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SPECTRAL SKIN SENSITIVITY IN ERYTHROPOIETIC PROTOPORPHYRIA

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In 1961 Magnus *et al.* (6) described a case of erythropoietic protoporphyria (EPP). Up to the present time about fifty cases of this condition have been published. Some special features of photosensitivity in EEP have lead us to examine the skin sensitivity to various wavelengths of sunlight by means of spectral filters used in light microscopy.

Case Report

We observed a 26-year-old female nurse who had suffered from hypersensitivity to light since two years of age. This hypersensitivity presented itself by burning sensations, itching and erythema and sometimes even by oedema of the skin exposed to light. These sensations appeared immediately after insolation and faded away in the course of 3 to 4 hours.

She had epidemic hepatitis at 9 years of age. Otherwise she had always been in good health. We observed no growth changes, curly hair, leuconychia or absence of the nail lunules (4, 5). Her hair was dark and eyes blue.

At the time of examination chronic eczematous changes on the back of the hands, on the nose and the forehead (Fig. 1), perioral painful fissures, dry desquamation of the lips and chronic anguli infectiosi were the outstanding features of the clinical picture.

The patient stated that the signs of hypersensitivity appeared when she was also exposed to sunlight passing through windowglass, the symptoms reaching considerable intensity. The difficulties also appeared in the winter season and were not reduced by topical sunscreens. During the summer the symptoms abated if the patient acquired a tan. Previous treatment with antihistaminics, antimalarial drugs and vitamins had not diminished her troubles.

An older sister of the patient and a cousin on the father's side had also suffered from hypersensitivity to sunlight from their early childhood. From the described distresses, clinical picture and familial occurrence we suspected an EPP condition. The finding of fluorescent erythrocytes in peripheral blood, a positive screening test according to Rimington and Cripps (11) confirmed the diagnosis. This is the second case of this condition reported in Czechoslovakia after Bielický (2) in 1967.

The presence of hyalin perivascular material in the papillae of the affected skin was observed in a biopsy specimen. Quantitative values of porphyrins and their precursors in red-blood cells, stool and urine of the patient are recorded in Table 1. The free red-cell protoporphyrin (PP) was

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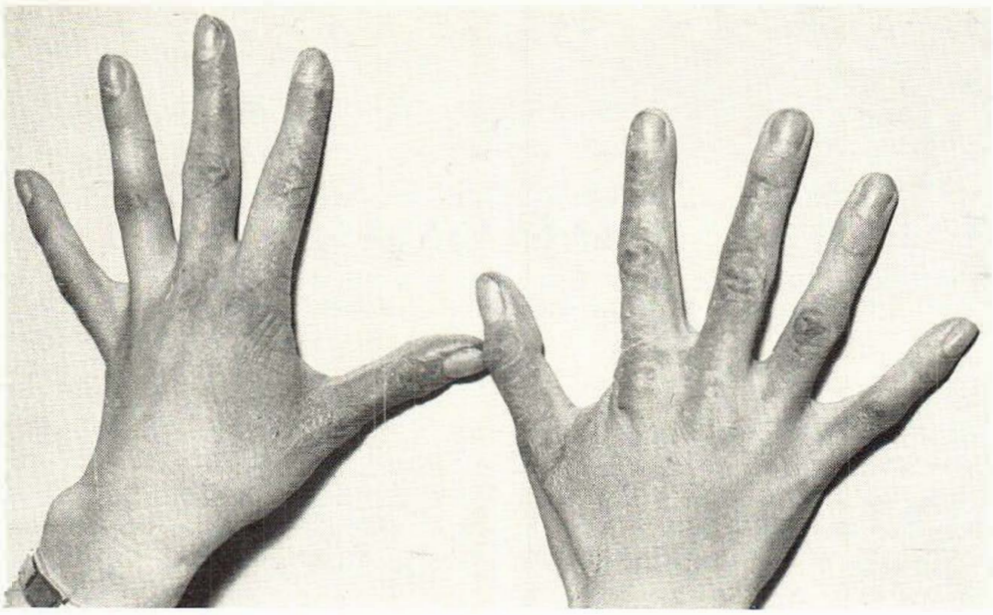


Fig. 1. Chronic skin rash on the hands of the patient with EPP.

Table 1. *Porphyrins and their precursors in the observed patient with EPP*

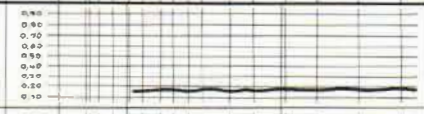
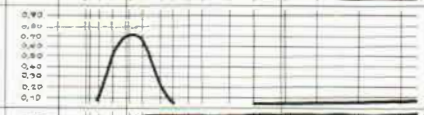
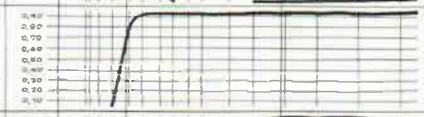
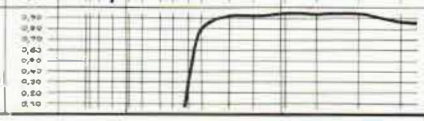
	R.B.Cs.	Stool		Urine			
	PP	PP	CP	CP	UP	ALA	PBG
	µg/100 ml packed cells	µg/1 g dry weight		µg/24 hours		µg/100 ml	
the patient	1184.1	488.2	167.0	54.4	34.5	99.5	63.0
normal values	< 52	< 30	< 20	< 176	< 30	< 200	< 57

