Leucomelanoderma in Blacks

A RECENT EPIDEMIC

M. DOGLIOTTI, I. CARO, R. G. HARTDEGEN, D. A. WHITING

SUMMARY

A recent epidemic of leucomelanoderma in Blacks is described. A total of 347 patients was seen in two hospitals during the survey period. The ratio of females to males was 7:1. A striking pattern af patchy depigmentation and mottled hypermelanosis occurred predominantly on the face and neck, but sometimes extended to other areas. Most but not all cases later showed repigmentation.

The cause of the dyschromia appeared to be monobenzone, a bleaching agent recently included in certain overnight creams packed in wide-mouthed jars.

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CLINICAL FINDINGS

In recent months (1973/4) many Blacks have attended our clinics complaining of colour changes in the skin. They showed a striking leucomelanoderma predominantly affecting the face, neck and upper chest, although a few had more extensive involvement. Guttate and larger patches of partial or complete depigmentation, discrete or confluent, were found mainly on the forehead, the eyebrow skin, the sides of the neck, and in males, on the beard area (Fig. 1). The arms, hands, chest and abdomen were more rarely involved (Fig. 2). In addition, mottled areas of hyperpigmentation were often present (Fig. 3). A preceding mild erythema and irritation had occurred in some patients, without subsequent scaling. No uniform history of the ingestion of a drug or a toxic substance was obtained.

During a 6-month period, 347 cases of leucomelanoderma were seen, 221 of whom attended Baragwanath Hospital and 126 the Johannesburg General Hospital. The ratio of females to males was 7:1. Many additional cases were seen outside these survey months. The age incidence of the condition in patients at Baragwanath Hospital is shown in Table I.

Initial investigations proved fruitless. No infective agent could be found, nor any internal metabolic disorder. Skin biopsies of the lesions showed a normal epidermis

Baragwanath and Johannesburg Hospitals and Department of Dermatology, University of the Witwatersrand, Johannesburg

M. DOGLIOTTI, L.M.C. (TURIN)
I. CARO, M.B. B.CH., F.F. DERM. (S.A.)
R. G. HARTDEGEN, M.B. B.CH.
D. A. WHITING, F.R.C.P., M.MED. (DERM.), D.C.H., D.OBST.

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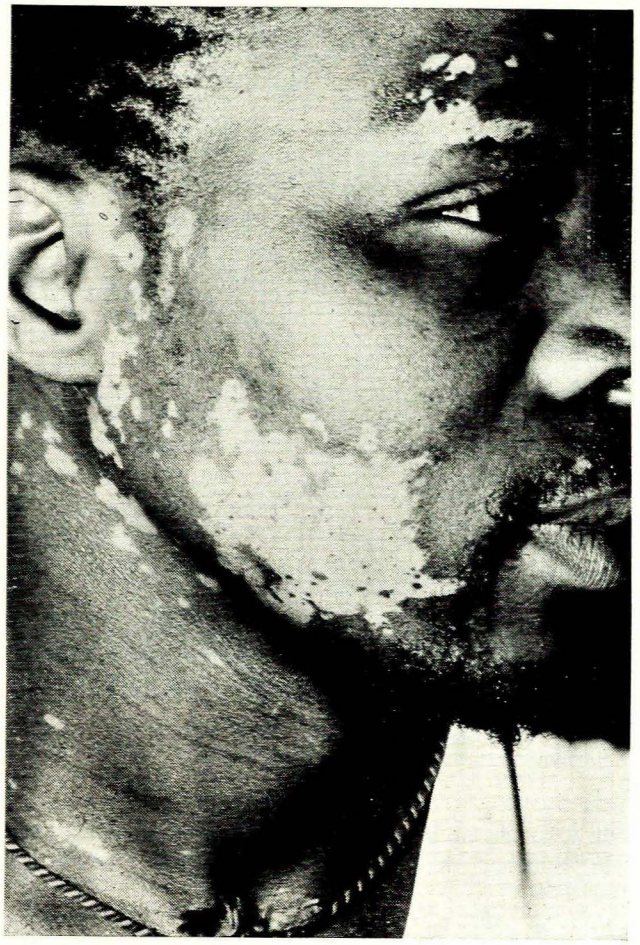

Fig. 1. Patchy leucoderma is present on the face and neck.

