

The Influence of Locally Administered Ultraviolet Light (UVB) on the Allergic Contact Dermatitis in the Mouse

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A quantitative model of contact allergy to picryl chloride in the mouse was used to evaluate the influence of locally administered ultraviolet light (UVB) on sensitization and challenge. UVB was given in three different doses immediately before and 24 h before sensitization and challenge, respectively. A suppressive effect was demonstrated on the afferent as well as on the efferent limb of the allergic reaction. *Key words: Contact allergy; mouse; Sensitization; Challenge.* (Received March 23, 1985.)

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During the last decade there has been an increasing interest in the pathogenesis of the allergic contact dermatitis. In this connection, the possible influence of ultraviolet light on the allergic reaction has been the subject of several experimental studies, directed on the afferent as well as on the efferent limb. Several of the results reported though, have been contradictory, perhaps due to differences in protocols or in species. The present study was initiated to investigate the possible effects of UVB on the allergic contact dermatitis in the mouse using a quantitative and reproducible technique.

MATERIALS AND METHODS

Animals. Female NMRI albino mice were obtained from Anticimex AB, Stockholm, Sweden. Their weight was about 25 g, and their age 2-3 months when starting the experiments. Each experimental group contained 10 animals.

Drugs. Picryl chloride (PC) a well known sensitizer, was obtained from BDH Chemicals Ltd, Poole, U.K. Mebumal Vet® 60 mg/ml was obtained from ACO Läkemedel, Solna, Sweden. It was dissolved in saline to a concentration of 6 mg/ml.

Epicutaneous sensitization

PC 7% dissolved in ethanol was painted on the shaved abdominal skin once.

Challenge and evaluation

One week after sensitization the animals were painted on the dorsal side of both ears with 0.25% PC dissolved in olive oil (1). The mice were killed 24 h later by a blow on the head. The ears were excised and weighed before and after a drying procedure consisting of exposure to 110°C for three hours in an oven. The relative water content of the tissue, the "wet weight" (WW), was calculated as follows.

$$WW = \frac{WE - DE}{WE} \times 100$$

WE=wet ear weight, DE=dry ear weight.

Mean values for each group were used for statistical evaluation which was performed with the Student's *t*-test. When variances differed too much the Wilcoxon two sample test was used.

Irradiation

Exposure with ultraviolet light was given once with two FS-40 Sunlamps (Westinghouse, Bloomfield, NY). The average irradiance for the integrated 280-320 nm (UVB) waveband was 2.5 m W/cm², as

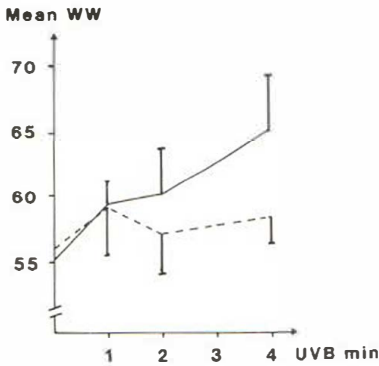


Fig. 1. The tissue wet weight of mouse ears 24 h (---) and 48 h (—) after different UVB doses. Mean values and SD.

measured with a UV meter (Waldmann AG, Schwenningen, FRG) at a distance of 12 cm from the light source agreeing with the distance to the exposed mouse skin.

Fixation

An i.p. injection of 1.8 mg Mebumal Vet® kept the animals unconscious for 90 min. Anesthetized animals were fixed with a shield for the eyes enabling the dorsal aspects of the ears or the abdomen to be fully exposed to the irradiation. All animals recovered completely after anesthesia.

Experimental design

Study I: The effect of UVB only. Eight groups were examined: A control group receiving no UVB; three groups of animals given 1, 2 or 4 min of UVB corresponding to 150, 300 and 600 mJ/cm², respectively. The WW of the ears was measured 24 h later; a control group receiving no UVB; three groups of animals given 1, 2 or 4 min UVB. The WW of the ears was measured 48 h later.

Studies II-III: The effect of UVB on sensitization. Study II: Animals were sensitized by PC on the abdomen and the test solution was administered 7 days later on the ears. Five groups were examined: Animals sensitized only; animals sensitized and challenged; three groups of animals given 1, 2 or 4 min UVB irradiation on the abdomen 24 h before sensitization and challenged 7 days later. Study III: This study was designed exactly like study II except that the irradiation took place immediately before sensitization.

