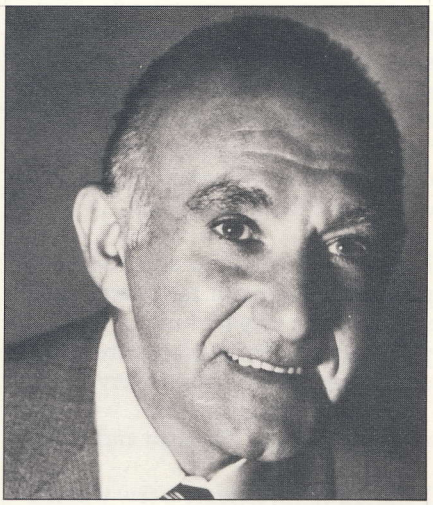
Experience in the Treatment of Skin Conditions Caused by Skin Lighteners

– Dr D Cowan



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Curriculum vitae

David Cowan was born and educated in Dublin; he qualified in 1928 and after 20 years of General Practice in London, immigrated to South Africa in 1948. He first served a white population in Johannesburg as a GP, and then moved to a wholly black practice in Johannesburg and Soweto where he worked for 26 years, till he retired in 1985. He is still serving the community on a part-time basis, and his special interests are still hyperpigmentation, Ochronosis and Cosmetic Acne. He is married and has 3 married daughters.

Summary

There are many publications available on the subject of exogenous ochronosis, but nobody suggested any form of treatment. The author describes an "informal study" on some 7 000 black women with ochronosis over the past 13 years, in which he successfully treated them with his own formula. The need for a well-planned research project with this formula is emphasized.

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KEYWORDS:
Ochronosis; Drug Therapy; Physicians, Family.

While a plethora of articles by dermatologists on the subject of exogenous ochronosis has appeared during the past fourteen years, no one has ventured to suggest any form of treatment. All have agreed that the affliction is permanent and irreversible. A treatment is discussed herein that has proved successful in over seven thousand patients, during a period of thirteen years. The same formula is capable of treating cosmetic-induced acne and its stigmata (including the cystic type), and of depigmenting temporarily the normal skins of blacks, thereby eliminating the risk of any future incidence of ochronosis. Despite the approval of the Medicines Control Council, in January 1987, of a protocol for inaugurating clinical trials as suggested by a well-known South African pharmaceutical manufacturer, neither the teaching staff of academic dermatological departments, nor the SA Society of Dermatologists are prepared to be involved. The reasons for this are discussed.

It has been estimated that in the Pretoria area where a survey was conducted during August 1988 by the SA Consumer Council[1] into the use of skin lighteners, 42,5% of black women users had suffered harmful effects. Although the nature of these effects is not mentioned, it is possible that it was exogenous ochronosis, as first described by Findlay et al[2] in 1975.

Ochronosis is a severe form of hyperpigmentation (HP) which develops on the skin of the face after a few years use of skin lightening creams (or lotions) containing hydroquinone (HQ). It develops with the presence also of colloid milium, and has the appearance of, in some cases, being spotted with caviar.[2] The skin is coarsened and very black, with large black papules. There was a predilection for areas with underlying bony structures such as the zygomae, the nose, forehead, upper lips and chin, presumably because firmer rubbing-in occurred in these areas. All the articles (see references) agree in the description and histology, and the causative factor of prolonged use of HQ in various concentrations, from 3,5% to 7,5%.[5] Ochronosis is the severest form of HP; others less severe are chloasma – "the mask of pregnancy", the HP seen in young adult women on contraceptive pills (seen in white women also) and "rich ladies neck", an HP formerly seen on the sides of the neck caused by dabbing perfume containing oil of Bergamet. This oil is now modified.

Despite the publication of the abovementioned articles of the dire results of using the skin-lighteners, many well-known pharmaceutical

manufacturers continue to market them. The number of preparations was 52 in 1986.[6] Eventually, Government ordered in 1980, Government Gazette 1982,[7] that no skin-lighteners, sold over-the-counter, should contain more than 2% of HQ. All the manufacturers know that the lightening effect is weak and transitory and that they eventually cause permanent damage to the skin. Their motives are therefore questionable.

