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5-S-CYSTEINYLDOPA AND PIGMENT RESPONSE TO UVA LIGHT

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Abstract. 5-S-Cysteinyldopa concentrations in serum were studied in healthy individuals exposed to daily high-intensity UVA radiation. A marked increase in 5-S-cysteinyldopa was found after 3 days, and in some individuals concentrations were still higher after 7 to 10 days. The immediate pigment darkening (IPD) and delayed tanning (DT) were weak or absent at pressure sites, i.e. in skin with a low concentration of oxygen.

Key words: 5-S-Cysteinyldopa; UVA light; Melanocytes; Immediate pigment darkening; Delayed tanning; Pressure sites; Oxygen

Evaluation of the risks and benefits of UVA radiation has achieved considerable importance owing to the proliferation in recent years of private "clinics" and beauty salons for administering UVA for cosmetic reasons. There is also medical concern about the marketing of sunbeds for use at home. The average sunbed consists of a transparent Perspex (polymethyl methacrylate) plate for the subject to lie on, over a bank of UV-emitting fluorescent low-pressure mercury-discharge tubes (4). Skin is exposed, front and back, for about 30 minutes each day. With such a unit the skin might receive 20 J/cm² of UVA, which is roughly twice the dose received during a similar length of time in the tropical midday sun (4).

UVA irradiation causes both immediate and delayed melanin pigmentation (12, 14). We have reported a marked increase in the urinary excretion of the melanocytic metabolite 5-S-cysteinyldopa and increased concentrations in serum of patients with psoriasis after 3 days' PUVA treatment, at which time no pigmentation could be observed. The highest urinary and serum concentrations of 5-S-cysteinyldopa were noted after 1 to 2 weeks' treatment (1, 9).

The aim of the present study was to investigate the chemical events in the melanocytes after exposure to UVA light alone, as reflected by changes in the serum concentrations of 5-S-cysteinyldopa.

MATERIAL AND METHODS

10 healthy volunteers were studied. None were receiving any drugs. There had been no exposure to strong sunlight or other ultraviolet radiation during the 2 to 3 months before the investigation, which took place in December and February in order to avoid influence of sun exposure (15).

The light source was a high-intensity UVA system (Philips TL 85 W/09 T) with an emission spectrum of 310–420 nm and a peak emission of 355 nm. About 0.4% of the radiant energy output of this light source is in the UVB region. The light source consisted of 10 tubes above which was a transparent plate of acrylic plastic for the individual to lie on. Using a Waldmann UVA-meter (H. Waldmann Werk für Lichttechnik, Germany) the intensity of the lamp in the UVA region primarily around the 360 nm band was estimated to 11 mW/cm² just above the plate. Skin was exposed, front and back, for 30 minutes on each side per day on 10 successive days.

10 ml venous blood samples for 5-S-cysteinyldopa analysis were collected in glass tubes containing 10 mg sodium metabisulphite 3 days before and just before the UVA irradiation series was started, and after 1, 3, 4, 7, 8, and 10 days' irradiation. Centrifugation of the samples was at 4500 rpm for 10 min within 1 h. Serum was precipitated with 1/10 volume 4 M perchloric acid, centrifuged at 15000 rpm, and filtered. 5-S-Cysteinyldopa was absorbed onto Al_2O_3 at pH 8.6, eluted with 1 ml 1 M perchloric acid, and then determined by high-performance liquid chromatography (HPLC) and electrochemical detection (6).

RESULTS

Pigment response

The immediate pigment darkening (IPD) and delayed tanning (DT) were studied. A shielded rectangular area on one of the buttocks served as control for judging pigmentation on exposed areas.