TABLE I. AGE INCIDENCE OF LEUCOMELANODERMA AT BARAGWANATH HOSPITAL

Age in years	Females	Males	Total
16 - 20	20	1	21
21 - 30	36	7	43
31 - 40	68	5	73
41 - 50	50	12	62
51 - 60	22	0	22
	196	25	221

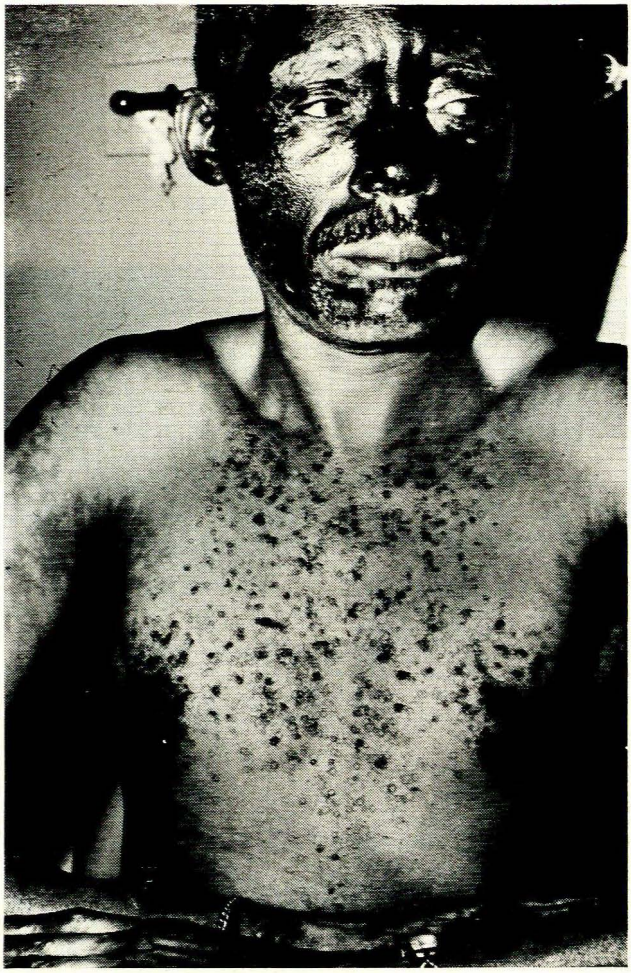

Fig. 2. Partial depigmentation is widespread over the trunk and upper arms and patchy on the hands.

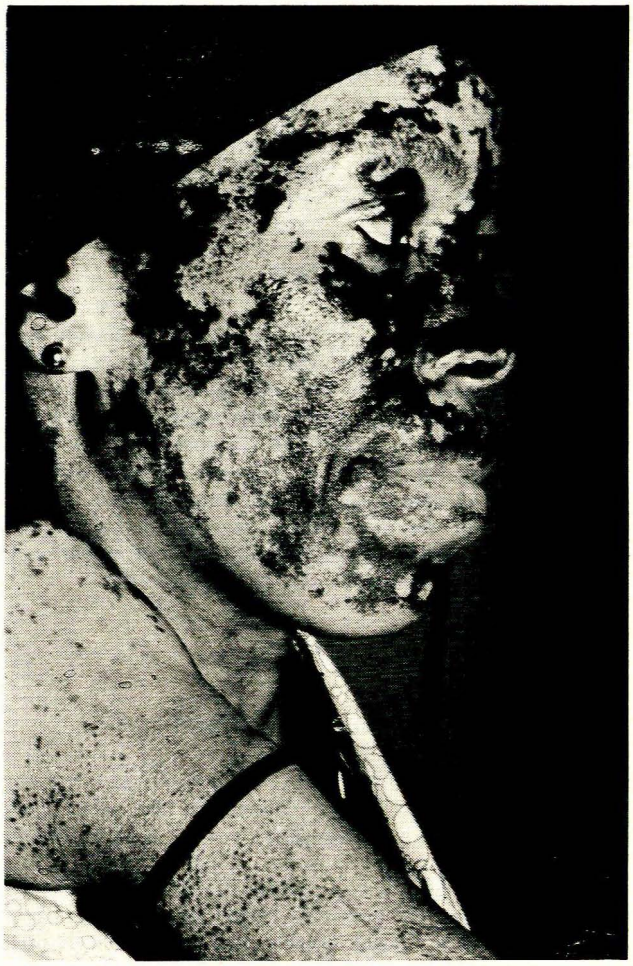

Fig. 3. A striking mixture of depigmented, normal and melanotic skin is shown here.

with some incontinence of pigment and a mild inflammatory infiltrate in the upper dermis on histological examination.