Ochronosis had become an epidemic;[2] Findlay and de Beer[5] at Kalafong Hospital state that 30% of patients at the skin out-patients wanted treatment for ochronosis. Others are described elsewhere.[3,4,5,6] The reduction in strength of HQ to 2% did not reduce the adverse effects; they continued to be seen up to 1986.[7]

In the same year that the article by Findlay et al[2] was published (1975) there appeared a paper "A new formula for depigmenting human skin" by Kligman and Willis of the Department of Dermatology of Philadelphia, Pennsylvania.[8] As the

More than 42% of black women in Pretoria have suffered badly

authors put it "after many trials that led us through a maze of trails, we finally arrived at our destination. The formula that eventuated was the following:-

Tretinoin (tetinoic acid, Vitamin A acid) 0,1%;
Hydroquinone 5%; and
Dexamethasone 0,1%

The base was hydrophilic ointment (USP) or a solution consisting of equal parts of ethanol and propylene glycol".

Kligman and Willis, after temporarily depigmenting the skins of black male prisoner volunteers, by twice daily application to squares of back skin outlined by a cardboard stencil, turned to the problem of HP in

More than 52 pharmaceutical preparations available in 1986

blacks and wrote, "one tends to think of HP as mainly a problem in whites, until one begins to acquire experience with blacks. In the latter, the most trivial chemical and physical traumata, frequently unrecollectable, tend to produce persistent HP. Extensive patch testing of blacks with various irritating and allergenic chemicals awakened our sensibilities to the problem of HP in blacks." I, personally, had noted long before this, that in black women, the too-tight shoulder straps of slips and bras caused marks of HP across their clavicles. The same HP due to pressure was also noted on knees and elbows.

Kligman and Willis' discussion was restricted, with limited success, to post inflammatory HP. It was obvious that they were not aware of the ochronosis as seen in South Africa.

I formed the idea that if the formula had such a profound effect in depigmenting black skin, which, to put it crudely, is after all, hyperpigmented white skin, would it have the effect of depigmenting, to some degree, hyperpigmented black skin? It seemed a far-fetched idea and after some deliberation decided to "give it a go", but before reporting on the outcome, I would like to discuss the formula further.

I started to treat a few selected patients, I had never taken very much notice of the varying hues of my patients' skin. Some blacks are light-complexioned and others very dark. The article "awakened my sensibilities" a la Kligman and Willis.

I started to investigate a few women with HP and met with limited success. I found the cream to darken from a light yellow to a brown within a few days. The authors had also reported this discolouration and mentioned that the same darkening had been reported by a previous investigator.[9] I had seen the Certificate of Analysis of Dexamethasone and of Tretinoin, and no mention of discolouration in solution was mentioned. I then made enquiries of the suppliers of the HQ. I was told that solutions turn brown on exposure to daylight because of its

Black skin is, after all, hyperpigmented white skin!

alkaline pH. This, it appears, is desirable in preparing the "developer" in photography and in developing x-ray plates. To avoid the discolouration I was advised to lower the pH to approximately 4,8. To do this I finally settled on Ascorbic acid (Vitamin C) and the result was satisfactory. This was most fortuitous and I believe that the outstanding result was due to this acidification.

The proportions of the three (now four) active ingredients must be exactly as specified by Kligman and Willis. They stress, in their paper, of having tried many variations before arriving at the optimum results. The apparent paradox of the preparation containing HQ to treat skin damaged by HQ is puzzling to dermatologists and hence their prejudice. I believe that the use of *HQ per se* is the cause. HQ is agreed to be a skin-lightener, albeit, a weak and transient one.[9] The deleterious effect is nullified by the presence of tretinoin and dexamethasone.