determined by the method of Wranne (14). Protoporphyrin (PP) and coproporphyrin (CP) in stool by the method of Rimington (9), coproporphyrin (CP) and uroporphyrin (UP) in urine also according to Rimington (10), delta-aminolaevulic acid (ALA) and porphobilinogen (PBG) according to Mauzerall and Granick (7). Other laboratory findings were: Red-cells in the blood count: 3.6 million per c.mm., haemoglobin 9.76 g per cent, Cl 0.84, haematocrit 33.5, reticulocytes 43 pro mille. Marked anisocytosis, poikilocytosis, hypochromia, abnormal Price-Jones's curve. White cells 3200 per c.mm. (eosinophils 9 per cent), thrombocytes 76,000 repeatedly. Normal myelogram. Serum iron from 107–121 gamma per cent. Normal BSP test, other liver function tests show normal values. A low level of haptoglobin (0–50 mg per 100 ml).

Methods

In our patient an exposure skin test was carried out by using selective spectral Zeiss-Jena filters. The filters were placed on the arms and forearms where the skin was adequately pigmented and free from pathological signs. The source of radiation was September midday sunshine; the period of exposure lasted one hour. The reaction was read immediately after the filters had been removed, and after one, two, four, six and twenty hours.

Table 2. *Results of the skin exposure test in the patient A. L. (Source of radiation: September midday sunshine; time of exposure: 1 hour)*

FILTER		REACTION					
		IMMEDIATE	AFTER				
COLOUR	LIGHT TRANSM.		1 HOUR	2 HOURS	4 HOURS	6 HOURS	20 HOURS
CARL ZEISS JENA NG 10 THICKNESS 1 mm		—	—	—	—	—	—
CARL ZEISS JENA UG 1 THICKNESS 1,5 mm		ITCHING BURNING ERYTHEMA +	ITCHING BURNING ERYTHEMA	ERYTHEMA	—	—	—
CARL ZEISS JENA BG 12 THICKNESS 2 mm		ITCHING BURNING ERYTHEMA +	ITCHING BURNING ERYTHEMA ++	ERYTHEMA ++	ERYTHEMA +	—	—
CARL ZEISS JENA GG 13 THICKNESS 2 mm		ITCHING BURNING ERYTHEMA ++	ITCHING BURNING ERYTHEMA ++	BURNING ERYTHEMA +++	ERYTHEMA + WEAL +	WEAL +++	PETECHIAE +++
CARL ZEISS JENA OG 2 THICKNESS 2 mm		ITCHING BURNING ERYTHEMA ++	ITCHING BURNING ERYTHEMA ++	BURNING ERYTHEMA ++	ERYTHEMA + WEAL	WEAL ++	PETECHIAE +
WITHOUT THE FILTER (THE FORARM)		ITCHING BURNING ERYTHEMA	ITCHING BURNING ERYTHEMA	ERYTHEMA ++	ERYTHEMA +	—	—
WITHOUT THE FILTER (THE AREAS OF CHRONIC CHANGES)		ITCHING BURNING ERYTHEMA	ITCHING BURNING ERYTHEMA	BURNING ERYTHEMA	ERYTHEMA WEAL	WEALS	WEALS PETECHIAE

Results

Results of the exposure tests are recorded in Table 2. The fact that the maximum cutaneous changes i.e. marked erythema, massive oedema and petechiae after 20 hours (Fig. 2) were found with a GG 13/2 filter transmitting the wavelength of Soret's maximum—but also the wavelength of the visible and infrared part of the spectrum in full intensity—is not surprising. It is in agreement with the results of Magnus *et al.* (6) using a quartz-xenon monochromator. He concluded that the maximal irritative effect is caused by light of the wavelength of Soret's maximum, i.e. 405 mμ, which is strongly absorbed by porphyrins. This view is generally accepted and the results of our experiments do not argue against it.

The finding of the same sequence of skin reactions with a OG 2/2 filter transmitting wavelengths over 578 mμ agree again with the results of Magnus (6) who interpreted the reaction to this wavelength band as a high degree sensitivity of the patient to light in December. These authors also suggested that this strongly evident sensitivity was directly conditioned by the high level of free red-cell protoporphyrin, present just in this season. The studies of other authors like Waldenström (14), Hæger-Aronsen (3), Redeker (8), Lynch (5) could not support such a direct relationship.

