. Each subject was irradiated 4 times a week for three weeks. The initial dose was related to skin type starting with a minimum of 30 s and then steadily increasing with 30 s at a time if erythema was not present, resulting in a total mean dose of UVB 5.3 J/cm^2, range 3.3–8.3 J /cm^2. Before each irradiation the same area (15×10 cm) on the upper right back was covered with a material allowing no penetration of ultraviolet light.

Table I. *Test scores for each subject before and after UVB irradiation*

		Retesting after UVB	
Subject	Testing before UVB	Irradiated site	Non-irradiated site
1[a]	10	4	9
2[a]	10	8	8
3[a]	11	3	4
4[a]	8	4	5
5[a]	9	4	8
6[a]	5	3	3
7[a]	8	1	6
8	4	0	1
9	4	0	3
Total	69	27	47

[a] These subjects participated also in the UVA part of the investigation.

Table II. *Test scores for each subject before and after UVA irradiation*

		Retesting after UVA	
Subject	Testing before UVA	Irradiated site	Non-irradiated site
1[a]	11	10	10
2[a]	11	8	10
3[a]	11	7	10
4[a]	6	7	5
5[a]	10	9	9
6[a]	11	9	11
7[a]	6	7	8
8	10	10	11
Total	76	67	74

[a] These subjects participated also in the UVB part of the investigation.

Irradiation with UVA

After primary hypersensitivity screening 8 subjects started whole-body UVA irradiation. The light source was 20 Philips TL 85–100 W/09N UVA fluorescent bulbs mounted in a Philips UVA solarium unit (type HP3126 and type HP3016) emitting a spectrum of 300–430 nm with a maximum at approximately 350 nm. The irradiance of UVA was 9.5 mW/cm^2 at a distance of 5 cm as determined with a PUVA-meter, Herbert Waldmann, Werk für Lichttechnik, Schwenningen, FRG. The irradiance of UVB from these bulbs was 0.0001 mW/cm^2. Each subject was irradiated for 30 min 4 times a week for 3 weeks resulting in a total dose of UVA 205.2 J/cm^2 and UVB 0.02 J/cm^2. Here too a 15×10 cm area on the right back was covered before each irradiation.

Retesting after UVR

Immediately after the last UVB or UVA exposure each subject was retested with the same nickel concentrations as before UVR exposure on the irradiated and non-irradiated upper right back, respectively. The results of the test readings before irradiation were kept in a separate file to avoid influence on the reading after UVR exposure. The test scores (before as well as after UVR) for each concentration and individual subject were summarized and the results compared to each other by the use of Wilcoxon paired rank sum test for non-parametric variables.

RESULTS

UVB irradiation

The results of the test reading before and after UVB irradiation are presented in Table I. Comparing the scores at primary testing with the scores after UVB on irradiated as well as non-irradiated sites significant differences were observed ($p<0.01$ and $p<0.01$, respectively). There was also a significant difference ($p<0.01$) between the retested irradiated and non-irradiated areas.

UVA irradiation

The results of the test reading before and after UVA irradiation are presented in Table II. No significant differences between the test scores before and after irradiation were observed.

DISCUSSION

With reservations for the difficulties in performing the present experimental study under double blind conditions due to the hyperpigmentation, we believe it was clearly shown that the elicitation of human ACD was suppressed by suberythema cumulative doses of UVB. The effect was evident on exposed as well as on covered skin implying both a local and a systemic suppression. This effect could not be demonstrated by UVA, neither locally, nor systemically.

Seven subjects participated in both studies. They were retested before entering the second part. At that time, they had regained their original hypersensitivity indicating that the suppressive effect of UVB did not last nine months. An interesting observation refers to patient number 6. As shown in the tables this subject had a lower degree of hypersensitivity before entering the UVB part than before entering the UVA part of the study. Later on it turned out that this subject was pregnant in the fourth week when tested before the UVB part (Table I) but was tested before the UVA part five weeks after delivery (Table II). This observation is in agreement with results reported in the guinea pig (18).

Our study is solely based on morphological observations, and we can only speculate about the pathogenetic mechanisms involved.

In several studies reviewed by Silberberg-Sinakin & Thorbecke (19), it is indicated that Langerhans' cells (LC) play an essential role during the elicitation phase of ACD. Several studies in humans as well as in experimental animals indicate that LC density and

morphology is affected by UVR, especially when higher doses are applied (20-22). This alteration in LC, however, cannot alone be the explanation of the diminished ACD following UVB exposure (11).

This diminished ACD following UVB exposure in mice is associated with the development of antigen-specific suppressor T lymphocytes (1). This is true, if the antigen is applied on directly exposed sites, but also (although larger doses of UVB are needed) when applied on a non-irradiated site. This might be one explanation why UVB diminishes ACD (23).

To bring about an optimal helper T cell stimulation a non-specific hormonlike substance, Interleucin I (Il-I) is needed (24). Il-1 is produced by macrophages and LC and a similar substance called ETAF by the keratinocytes. The production of ETAF is decreased by UVB (25) and this might be another reason for diminished ACD after UVB exposure.

Recently it has been proposed that E-urocanic acid, a metabolite of histidine which accumulates in the skin, serves as a chemical photoreceptor for UVB irradiation and transduces this stimulus to the immune system (26). Till now it has not been shown, however, if urocanic acid is the trigger factor for initiation of formation of suppressor T lymphocytes.

Granstein et al. suggest that there are two different kinds of antigen presenting cells in epidermis (27). One is the UV-sensitive LC, which by activating helper T-cells enhances the ACD. The other cell is UV-resistent and activates the suppressor T lymphocytes.

Whatever the mechanisms are, Mørk & Austad (28) have reported a good clinical effect of UVB in patients with ACD of the hands. Whole-body exposure together with extra exposure of the hands, taking advantage of local as well as systemic suppression by UVB, might be an even more effective therapeutic regimen in patients with severe ACD of the hands. Another practical conclusion of the present result is, that in order to avoid false negative test reactions, patch testing in connection with UVB treatment or overt sun exposure should not be performed.

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