However, Kligman and Willis[8] and Mills and Kligman[12] put forward, in detail, an endeavour, scientifically, to explain how the formula works in depigmenting. "HQ is known to interfere with the tyrosine - tyrosinase pathway of melanin synthesis. This drug also causes subcellular membrane damage and inhibits the formation of melanosomes, the organelles in which melanin is packaged. How tretinoin and the steroid contribute to the depigmenting action is conjectural . . . Both tretinoin and the steroid are known to have skin-lightening propensity.[8]

I have never found a single patient who did not respond to this therapy

"While every ingredient was crucial to attain our established end-point, we could form a crude estimation of the relative importance of each. The ranking of depigmenting was (in descending order) HQ, tretinoin and the steroid. Without tretinoin, moderate depigmentation was usually possible. Leaving out the steroid clearly lessened effectiveness, but not to the extent that occurred when tretinoin was omitted. In no instance in a group of four subjects did application of one-ingredient formulations produce substantial depigmentation within three months. Without HQ only very slight and inconsistent depigmentation could be obtained. This component (HQ) has overriding importance. No loss of pigment occurred when retinoic acid and the steroid were applied alone. No adverse effects other than irritation were encountered. The well-known local side effects of steroid therapy; atrophy, striae, acne, telangietasia have not been noted and are highly unlikely. Tretinoin is a recognised antagonist of steroid therapy; it counteracts, for example, steroid - suppressed wound healing.[13] Tretinoin apparently overcomes the potentially deleterious effects of steroids.[13] The formula is not a bleaching agent and will not de-colourize melanin."

My big surprise was the success of this formula on cosmetic-induced acne and the stigmata

In a later article in 1978 by Mills and Kligman[12] further observations are made; "it is necessary to explain that we never encountered adverse steroid effects in chronic users of the depigmenting cream . . . owing to the presence of tretinoin in the formulation. The biologic effects of tretinoin are virtually opposite to those of steroids; for example, it stimulates mitosis while steroids are inhibitory.[14] It promoted wound healing, while steroids are inhibitory.[15] The tretinoin is comedolytic;[15] steroids enhance the formation of closed and open comedones,[16] and so the potential damages that steroids could exert on skin structure, especially atrophy, are completely nullified by tretinoin".

I was the senior partner (of three) in a wholly black practice with consulting rooms in west-central Johannesburg and three branch consulting rooms in Soweto, for twenty six years.

The bulk of the practice was fully dispensing, made up of members of three Industrial Medical Benefit Societies, accounting for approximately ten thousand persons, two-thirds whom were women. We, therefore, had plenty of black skins to inspect.

After the formula had the addition of the ascorbic acid I started anew. I selected three women with histories of hyperpigmentation of between 15 and 30 years. Their informed consent was obtained. After patch testing they were given a jar of 30 grams and instructed to apply the cream at night and in the morning (Kligman and Willis found twice-daily to give the best results). To my (and their) pleasant surprise they started to improve within a matter of days and by twelve weeks their ochronosis had

Vaseline is a potent hyperpigmenter

very markedly improved. This encouraged me to extend the number of participants, with excellent results (fig 1 and 1A). This trial was in 1976. It was not until a few years later when I had experience with the treatment of cosmetic-induced acne, including severe cystic types and acne stigmata, that I started to photograph some types of patients before and after. Since starting to treat patients with pigmentary problems, with the formula, I have never found a single patient who did not respond to therapy.

Some were slower than others and I found that these were irregular users. Some users developed reddening and irritation initially as also described by Kligman et al. Most were due to too exuberant rubbing and few who denied rubbing too briskly. In all cases, ceasing use for a few days, and applying a calamine cream, cleared the irritation and therapy continued. In time the skin became accustomed to the tretinoin to the extent that irritation ceased altogether. The original authors found that the irritation enhanced depigmentation but was not a prerequisite for it. Patients on treatment were advised to avoid undue exposure to sunlight. I strongly feel that the addition to the formula of a sunscreen eg PABA (para-amino benzoic acid) would increase its efficiency.