After a while it became apparent, on repeated direct questioning, that most of the patients had been applying a bleaching cream packed in a wide-mouthed glass jar. Its use was then forbidden and thorough washing advised. For some a topical corticosteroid was prescribed. Most cases showed repigmentation within the next 2 - 6 months, often of considerable intensity in the earlier stages. As in vitiligo, the new pigment usually spread out from hair follicles in a spotty fashion. Sun exposure seemed to accelerate the process. Some patients have reverted to normal pigmentation, but others are still severely affected up to 7 months after the onset of the condition. Sites such as the hairline area of the brow, the eyebrow skin, the shaded areas of the neck and unshaved facial skin were often slow to repigment.

It was notable that many patients had used the same brand of overnight cream for years. However, consultation with the manufacturers showed that the formulation of the creams had been changed at the end of 1972, depending upon the pack. Prior to that, ammoniated mercury, a mild skin-bleaching agent, had commonly been used, despite its ability to produce sensitisation and postinflammatory hyperpigmentation of the skin in susceptible subjects. Reports of renal damage following repeated application to the skin had led to its recent withdrawal from the market. A more active substitute now employed is hydroquinone, which has the disadvantage of being subject to oxidative blackening on exposure to air. This does not prevent its use in tubes with small nozzles, but it cannot be dispensed in wide-mouthed containers. As these jars still enjoy considerable consumer popularity, the monobenzyl ether of hydroquinone, known as monobenzone, was included in the cream for this pack in a 2% concentration. It was chosen for its marked skin-bleaching effect and its resistance to oxidation. Salicylic acid was often added in 2% concentration. The cream was thick and sticky, in order to remain on the skin overnight. It transpired that many of our patients had obtained a jar of the new cream 2 - 4 months before the onset of the leucomelanoderma.

Experimental patch testing with a patent overnight cream containing monobenzone 2% was carried out by us in 3 unaffected volunteers. Two 3-cm-square areas a few cm apart were selected on the back and the cream applied under occlusion twice daily for 3 - 5 weeks. In one of the patch areas skin stripping was carried out daily. Leucoderma occurred in the stripped site in 1 case after 2 weeks (Fig. 4) but the other cases did not depigment after the limited time of the test.

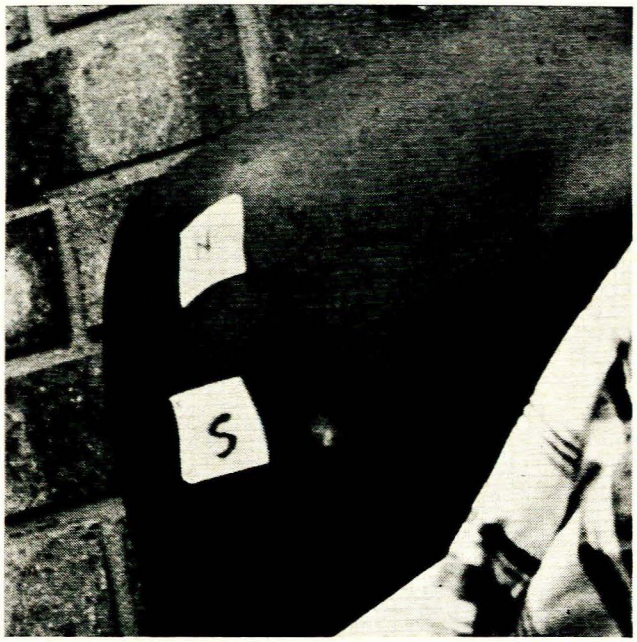

Fig. 4. Patch testing with a 2% monobenzone cream for 2 weeks has produced leucoderma on the stripped site.