The finding of much smaller skin changes e.g. itching, burning sensations and a rapidly disappearing erythema with a BG 12/2 filter transmitting wavelengths of Soret's maximum exclusively was rather

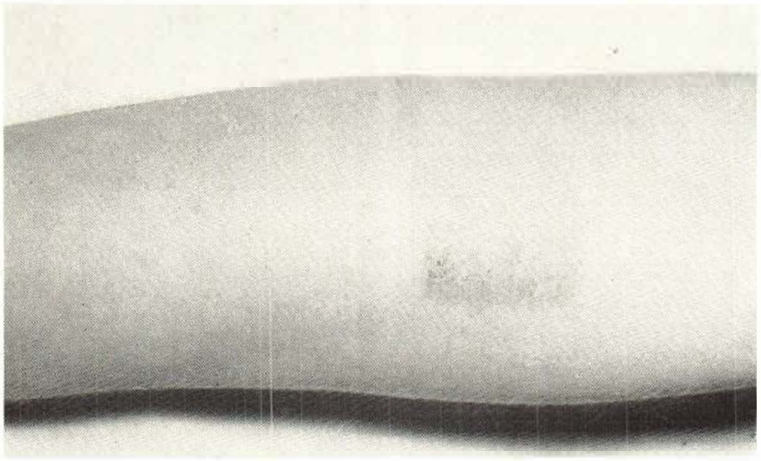


Fig. 2. Petechiae appearing on the skin of the forearm under filter GG 13/2 after 20 hours following the exposure test.

surprising. It seems unlikely that this result can be explained by a smaller degree of transmission of light of this wavelength with this filter than when using the filter GG 13/2, the difference of transmission being only 10 per cent. We rather believe that the changes in the capillaries (oedema, petechiae) in this condition are due to the light of the wavelength over 578 mμ where also the fluorescent emission of porphyrins is elicited. These wavelengths were transmitted through the filters GG 13/2 and OG 2/2 in full intensity, while they were not let through the BG 12/2 filter. Burning sensations, itching and a slight erythema which disappeared after 4 hours occurred with the UG 1/1.5 filter. The band of transmission of this filter is in the melanogenous zone of the spectrum which did not cause abnormal reactions even in Magnus's experiments. No changes were seen under the protective filter NG 10/1. All mentioned cutaneous changes including oedema and petechiae were strictly limited to the area of the filtered light.

Discussion

The experiment was carried out during one session so that variations of protoporhpyrin-levels could be disregarded, as well as the changes of the radiation source and fluctuating reactivity of the skin capillaries. At the same time we were able to compare the effect of the whole sunlight on a control area of the skin of the forearm which was not covered by any filter. In this area the cutaneous changes observed were a degree of mild itching, burning and a slight erythema, similar to the changes observed when using UG 1/1.5 and BG 12/2 filters transmitting ultraviolet wavelengths. This observation deserves the greatest attention, especially when we take into account that the control skin-area of the forearm was affected by wavelengths of 405 mμ or more in the same time period and in the same intensity. These wavelengths isolated with GG 13/2 and OG 2/2 filters led to serious capillary changes (oedema and petechiae). It therefore appears paradoxical that the absence of lower, i.e. ultraviolet wavelengths should give rise to capillary damage.

It is also interesting that the areas of the hand affected with chronic eczematous changes (sharply demarcated dryly desquamating patches of the skin with a brown-red tinge) after one hour's exposure reacted in the same manner as the skin of the forearms and arms when using GG 13/2 and OG 2/2 filters, transmitting visible and infrared light. The oedema and petechiae of the hand were not limited to chronic eczematous patches but afflicted

extensively also the adjacent areas especially the ulnar side of the hand.

On the basis of the associations observed we believe that the melanin-stimulating zone of ultraviolet light has a protective effect on areas which are not affected by manifest signs in a photosensitive condition like EPP.

Accepting this hypothesis the clinical observations can be explained:

1) The patients with EPP suffer from signs of hypersensitivity to solar radiation even behind the windowglass (2, 5 and own observation).
2) The difficulties occur also during the winter season, especially on clear windy days (2 and own observation).
3) After getting tanned the degree of hypersensitivity of the same patient will temporarily decrease (2 and own observation).
4) The skin of the trunk remains unaffected on sunbathing (12 and own observation).
5) Topical sunscreens with filters against UV radiation remain completely ineffective in this condition (4, 5 and own observation).
6) The severity of the pathological changes and presence or absence of an eczema do not seem to depend on the level of protoporphyrin in the red-blood cells (3, 5).
7) Up to the present time EPP has been described in only one Negroe (1) but entirely without the clinical signs of photosensitivity. From 1150 to 1590 µg of free erythrocytic protoporphyrin per 100 ml of packed red-blood cells was a secondary finding on haematological examination for anaemia. Thus the question arises if the usually efficient capacity of the pigment is concerned in the occurrence of latent forms of EPP.

SUMMARY

In a 26-year-old female patient with erythropoietic protoporphyria and chronic cutaneous changes maximal irritative effect of sunlight was found to result from wavelengths of more than 405 mµ when using selected filters placed on unaffected skin. The changes were much less marked when using filters transmitting ultraviolet light and were similar to those observed on unaffected uncovered skin.

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