The irritation caused by the small concentration of tretinoin 0,1% in the formula which is further reduced by the dexamethasone (see above) contrasts markedly with the severe irritation caused by two preparations for use in acne, viz Airol (Roche)[10]

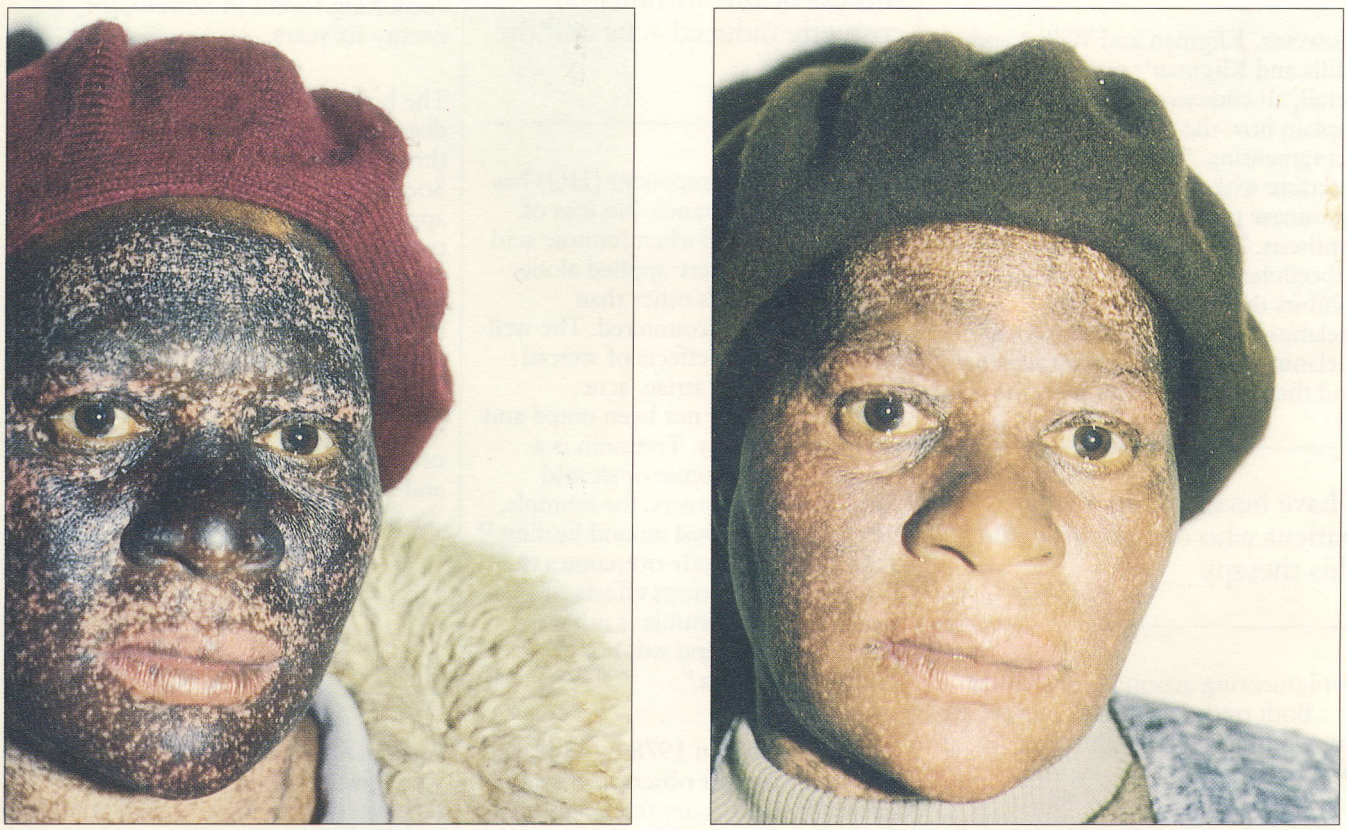

Fig 1 and 1A: JA aged 42 years. History of using skin-lighteners for 24 years. When she looked like the photo no 1 she went to a large Johannesburg teaching hospital skin department; was given Betnovate Cream and an "alcoholic" lotion, which she used for many months, without result. From her first application of the formula to the time of the second photograph the period of time was from 25 July to 7 October, ie twice daily application for 11 weeks. After that I lost contact with her. I was told she "returned to the farms". Doubtless, without a maintenance application, she will have regressed.