Monobenzone

Monobenzone, or *p*-benzyloxyphenol monobenzone, is a whitish, crystalline powder easily soluble in ethanol and acetone, slightly soluble in liquid paraffin and glycerine, but almost insoluble in water. Being stable, it is a potent anti-oxidant, and an inexpensive form of it known as agerite alba has been used for years in the processing of rubber to prevent perishing. Its ability to bleach skin was discovered on investigation of an outbreak of leucoderma in factory workers wearing rubber gloves.[1] It has also proved to be a ready skin sensitiser but can cause depigmentation independent of this property. Encouraging reports of its ability to bleach hyperpigmented patches of skin did appear,[2] although it was found ineffective in treating melanomas, *café-au-lait* spots and other pigmented naevi. Further clinical experience showed that monobenzone could cause a disfiguring leucomelanoderma, both at and distant from the sites of application.[3,4] This was confirmed experimentally when monobenzone was applied topically in various concentrations to 42 Negro males.[5] Several weeks of treatment were required to produce the characteristic dyschromia which was not always preceded by erythema. The hypopigmentation commonly extended beyond the area of application and might appear at unrelated sites. Stopping the treatment did not necessarily limit the spread of leucoderma and the first white spot sometimes appeared several months after the last application. After 4 years one-third of the affected cases had not repigmented. These findings showed that monobenzone should be used with great caution as a therapeutic agent.

Although monobenzone is a strong bleaching agent clinically, it has no effect *in vitro* and its exact mode of action is unknown. It interferes with the biosynthesis of melanin, preventing the oxidation of tyrosine to phenylalanine. As its effect is not on preformed melanin its action takes several weeks to become apparent. If the depigmentary activity of monobenzone were totally reversible, then its action could be explained solely on the basis of tyrosinase inhibition[6] or the tyrosine analogue effect[7] or redox properties of a para-substituted phenol derivative. However, the persistent leucoderma occurring in some patients could better be explained if monobenzone acted like topical *N*-mercapto-ethyl-dimethylamine which causes pigment to disappear and after continuous use for 2 - 3 months destroys melanocytes,[8,9] implying a cumulative and eventually cytocidal effect. This lasting cell injury might be due to lipid peroxidation caused by derivatives formed by tyrosinase acting on certain phenols, as postulated for other bleaching agents.[10,11] An antigen-antibody reaction has been suggested[12] to account for the leucoderma found on untreated sites.

DISCUSSION

Although a definite history of the use of a monobenzone cream was not found in all patients, it was obtained often enough to seem significant. The low content of monobenzone in the cream was misleading, in that its presence in undissolved granular form could lead to patchy areas of highly concentrated chemical on the skin. Its penetration through keratin layers was aided by the salicylic acid. The differing degrees and patterns of dyschromia seen might also have been due to a cyclic variation in melanocyte sensitivity.[12] Although many patients have regained a normal skin colour, the fact that some have not is in accordance with the known permanent effects of monobenzone.

The cause of the marked degree of melanosis seen in many cases was not always clear. In some it may have been a postinflammatory hyperpigmentation, but preceding erythema was not a feature in all cases. A photosensitisation effect from one or other constituent of the cream was another possibility, as occurs with vaseline.[13] Perhaps the monobenzone itself is subject to oxidative darkening, as has been suggested for other phenols causing exogenous ochronosis.[14]

The distribution of the skin lesions in relation to the stated sites of application of the cream was not easy to explain. However, the predilection for hairy areas of the face and neck may have been due to difficulties in removing the sticky cream. Leucoderma around the neck in the collar area, in the armpits and under the waistband

would seem to conform to patterns of clothing dermatitis due to chafing by fabric impregnated with bleaching cream and sweat. Other seemingly unlikely areas of involvement may have arisen from repeated physical contact with a partner using the cream or with the surrounding bedding.

CONCLUSIONS

It seems reasonable to conclude that the recent epidemic of leucomelanoderma has been caused by the inclusion of monobenzone in certain bleaching creams. This change in composition was not always advertised, so the unsuspecting individual might well buy fresh supplies of a preparation used safely in the past. The resultant changes in skin colour bewildered the user who tended to continue applying the cream as before. The extended exposure to monobenzone which resulted was enough to produce severe and prolonged effects.

The dyschromia in this epidemic can only be described as a cosmetic disaster for a dark-skinned individual. It is suggested that any new bleaching preparation be thoroughly tested by clinical trial before its release for general use. If a powerful skin-lightener like monobenzone is to be used at all, it would be better if it were made available only on prescription.

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