

Albinism and skin cancer in Southern Africa

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The presence of skin cancer was investigated in 111 albinos belonging to the black (Negro) population of Johannesburg, South Africa. The overall rate was 23.4%, the risk increasing with age. Identifiable risk factors included: environmental exposure to ultraviolet radiation; inability to produce ephelides ('freckles'); and possibly ethnicity. The head was the site most commonly affected, and squamous was far more common than basal cell carcinoma. No melanomas were detected. Recommendations are made regarding prevention of skin cancer in the at-risk group.

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Albinism is a 'congenital heritable hypomelanosis that ... involves the eye and integument (oculocutaneous albinism, OCA) and in which nystagmus, photophobia and decreased visual acuity are present' (Witkop et al. 1983). The prevalence rate is 1 in 3900 in the Southern African black population (Kromberg & Jenkins 1982). Apart from the eye disorders, the major medical problems for the albino in Africa are associated with the hypopigmented skin and the consequent susceptibility to carcinomas. The photosensitivity of the skin of albinos has been recognized for centuries. In 1666, Vossius (quoted in Pearson et al. 1913) wrote that African albinos disliked the sun and used protective ointments. Livingstone (1857), during his travels in Africa, noted that the bodies of albinos always 'blistered' on exposure to the sun. In 1910, Watkins-Pitchford commented that the 'true' albino should display the greatest liability of all to cancer, since this liability increased as pigmentation decreased. Cohen et al. (1952)

found that albinos accounted for one fifth of all skin cancer in Transvaal blacks, which was grossly disproportionate to the albinism rate in that group. Schrire (1958) suggested that albinos appeared to die early of skin cancer and that exposed areas were most commonly affected. Oettle (1963) found that albinos represented 9.6% of all cutaneous squamous cancers in blacks in the Transvaal.

Rates of skin cancer in albinos throughout Africa do not appear to be uniform. Rose (1973) reported that such cancer was infrequent in the Transkei and Burrell (unpublished data) noted only one case (a 50-year-old woman with a melanoma) in 458 albinos there. In Nigeria, on the other hand, Okoro (1975) found that all albinos over 20 years of age had malignant or premalignant lesions, and that overall, 50% of his subjects had keratoses and/or superficial ulcers. Rippey & Schmarman (1972) investigated squamous and basal cell carcinoma in black patients in Johannesburg and found 11%

of the former and 41% of the latter type were in albinos. Similarly, Isaacson et al. (1978) in a 10-year survey of the black population found that 6.9% of squamous and 33% of basal cell carcinomas were in albinos.

Since specific carcinoma risks for albinos living in South Africa had not been assessed previously, the aims of the present study were to: investigate the risk of skin cancer in albinos in terms of age and ethnic group; assess any correlation between presence of ephelides and susceptibility to carcinomas; identify the types of cancer found and the body sites affected; and compare the rate of skin cancer in albinos in Soweto, Johannesburg, with that reported for the Transkei. It was hoped that through these results those at high risk could be identified and the importance of instituting preventive measures for specific target groups could be evaluated.

Subjects and Methods

Subjects were ascertained during a population survey of albinism aimed at determining the prevalence of the condition in the South African black population. The study was undertaken in Soweto, a satellite city with about one million inhabitants, situated close to Johannesburg. Every school, health clinic, hospital, and welfare organization in the area was approached and requested to refer affected people to the authors. Families were then visited and interviewed and they often gave names of other affected families. The families were asked to cooperate in various studies on albinism. The inducement was a supply of free anti-actinic skin cream for the albino subjects and transport expenses were paid to encourage each one to come in to the medical centre for physical examination. Also free genetic and health counselling were offered and, occasionally, where necessary, poverty-stricken families

were provided with food parcels and clothing. Several findings from this study, regarding prevalence, genetic counselling considerations, genetic and psychosocial issues, reasons for the high frequency of albinism found in this population, maternal responses to the birth of an albino infant, and the prenatal diagnosis dilemma, have been reported previously (Kromberg & Jenkins 1982, 1984, Kromberg 1986, 1987, Kromberg et al. 1987 a, b, respectively).