and Retin A (Cilag).[11] Both of these preparations have tretinoin as the only active ingredient with a concentration of 0,5%. The package insert of both preparations warn against severe reactions." [11]

My big surprise was the effect of the formula on cosmetic-induced acne and the stigmata (Fig 2 and 2A). This was the most appreciated result in therapy of hyper-pigmentation that was short of true ochronosis. These were, of course, in the younger patients whose use of skin lighteners was of shorter duration (under ten years).

I had also found patients who had used vaseline regularly and to a lesser degree glycerine, developed an all-over evenly distributed HP of the face, without the usual emphasis on the areas with underlying bony structures. These vaseline users, however, developed ochronosis quicker from skin-lighteners than non-vaseline users. This HP due to vaseline was reported by Dr JA Warndorff, Senior Dermatologist at ALERT (the all Africa Leprosy and Rehabilitation Centre in Addis Ababa)[19] who says that vaseline is a potent hyperpigmenter.

While my acne patients who represented 30% of all HP patients had black spots (stigmata) of healed pustules, some patients with ochronosis on the cheeks showed variable amounts of white puntate stigmata of similar size to the black stigmata of acne. The white spots disappeared during therapy, to blend in with the whitening skin. The same was found in treating patients with HP and patches of vitiligo.

The general manager of one of the largest makers and distributors of skin-lighteners, in Readers Digest, July 1984[17] in answer to a question "How safe are current skin-lighteners?" denied that any of their cosmetics was or is dangerous. "It is misuse by people that causes the trouble" he claims, "they mix lighteners with tooth paste, battery acid and tea-bags."

I believe that hitherto no skin-lighteners lighten skin in the long term, they all eventually cause severe and intractable damage. In 1977, some time after my success in treating ochronosis etc, I started trying to interest dermatologists in the hitherto untreatable ochronosis,