The IPD reaction was first seen when the subject turned on the sunbed after the first 30-min irradiation. It was present over the whole body except for the most prominent parts of the scapulae, the medial sacral areas, the skin over the ventral prominence of the head of the humerus, and the prominent areas of the anterior ribs. These areas showed pallor lasting 1 or 2 seconds after turning or rising from the

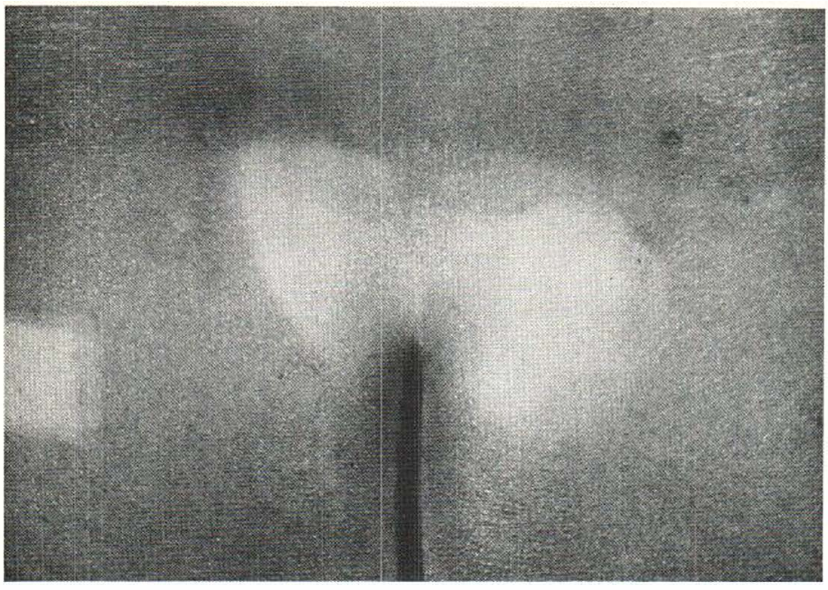

Fig. 1. Lack of pigmentation at pressure sites over the medial sacral area after 10 days' UVA irradiation. Shielded control area on the left.

sunbed, followed by erythema lasting 10–15 min, followed by paling (Table I). The areas of pallor contrasting to the general IPD reaction were seen in 9 of the 10 subjects, and were most pronounced in lean persons. The only subject who did not display areas of weak or absent IPD reaction was a rather obese man. The IPD reaction was most pronounced in individuals with skin type IV, and weakest in those with skin type I (Table II) (2, 12).

The DT, which appeared after 2 to 3 days, was most pronounced in persons with skin type IV and weakest in those with skin type I. After 2 to 3 days all but the skin type IV subjects developed an erythematous reaction on the previously non-sun-exposed buttock skin. Subjects P-I. C. and F. N. (skin type I) developed erythema also on the abdomen and dorsum, and reported some itching on these areas for 2 to 3 days. Areas where IPD was weak or absent also showed weak or absent DT (Figs. 1 and 2). No erythematous reaction occurred in these areas, except during the first 10–15 min after irradiation (Table I). After 1 to 2 months these hypopigmented areas were still discernible although the tanning of surrounding skin was fading.

Table I. *Skin reactions during UVA irradiation in areas exposed to pronounced pressure compared with other skin areas.*

	Pressure areas	Other areas
Immediate pallor (a few sec. duration)	Yes	No
Immediate erythema (10–15 min duration)	Yes[a]	No[b]
Delayed erythema (starting after 2–3 days)	No	Yes[c]
Immediate pigment darkening	No	Yes
Delayed tanning	No	Yes

[a] This erythema appeared after 30 min even when the lamps were not switched on, and must therefore have been caused by the pronounced pressure.
[b] Slight erythema probably caused by the heat sometimes appeared on areas not exposed to pronounced pressure.
[c] This erythema was observed on previously non-sun-exposed gluteal region.

Table II. *Clinical data on 10 healthy individuals*

Individual	Age	Sex	Hair colour	Eye colour	Skin type[a]
P-I. C.	32	♂	Brown	Blue	I
F. N.	25	♂	Brown	Green	I
F. N-n.	29	♂	Blond	Green	II
C. B.	25	♀	Brown	Brown	II
P. O.	31	♂	Brown	Blue	II
U. M.	25	♀	Brown	Blue	III
D. F.	25	♂	Blond	Blue	III
B. M. B.	24	♂	Brown	Brown	IV
A. M.	25	♂	Brown	Blue	IV
P. S.	23	♀	Blond	Blue	IV

[a] The following criteria were used: Skin type I = always burn, never tan; II = always burn, then slight tan; III = sometimes burn, always tan; IV = never burn, always tan.