Study IV-V: The effect of UVB on elicitation. Study IV: This study was designed exactly like study II except that UVB was given 24 h before challenge instead of before sensitization, and on the ears instead of the abdomen. Study V: This study was designed like study IV except that UVB was given immediately before challenge.

RESULTS

Study I

UVB alone induces an edema at exposed sites. To measure this effect and make it possible to separate the UVB edema from that induced by the allergic contact dermatitis in studies IV and V the following study was performed: the same doses of UVB and the same time lapses between exposure and sacrifice of the animals were used in this study as in studies IV and V (Fig. 1).

UVB irradiation of mouse ears for 1-4 min induced a statistically significant edema at 24 h though not more with 2-4 min than with 1 min. Also when measured after 48 h, 1-4 min of UVB irradiation resulted in a statistically significant edema. In this study, however, the edema from 4 min UVB was significantly stronger than that from 1-2 min (Fig. 1).

Study II

This study examined the effect on the allergic reaction of UVB given 24 h before sensitization. The results together with the statistical evaluation are summarized in Table I.

Table I. UVB given 24 h before sensitization

The mean wet weight of mouse ears and statistical difference between the experimental groups

Group No.	UVB (min)	Sensitization	Challenge	Mean WW	I	II	III	IV	V
I	—	+	—	56.3					
II	—	+	+	62.7	***				
III	1	+	+	60.8		**			
IV	2	+	+	58.8		***	***		
V	4	+	+	57.9		***	***	*	

*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$.

Compared to the nonexposed animals the groups which were irradiated 24 h before sensitization all showed a diminished response to the challenge. The reduction was more pronounced the more irradiation was given.

Study III

This study examined the effect on the allergic reaction of UVB irradiation given immediately before sensitization. The results together with the statistical evaluation are summarized in Table II.

Compared to the nonirradiated animals the group receiving 1 min UVB immediately prior to sensitization showed no significant reduction in ear wet weight. The groups exposed to 2 and 4 min UVB, however, showed a reduction in the edematous response. This reduction was more pronounced after 4 min exposure to UVB than after 2 min.

Study IV

This study examined the effect of UVB irradiation on the allergic reaction of the ears when given 24 h before challenge. The results together with the statistical evaluation are summarized in Table III.

Compared to the nonirradiated control group the animals receiving 2 and 4 min UVB had significantly higher WW. The group exposed to 4 min UVB had significantly more edema compared to the group exposed to 1 and 2 min UVB. Considering the edema induced by UVB alone (see study I), however, one would have expected an even higher WW if UVB had no decreasing effect (see below).

Table II. UVB given immediately before sensitization

The mean wet weight of mouse ears and statistical difference between the experimental groups

Group No.	UVB (min)	Sensitization	Challenge	Mean WW	I	II	III	IV	V
I	—	+	—	55.7					
II	—	+	+	63.9	***				
III	1	+	+	63.1		NS			
IV	2	+	+	61.7		***	*		
V	4	+	+	60.0		***	***	*	

*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$. NS = not significant.

Table III. UVB given 24 h before challenge

The mean wet weight of mouse ears and statistical difference between the experimental groups

Group No.	UVB (min)	Sensitization	Challenge	Mean WW	I	II	III	IV	V
I	—	+	—	56.1					
II	—	+	+	62.6	***				
III	1	+	+	63.2		NS			
IV	2	+	+	64.6		***	*		
V	4	+	+	69.9		***	***	***	

*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$. NS = not significant.*Study V*

This study examined the effect of UVB on the ears given immediately before challenge. The results together with the statistical evaluation are summarized in Table IV.

Compared to the nonirradiated animals the group receiving 1 min UVB immediately prior to irradiation showed no decrease in the challenge response.

The other groups, however, showed a slight but significant decrease in the challenge response.

DISCUSSION

These studies demonstrate that exposure of mice to UVB irradiation reduces the allergic contact dermatitis to PC. This is clearly shown when UVB is given before sensitization and immediately before challenge, but there is probably a suppressive effect when UVB is given 24 h before challenge too. According to study I there is a marked edema of the mouse ears from the UVB doses used throughout the studies. The edema after 1 min irradiation is about the same when measured after 24 and 48 h. However, there is no further increase after 2 and 4 min exposure when measured after 24 h. After 48 h, however, there is a significantly higher and increasing WW after the same light exposures (Fig. 1). Consequently, the edema expected from the exposure 24 h before challenge would be even stronger than the edema actually observed (Table V).