Altogether 140 albinos were ascertained and they participated either fully or partially in a wide range of studies. The tyrosinase-positive (ty-pos) type of albinism was established in 71 cases, who clinically appeared to have ty-pos albinism, by means of the hair-bulb incubation test (Witkop et al. 1970). Those subjects (40 cases) who did not have the hair-bulb test, but had the clinical features of ty-pos albinism (i.e. yellow hair, blue to brown irides, sometimes pigmented ephelides but otherwise generalised lack of pigment in the skin, and nystagmus) were included in the ty-pos group, and the total therefore numbered 111. The ages of the subjects ranged from 1 to 72 years (mean age 17.8 years) and each subject was clinically examined for the presence of skin lesions (which included solar keratoses and chronic superficial ulcers) and ephelides (heavily pigmented large spidery freckles). It was not feasible to do skin biopsies on all subjects, but 13 albinos had skin biopsies for treatment purposes and these individuals are included. This group of subjects (Group 1) provided the first data source.

Two additional sources of data were used. The reports on 100 skin biopsies (17 of which were from albinos) on patients from the black population groups investigated at a local hospital in Johannesburg, over the period January 1976 to March 1980 were reviewed. This time period was selected because good records were available regarding the findings from the biopsy, the type and

site of carcinoma and whether the subject was an albino. These details were recorded and provided the second data source (Group II).

Then patient records of 19 albinos attending the local Johannesburg cancer clinic for dermatological assessment were analysed for further information regarding type of skin lesion, and this material provided the third data source (Group III).

Statistical analyses were performed using the chi-square test throughout, with one exception (indicated below) where the Mann-Whitney test (Siegel 1956) was required; a p -value < 0.05 was considered significant.

Results

Age and Ethnic Group

The data on the 111 Soweto subjects (Group I) examined for skin lesions were analysed according to the age of the subject at examination. The data are presented as cumulative percentages in Fig. 1. The overall prevalence of lesions was 23.4% (26 of 111 individuals), and the rate increased with age, rising from 6.0% (2 of 32) for those individuals below 10 years of age to 14% (6 of 44) in those aged 10–19 years, 21% (3 of 14) in the group 20–29 years, 62% (10 of 16) in the subjects 30–49 years and 100% (5 of 5 individuals) for those over the age of 50.

To assess whether lesions occurred at different rates in different ethnic groups, the Group I data were analysed according to age and ethnicity (Table 1). The subjects were divided into the two main ethnic groups found in South Africa: the Sotho-Tswana and the Nguni. The mean age of the Sotho-Tswana group was 17.5 (standard error 1.7) and of the Nguni 19.1 years (standard error 2.03), so the groups were similar. In the total group the mean age of subjects with skin lesions was very significantly higher than those without (31.0 years compared

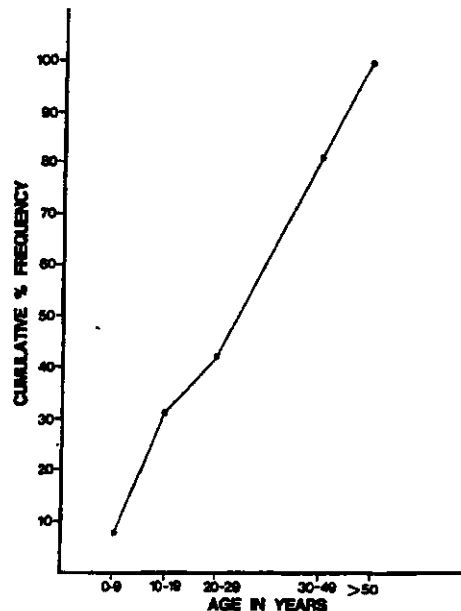


Fig. 1. Cumulative percentage frequency of albinos with skin lesions by age at examination.

with 13.9 years; $p < 0.001$, Mann-Whitney). The Sotho-Tswana group had an overall frequency of lesions which was greater than that for the Nguni (28% compared with 16%), but the difference was not significant (chi-square = 2.28; $p > 0.10$).