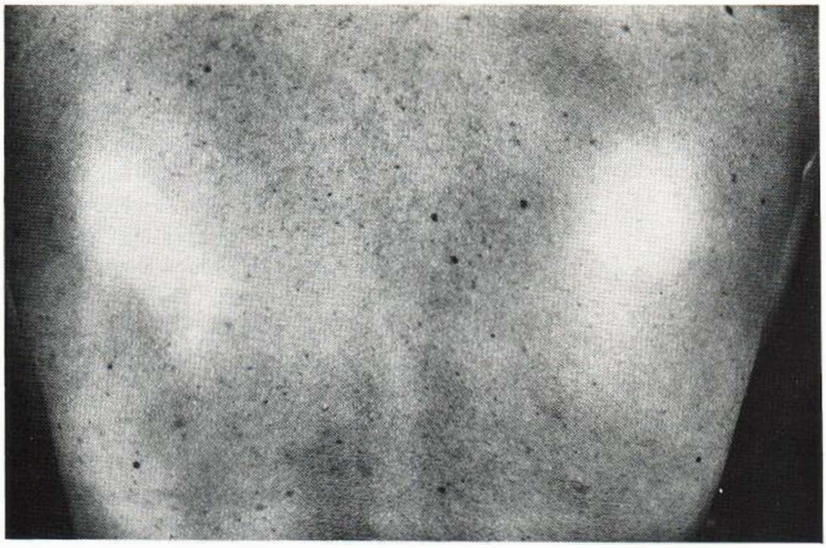

Fig. 2. Lack of UVA-induced pigmentation at pressure sites over the scapulae.

5-S-Cysteinyldopa response

The concentration of 5-S-cysteinyldopa in serum just before irradiation was 1.2–5.0 ng/ml (mean 2.6 ng/ml serum) (Table III), i.e. within the normal range (7, 8). After 3 days 5-S-cysteinyldopa values had increased in all persons (Table III and Fig. 3). All now showed increased pigmentation, and all but those with skin type IV had erythematous reactions. After 4 days the mean concentration in serum was 2½ times higher than the initial value, and it remained at this level to the end of the experiment after 10 days (Fig. 3). In 4 persons a further blood sample was collected 18 days after starting irradiation, i.e. 9 days after completing the course of the irradiation; in 3 the serum concentrations of 5-S-cysteinyldopa had returned to roughly the initial values, but in 1 (F. N.) the 5-S-cysteinyldopa level remained at about twice the initial value. However, this man showed one of the greatest increases in serum 5-S-cysteinyldopa at the end of the course of irradiation (Table III). The weakest 5-S-cysteinyldopa response was noted in 2 persons (D. F. and A. M.) with skin types III and IV. Another (B. M. B.), with skin type IV, showed a high 5-S-cysteinyldopa concentration after 10 days. 2 with skin types I and II (P–I. C. and C. B.) showed a marked 5-S-cysteinyldopa response.

DISCUSSION

All except persons with skin type IV developed erythema on the previously non-sun-exposed gluteal

Table III. *Serum concentrations (ng/ml) of 5-S-cysteinyldopa during UVA irradiation*

Individual	Before irradiation		Days after starting irradiation 1	3	4	7	8	10	18
P–I. C.	1.7	1.9	1.9	4.9	6.7	7.7	7.7	8.6	
F. N.	1.8	2.7	4.4	6.3	9.4	5.8	9.0	9.3	5.6
F. N-n.	2.6	2.1	4.1	5.1	5.0	5.4	5.3	4.9	2.2
C. B.	1.8	1.2	2.7	3.2	4.4	5.6	4.8	4.3	
P. O.	1.3	1.3	1.6	2.7	3.2	3.1	3.6	4.4	
U. M.	1.6	2.2	1.6	3.3	4.9	4.7	4.7	5.2	
D. F.		5.0	3.3	5.4	7.4	8.9	6.8	7.4	
B. M. B.	2.4	3.0	5.7	5.6	5.6	4.7	5.5	24.2*	3.9
A. M.	2.5	3.5	4.7	4.1	4.3	3.8	4.8	5.9	3.7
P. S.		2.6	2.8	3.1	7.8	7.5	6.0	5.1	

* Excluded from Fig. 3.

