

# ADVANCED SKIN CANCER IN TANZANIAN ALBINOS: PRELIMINARY OBSERVATIONS

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**Ten cases of advanced squamous cell carcinoma of the skin in albinos, treated by radiotherapy from 1973 to 1979 at the Muhimbili Medical Center of Dar-es-Salaam, have been reviewed. Age, sex, duration of symptoms, anatomic distribution, stage of disease, and treatment are reviewed. The relationship between albinism, sunlight, and skin cancer is discussed and a practical program of prevention is suggested. Advanced carcinoma of skin in albinos may be managed successfully with judicious radiation therapy. Excellent objective responses have been noted. No assessment of long-term control is made due to poor follow-up of patients.**

The incidence of squamous cell carcinoma of skin in Africa ranges from 7.8 to 16 percent of all diagnosed malignant tumors.<sup>1</sup> In Tanzania, these skin cancers represent as much as 15.2 percent of all tumors<sup>2,3</sup> and are the most frequently reported squamous cell cancers in mainland Tanzania.<sup>4</sup> The susceptibility of albinos in tropical regions to skin cancer has been documented previously.<sup>5-7</sup> The increased risk of developing skin cancer in African albinos as compared to normally pigmented individuals has been reported to be 1 to 1,000.<sup>8,9</sup> Okoro in a recent survey of nearly 1,000 patients with albinism found no albino over the age of 20 years to be free of malignant or premalignant skin disease.<sup>10</sup>

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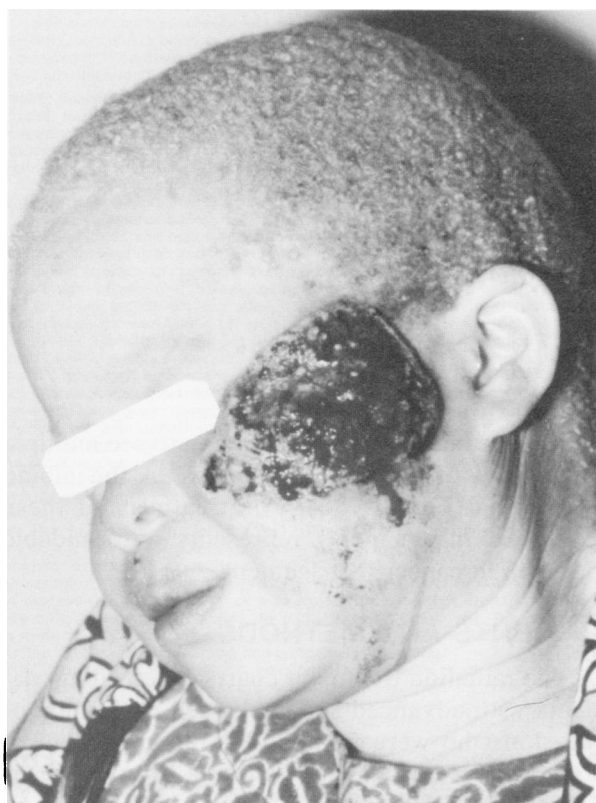
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In Tanzania, it is not uncommon to see multiple and/or advanced skin carcinomas in the albino population (Figures 1-3). The treatment of these advanced malignancies represents a formidable problem in cancer management.

## PATIENTS AND METHODS

The radiation treatment charts of ten albino patients with advanced squamous cell carcinoma of the skin who were treated at Muhimbili Medical Center, Dar-es-Salaam, Tanzania from January 1973 through December 1978 were reviewed. All patients had clinically diagnosed oculo-cutaneous albinism and histologically confirmed single or multiple squamous cell carcinomas. All were previously untreated except for one patient who had received several excisional procedures at another hospital.

Of the ten patients, the average age was 34.5 years (range 14 to 60 years). There were nine males and one female. The average duration of symptoms was 17.9 months. These patients were staged retrospectively according to the 1978 American Joint Committee recommendations.<sup>11</sup> A total of 21 squamous cell carcinomas were treated. All were radiated with a cobalt 60 teletherapy unit at Muhimbili Medical Center, the only radiotherapy facility in Tanzania. Treatment consisted of 200 rad per day, delivered four times per week. Where applicable, a 0.5 cm layer of bolus was used to deliver maximum doses to the skin and superficial tissues. The radiation response to treatment was defined as objective regression in the size of the primary lesion at completion of the teletherapy course. Eighty percent regression in tumor size was considered excellent, 50 percent regression was good, and less than 50 percent reduction in size was considered only as improved.