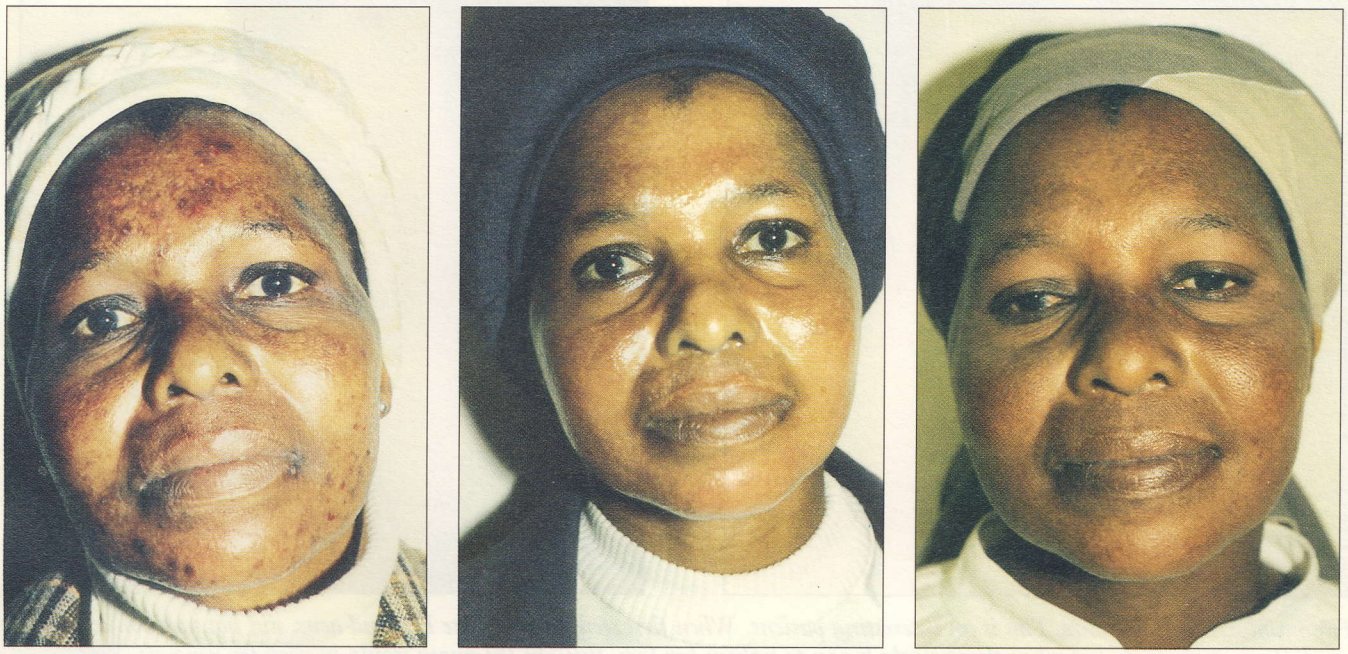

Fig 2A, B & C: History of 20 years. (A); Great improvement seen after 3 months. (B); Continued on maintenance for 2 years and left for Maritzburg and took some extra tubes with her. When she returned had had no cream for 3 months. (C).

but without success. I thought they would also like to know of a possibly efficient and safe skin-lightener (Fig 3 and 3A) to replace the dangerous rubbish on the market, bearing in mind that large numbers of users are, by their lack of sophistication and restriction of language and literacy, easy prey to unscrupulous vendors.

It is of no use begging the question, "why do people use skin-lighteners?" One must be pragmatic. Blacks desire to lighten their skins just as whites desire to darken theirs (to get a "nice tan"). They must be protected against themselves. Dermatologists have, for years, warned whites of the dangers of a "nice tan", of acquiring a skin like a dried prune, apart from the likelihood of skin cancer. At least, ochronosis has not been shown to predispose the skin to malignancy.

One head of a teaching hospital skin department in 1977 admitted that one of my (early) photographs showed the first he had ever seen of a reversal of ochronosis and suggested that the Vitamin C was the reason and told me to try a 2% cream with ascorbic acid, to get the same result. I did so and had no success from much-grumbling patients after up to 6 months of use. The head of a teaching hospital skin department asked me to do a punch biopsy. Another suggested applying the cream unilaterally in a controlled study. This