Skin Cancer and Ephelides

Ephelides were observed in Group I subjects in only 8 (25%) of the 32 albinos under 10 years of age, but were seen in 48 (61%) of the 79 subjects 10 years of age and older. This age-dependency of ephelides led us to exclude children under 10 years of age (an arbitrary cut-off point) from further analysis. In the group without skin lesions 40 of 55 (73%) had ephelides, while of the 24 subjects with lesions, only 8 (33%) had ephelides (see Table 2). The difference is highly significant (chi-square 9.28; $p < 0.01$). Of the 13 albinos with frank malignancy diagnosed as either

Table 1
Albinos (N=111) in Soweto with skin lesions by ethnic group and age

Ethnic group (No)	With lesions			Without lesions		
	No.	(%)	Mean age (SE) ^a (years)	No.	(%)	Mean Age (SE) (years)
SOTHO-TSWANA						
Tswana (33)	7	(21%)	32.8	26	(79%)	13.6
Pedi (2)	2	(100%)	23.0	0	(0%)	—
S Sotho (32)	10	(31%)	27.4	22	(69%)	16.9
Sub total (67)	19	(28%)	29.9 (4.1)	48	(72%)	12.5 (1.2)
NGUNI						
Zulu (25)	5	(20%)	44.0	20	(80%)	13.8
Xhosa (6)	0	(0%)	—	6	(100%)	19.0
Swazi (13)	2	(15%)	19.0	11	(85%)	14.2
Sub total (44)	7	(16%)	36.8 (6.2)	37	(84%)	15.8 (1.6)
Total (111)	26	(23%)	31.0 (3.5)	85	(77%)	13.9 (0.97)

^aSE: Standard error of the mean.

squamous or basal cell carcinoma on biopsy, only one had ephelides.

The ethnic origin of those subjects 10 years of age and older was analysed according to absence or presence of ephelides. The Sotho-Tswana had an overall lower rate of ephelides (27 of 47 subjects or 57%) than the Nguni (21 of 32 subjects or 65%), but the difference was not significant (chi-square 0.25; $p > 0.50$).

Type of Skin Cancer

The data from 100 skin biopsies (Group II) were analysed according to histological type of lesion (Table 3). The rate of both squamous and basal cell carcinoma in albinos

was grossly disproportionate to the rate of albinos in the population under survey, albinos comprising 17% of the total group with these conditions.

The data from the 19 albinos (Group III) attending the cancer clinic confirmed these histological findings, squamous cell being far more frequent than basal cell carcinoma; two patients had both types of malignancy. No melanomas were reported in either of these groups.

Site of Skin Cancer

The site of the skin biopsy was specified on only 83 of the 100 biopsy reports (Group II) and the findings from these 83 subjects

Table 2
Ephelides in albinos (79 subjects) 10 years and older with or without skin lesions

	With lesions		Without lesions	
	No.	(%)	No.	(%)
With ephelides (N=48)	8	(33%)	40	(73%)
Without ephelides (N=31)	16	(67%)	15	(27%)
Total	24	(100%)	55	(100%)

Table 3

Squamous and basal cell carcinoma in 100 skin biopsies from albinos and the general population

Type of carcinoma (No)	Skin biopsies			
	Albinos		General population	
	No.	(%)	No.	(%)
Squamous (87)	15	(17.2%)	72	(82.8%)
Basal cell (13)	2	(15.4%)	11	(84.6%)
Total (100)	17	(17%)	83	(83%)

are shown in Table 4. The site of the cancer in the majority of albinos was different from that reported for non-albinos, the head being involved more often in albinos, but the difference did not reach significance (chi-square 2.62, $p > 0.10$). The eye, eyelid, and cheek were the most susceptible sites on the head in albinos, whereas the scalp, neck and eye were commonly affected in non-albinos. There were no albino patients who had had biopsies on the torso, whereas 15% of the non-albinos had biopsies from this part of the body.

Discussion

The albinos in this study showed a high rate of skin lesions and the samples from which they came might be criticized as not being representative of the general albino population. The first group of subjects, however, was ascertained on the basis that they were albinos, not because they had skin cancer, and the present study was preceded by one on the prevalence of albinism, as well as several other studies. If the sample is biased at all, it could be biased in either of two

Table 4

Site of cutaneous biopsied carcinomas reported in albinos and the general black population in Johannesburg