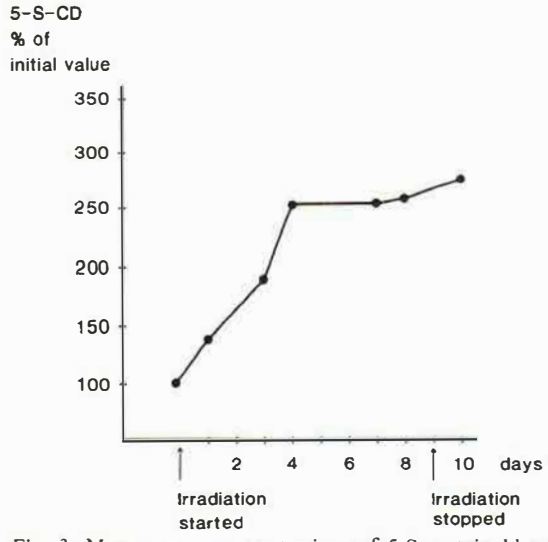

Fig. 3. Mean serum concentrations of 5-S-cysteinyldopa in 10 individuals during UVA irradiation (initial value = 100%).

region, and both with skin type I also developed widespread erythema. The erythematous reaction was first observed after 2 to 3 days. The inflammatory reactions were not unexpected, because the skin received daily doses of about 20 J/cm^2 of UVA. The minimal erythema dose for UVA is about 20–30 J/cm^2 (13). Detailed data on the time course of the erythematous response to UVA related to the dose of radiation of different wavelengths have been published by Kaidbey & Kligman (10). All our subjects showed increased serum concentrations of 5-S-cysteinyldopa after 3 days of irradiation, and some individual concentrations were still higher after 7 to 10 days. PUVA treatment leads to a greater increase in serum 5-S-cysteinyldopa (1, 9), and PUVA patients who developed pronounced erythema showed very high 5-S-cysteinyldopa concentrations at the time of the erythematous reaction. In the present study a great increase in serum 5-S-cysteinyldopa was noted in the type-I individuals who developed marked erythema, a finding which supports the hypothesis that increased 5-S-cysteinyldopa excretion from the melanocytes is related more closely to cell damage than to pigment response (1, 9).

The subjects lay fairly still on a hard transparent plate of acrylic plastic for 30 min at each session. After each irradiation the pressure sites showed reversible erythema, indicating transient disturbance of the circulation (5). The erythema disappeared after 10 to 15 min, and lack of pigmentation was noted at the pressure sites. These areas of pallor were observed even after the first irradiation, when the IPD reaction was noted on other areas. Oxygen is needed for the IPD reaction (3, 11, 14), and oxygen deficit at the pressure sites would probably explain the absence of the IPD reaction. However, in 9 of our subjects the pressure sites also showed weak or absent DT which could still be observed after 1 to 2 months. The man without obviously weaker pigmentation at pressure sites was rather obese, and had skin type I. His IPD and DT reactions were slight, so any contrasting effect would therefore be weak.

The weak or absent DT at pressure sites observed in our subjects is well known to laymen who use UVA-beds, but seems to have attracted little interest among dermatologists. According to Blum (3), erythema and melanization are not affected by oxygen deprivation during light-exposure. However, the oxygen deficiency is probably very pronounced at pressure sites under our experimental conditions, which may explain our findings of oxygen-dependent erythema and pigmentation. The weak or absent pigmentation of light-exposed skin at pressure sites with low oxygen concentration (5) suggests that light-induced oxygen radicals are of importance for erythema and the delayed pigment response.

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