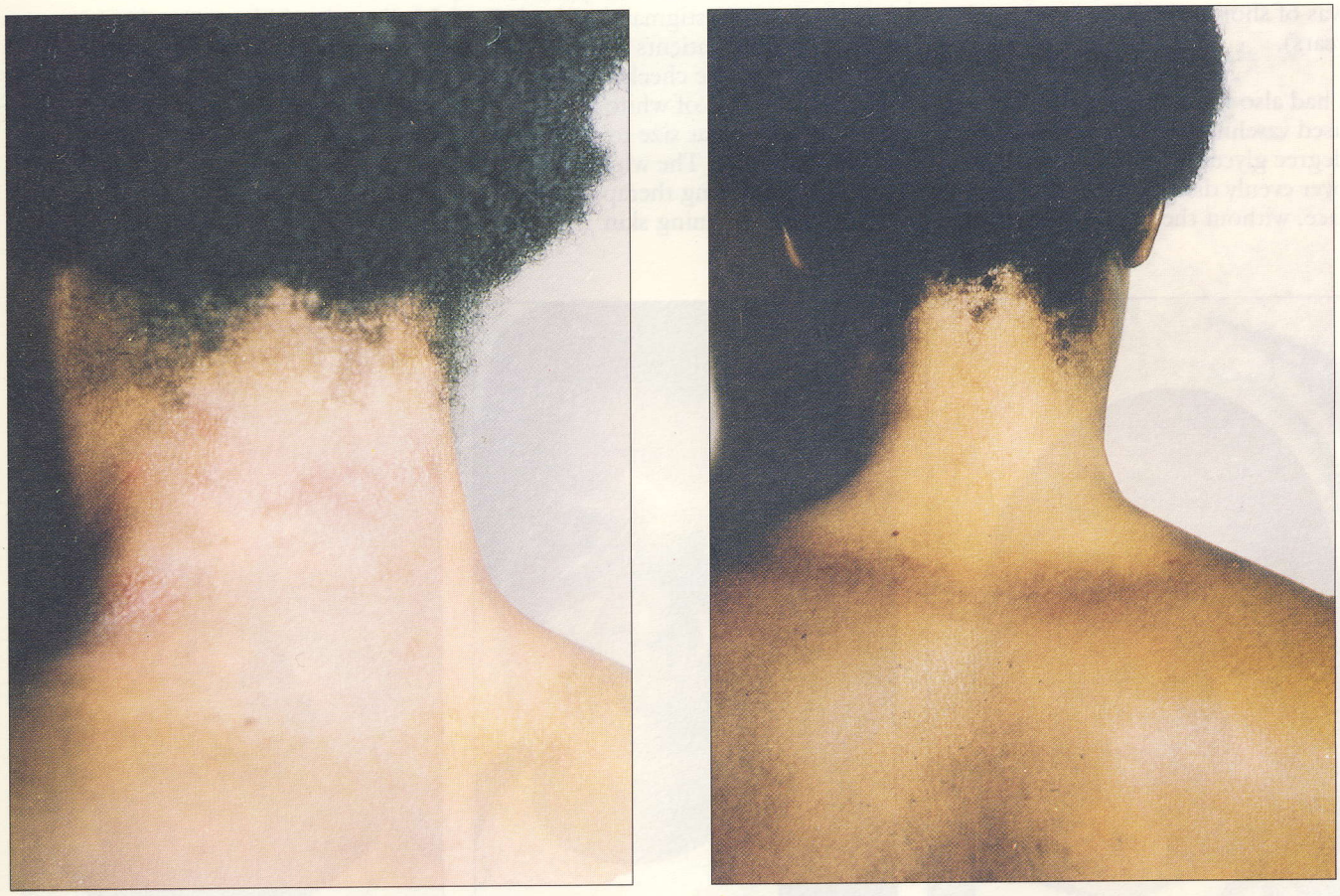

Fig 3 and 3A: LM 23 years. This is an interesting patient. When first seen for moderate HP and acne, did not mention a rash on the back of her neck, but when the formula began to lighten her face, thought the cream would be good for her neck. Was regular user and only mentioned her neck rash 3 months later. I found that the rash was still there (contact dermatitis from a cheap metal necklace) but the skin was completely depigmented. I gave her some calamine cream and saw her again 3 months later. The rash was gone and her skin was repigmenting.

surely would have been unethical and morally unjustifiable. The Dermatological Society's reason for not pursuing the study mentioned earlier was that "they felt that is was in no way the Society's business to either commend or condemn such a trial." [18]

Conclusions

The formula is successful in treating (reversing) ochronosis (Fig 1) and cosmetic-induced acne (Fig 2). It is also an efficient and safe skin-lightener (Fig 3). It is not a permanent cure but will keep the skin-troubles that have been discussed, at bay, on a maintenance application, as little as once a week, for an indefinite period. There are no deleterious side effects. After clinical trials and registration, it will be a Schedule 4 preparation and under present laws will be available only on doctor's prescription.

Hitherto no skin-lighteners really lightened skin in the long term; they did cause severe damage though

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I had no intention of initiating a formal study at first, and now regret it, since I was amazed at the results of my "informal study". While not attempting to portray a well controlled trial I wish to share my experience of over 7 000 patients between 1975 and 1989, with those practitioners who are regularly faced with these desperate people.

Mark H McCormack, mentor of the world's sports stars says, "the moment somebody says, 'that's a great idea', that's the very moment when most people decide how they can resent it, resist it, misrepresent it, misuse it, neglect it, or love it to death."

I appeal to the dermatologists to grasp the opportunity, sink their prejudices, cease their posturing and join in the solving of a problem of such great dimension and human anguish.

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