Site of carcinoma	Biopsies from albinos			Biopsies from the general population		
	Total	No.	(%)	Total	No.	(%)
Head	13		(81%)	40		(80%)
Face (unspecified)		3			4	
Forehead		0			3	
Eye (+ eye-lid)		4			8	
Cheek		4			2	
Nose		1			1	
Lip		1			2	
Scalp		0			10	
Neck		0			10	
Torso	0		(0%)	10		(15%)
Chest		0			7	
Back		0			3	
Limbs	3		(18%)	(17%)		(25%)
Leg		3			13	
Arm		0			4	
Total	16	16	(100)	67	67	(100)

directions. Subjects with severe cancerous states might have been missed, since these states are unsightly and the patients are either hospitalized or do not expose themselves to public scrutiny, and therefore may not be available for research purposes. Alternatively the subjects with cancer may have been more likely to present for research purposes in the hope that they would receive help of some kind, especially since free anti-actinic cream was offered as an inducement. It is probably impossible to determine the ascertainment bias in terms of these two alternatives and in fact they may compensate for each other, resulting in a relatively unbiased sample. The albinos themselves were generally most grateful for the interest being taken in them, and this encourages the authors to think that they came forward because of their condition. Many different ascertainment methods were used and this led to the finding of an unusually high prevalence of the condition in the defined area of Soweto, Johannesburg (1:3900, Kromberg & Jenkins 1982) suggesting that the ascertainment was almost complete, again minimising any possible bias.

The findings from the present study show that susceptibility to skin cancer increases with age. The risks, however, do not appear to be as high as those for albinos living nearer the Equator; for example in Nigeria, all those albinos over the age of 20 years were found to have premalignant or frankly malignant lesions (Okoro 1975) and most had advanced lesions as early as the third decade of life (Okoro 1975, King et al. 1980). In the present series only 31% of subjects exhibited lesions by the end of the second, and 42% by the end of the third decade. Skin cancer rates are negatively correlated with latitude (Scotto et al. 1982), and this factor, together with the possibly lower standard of living and of available health services, could partly explain the

raised risks of skin cancer in Nigerian albinos.

The difference between the rates for lesions in albinos in the two local subgroups of the black population was not significant, but the data are suggestive of a lower rate amongst the Nguni. Probably the sample size was too small for the difference to be significant. It may be either that the Nguni have less ultraviolet exposure in their rural area (Scotto et al. 1982, Mulvihill 1981), where they may spend part of their lives, especially in early childhood, or that they have some innate protection from carcinomatosis. The areas where the Sotho-Tswana live are at higher altitude, lower latitude and have less sky cover than those of the Nguni. These factors are correlated with high rates of ultraviolet radiation (Scotto et al. 1982), which is the chief environmental causal agent in skin cancer (Mulvihill 1981). On the other hand, other factors predisposing to malignancy, for example genetic constitution, susceptibility to infections, lifestyle factors (such as diet and sun exposure), cultural habits (for example, consanguineous marriages which are more common in the Sotho-Tswana than in the Nguni), occupation, and education, might determine varying inter-ethnic cancer rates, and should be investigated.

The correlation between presence of ephelides and a reduced susceptibility to skin cancer may possibly be explained simplistically. Those albinos able to produce ephelides presumably have a greater ability to produce the pigment which is so important in protection of skin from the carcinogenic effects of ultraviolet radiation. The distribution of ephelides is similar to that of skin cancer, namely the sun-exposed areas (head, hands and forearms), and this would imply that both these dermatological changes are secondary to the same environmental insult (that is, ultraviolet radiation). There was no significant ethnic difference

in the presence of ephelides, although there was a trend towards the Nguni having a higher incidence than the Sotho-Tswana, which would correlate well with the suggested decreased rate of skin cancer in Nguni albinos.

The fact that all the subjects most probably had the tyrosinase-positive type of albinism, but that only 61% of those 10 years of age and older exhibited ephelides, is noteworthy. It may be that the tyrosinase-positive group is more heterogeneous than is presently recognised, and perhaps it should be sub-divided into those who can make some pigment (i.e. those with ephelides) and those who cannot.

The protection from ultraviolet radiation afforded by dark skin pigmentation is dramatically demonstrated comparing the rates of skin cancer in albinos with that of the general black population. Higginson & Oettle (1960) estimated that albinos in Johannesburg, where ultraviolet radiation is especially high because of the high altitude, low latitude, high number of sunny days, and reduced sky cover, have a risk for developing skin cancer which is 1000 times higher than that of the local pigmented black population. Further, South African negro albinos have approximately ten times greater susceptibility to skin cancer than do whites in the United States of America, and it has been objectively demonstrated by skin reflectance measurements that South African negro albinos have significantly lighter skin than South African whites (Kromberg 1986, Wasserman & Heyl 1968). Itayemi et al. (1979) suggest that basal cell carcinoma in Nigerian albinos behaves more aggressively than in Caucasoids, further emphasising the increased danger in albinos.