There are at least two possible explanations for this difference in expected and found values. The first is that UVB does in fact produce a suppressive effect of the allergic

Table IV. UVB given immediately before challenge

The mean wet weight of mouse ears and statistical difference between the experimental groups

Group No.	UVB (min)	Sensitization	Challenge	Mean WW	I	II	III	IV	V
I	—	+	—	56.3					
II	—	+	+	64.1	***				
III	1	+	+	63.4		NS			
IV	2	+	+	62.2		**	NS		
V	4	+	+	62.6		*	NS	NS	

*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$. NS = not significant.

Table V. Edematous response (wet weight increase) to UVB exposure and to allergic challenge

These two events (arithmetic sum) are compared to the values actually found in study IV

UVB (min)	UVB alone (Study I) % increase in WW	Challenge alone (Study IV) % increase in WW	Summation % increase in WW	Study IV % increase in WW
1	7.6	11.6	19.2	12.7
2	10.2	11.6	21.8	15.2
4	19.1	11.6	30.7	24.6

contact dermatitis, but the edema induced by the UVB exposure alone is too marked to make this decreasing effect demonstrable. The second explanation is that it is not biologically possible to induce a higher tissue WW than 70%. It has been shown, however, that an experimental edema of mouse ears around 75% WW or more is far from unusual (1). This means an increase in WW of 33–35%.

In the guinea pig, it was shown (2) that UVB when given 7 days prior to sensitization and in the interval between sensitization and challenge at the site of challenge had a suppressive effect on the allergic contact dermatitis. From this study it was impossible to decide if the suppression was on the afferent or efferent limb of the allergic contact dermatitis. The difficulty is strengthened by the fact that UVB, when given to mice before sensitization, has a systemic suppressive effect (3–7). There are, however, studies investigating and separating the local effect of UVB prior to sensitization and challenge respectively.

Thus, Morison et al. (8) showed that UVB prior to elicitation had a suppressive effect on the allergic contact dermatitis in guinea pigs. This was later confirmed by Austad & Mørk (9), and, in the present work, now also in the mouse.

Morison et al. (8) found no suppressive effect in the guinea pig when UVB was given locally on the area of sensitization before and after this procedure. In mice, however, Toews et al. (10) showed that UVB given before sensitization upon that very spot inhibited the allergic reaction. This was confirmed in the present study using different time intervals between light exposure and sensitization.

For ethical and practical reasons, only few similar studies in man have been published. In psoriatic patients Nusbaum et al. (11) showed that UVB irradiation made these patients to a less extent allergic to a subsequent treatment with nitrogen mustard. According to Friedmann et al. (12) psoriatic patients undergoing an Ingram regimen (UVB + anthralin) showed a reduced responsiveness to DNCB sensitization. Kalimo et al. (13) treated patients with a known allergic contact dermatitis with UVB once on a limited area and showed that the allergy diminished by 80%. These findings were not confirmed in a similar study from our department (14). With repeated exposures to UVB given as whole-body treatment, however, the contact allergy was clearly reduced (15).

The contradictory results quoted above may be due to differences in protocols or in species. The mechanisms behind the suppressive effect of UVB on allergic contact dermatitis are not fully understood. Langerhans' cells (LC) are believed to be one important link in establishing an allergic contact dermatitis. It has been shown that UVB irradiation depletes the skin of recognizable LC both in humans (16, 17) and animals (18). Whether this absence of recognizable LC is the cause of the suppressive effect of UVB irradiation is still a matter of dispute.

With regard to the systemic depressive effect of UVB, however, it was recently shown (7) that the LC have no mediating importance. UVB may instead produce a photoproduct in the skin leading to the formation of antigen-specific lymphocytes (3).

Although the mechanisms behind the suppressive effect of UVB irradiation upon the allergic contact dermatitis are not yet known this effect may evidently be used clinically, e.g. for pretreating subjects with the risk of being exposed to potential allergens, or for treating patients with established contact dermatitis (19). We further believe that this therapy should be given as whole-body treatment to utilize the systemic suppressive effect of UVB irradiation.

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