The relatively high incidence of non-melanoma skin cancer in the albinos in the present series contrasts strongly with the extremely low rates reported for those domiciled in the Transkei (Burrell, unpub-

lished data; Rose 1974; Keen 1976, personal communication). Although the Transkei data require confirmation, a likely explanation for this discrepancy is that there is lower ultraviolet radiation resulting in reduced mutagenesis and skin cancer rates in the Transkei (Kubitschek et al. 1986). The Transkei is coastal, and spans a latitude of around 30°-32° South, while Soweto (Johannesburg) is at an altitude of 2000 m and latitude of 26° South; both altitude and latitude have been shown to influence amount of ultraviolet radiation (Scotto & Fraumeni 1982). Further, it has been shown that Durban, a coastal city just north of the Transkei, has lower annual solar radiation than does Johannesburg (Riemerschmid 1940). Thus these data perhaps serve as an *in vivo* demonstration of the relationship between exposure to ultraviolet radiation and non-melanoma carcinogenesis. One must bear in mind, however, that none of the small group of Xhosas (the usual inhabitants of the Transkei) in the present series had cancer, and that the Nguni groups (which includes the Xhosa) may have some inherent protection from skin cancer.

The proportion of basal to squamous cell carcinomas, appears to be similar in the present study and in the studies of Oettle (1963), Isaacson et al. (1978) and Luande et al. (1985), the former type occurring much less frequently than the latter in albinos and in the general population. The absence of melanomas in the present series was not unexpected, because the pathogenesis of malignant melanoma seems to be related to sunburn rather than prolonged minor radiation exposure (Editorial 1987), and albinos might tend to avoid such excessive sun exposure because of their skin sensitivity. Also melanomas are more common in the higher socio-economic and advanced age groups (Cooke et al. 1984) and our subjects were from the lower strata and younger age groups. The absence of mela-

noma in our sample may have been due to small sample size; however the low incidence of this form of skin cancer in albinos has been noted by others (Stoll et al. 1981, Scott et al. 1982).

Oettle (1963), King et al. (1980), and Luande et al. (1985) found a distribution of sites of skin cancer similar to that observed in the present study, the head being involved most commonly. Although no albino was reported in this study to have cancer on the scalp, this finding was probably due to the limited sample size, since we are aware of one case which has come to our attention recently. However, we do encourage our subjects to keep their hair long and wear hats whenever possible as a preventive measure. The back and chest were affected only occasionally in the subjects of Oettle (1963) and Luande et al. (1985), and not at all in subjects in the present series. Since squamous carcinoma occurs only in sun-damaged skin, the trunk must have been exposed relatively frequently in the cases from these two former studies (for example, through inadequate clothing). However, factors other than sun exposure might predispose to the development of skin cancer. These include trauma and/or burns, unusual diets, chronic bacterial or parasitic infections, and/or oncogenic viruses, which might indirectly predispose to malignancy by non-specifically interfering with immunological defences (Cervenka et al. 1979).

In order both to proceed with further investigations and to assist the local albinos with the problems and risks associated with their hypopigmented skin, a clinic, as has been described in Tanzania (Luande et al. 1985) should probably be set up specifically for these patients. Apart from promoting early treatment, which can be very effective, such a clinic should offer preventive health counselling. Albinos should be advised to take protective measures such as: application of anti-actinic skin cream (particu-

larly to the face, including the eyelids and ears, and to the neck); using sunshades or hats with large brims; wearing long-sleeved dresses and long trousers; avoiding sunlight at least between 11.00 and 13.00 hours (thus reducing ultraviolet exposure by 50% (Scotto & Fraumeni 1982)) and perhaps even from 10.00 to 15.00 hours as recommended in Tanzania (Alexander & Henschke 1981); keeping the hair long; and working indoors if possible. If albinos were taught to take these preventive measures, their risks for skin cancer would be reduced and their quality of life improved.

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