**Figure 1. Squamous cell carcinoma of the cheek in a 14-year-old albino girl**



**Figure 2. Multiple squamous cell carcinomas of the forehead in an adult male albino (age unknown)**

## RESULTS

The age distribution of the ten patients is shown in Table 1. Seven were between the ages 20-39 years. Table 2 describes the clinical features in each patient. Six patients had two or more squamous cell carcinomas. The lesions ranged in size from 0.5-16 cm. The anatomical distribution of lesions is listed in Table 3. Nineteen of 21 lesions were located in areas that were exposed to the sun and 15 of these were found in the head or neck region. The most frequent sites of involvement were the temple (5), cheek (2), post-auricular region (2), and neck (2). The forehead, eyelid, nose, and preauricular regions had one lesion each. Seven patients presented with T<sub>4</sub> lesions. Nodal involvement was seen in only two patients. No patients had distant metastasis at the time of initial presentation.

Results of treatment are illustrated in Table 4. Treatment doses ranged from 700-7,000 rad. Two patients discontinued radiotherapy for unknown reasons. Immediate responses to irradiation were

excellent in five patients, improved in four, and unknown in one. Five patients have been followed for 3 to 28 months after treatment. Two patients had recurrent disease at 4 and 13 months after radiotherapy. One patient developed a second primary carcinoma (Figure 4) at three months while in another patient, necrosis of the skin over the scapular region (Figure 5) was observed some 28 months after radiation therapy completion. One patient died after 16 months from persistent local disease of the neck. Five patients were lost to follow-up immediately after completion of treatment.

## DISCUSSION

Albinism is characterized by a decrease in pigment in the skin, hair, and eyes. It is due to an

inability of melanocytes to produce normal melanin. This genetic disease results from an enzyme defect in melanin synthesis. It generally is inherited as an autosomal recessive trait (oculocutaneous type). Certain pedigrees, however, have suggested dominant transmission (partial type) while others are sex-linked (ocular type).<sup>12</sup> From a biochemical point of view, albinism can be divided into two types, tyrosinase-positive and tyrosinase-negative.<sup>13</sup> In the former, the enzyme is present, but there is a limitation of availability of tyrosine. In the latter, there is complete lack of tyrosinase.

Albinism has a worldwide distribution. The highest incidences are recorded among the Caribe Cuna Indians of the San Blas Islands, which lie off the Atlantic coast of Panama. The Cunas have 63 albinos per 10,000.<sup>14</sup> In Africa, the frequency of albinism is reported to be between 1 in 2,600 and 1 in 10,000.<sup>1,10,15,16</sup>

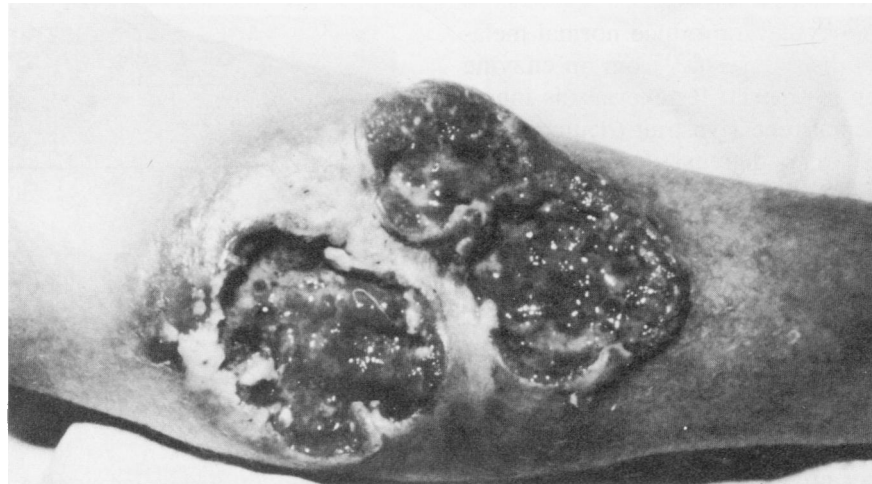
**TABLE 1. AGE DISTRIBUTION OF ALBINO PATIENTS**

Age Groups (years)	Patients
10-19	1
20-29	3
30-39	4
40-49	0
50-59	1
60+	1
<b>Total</b>	<b>10</b>

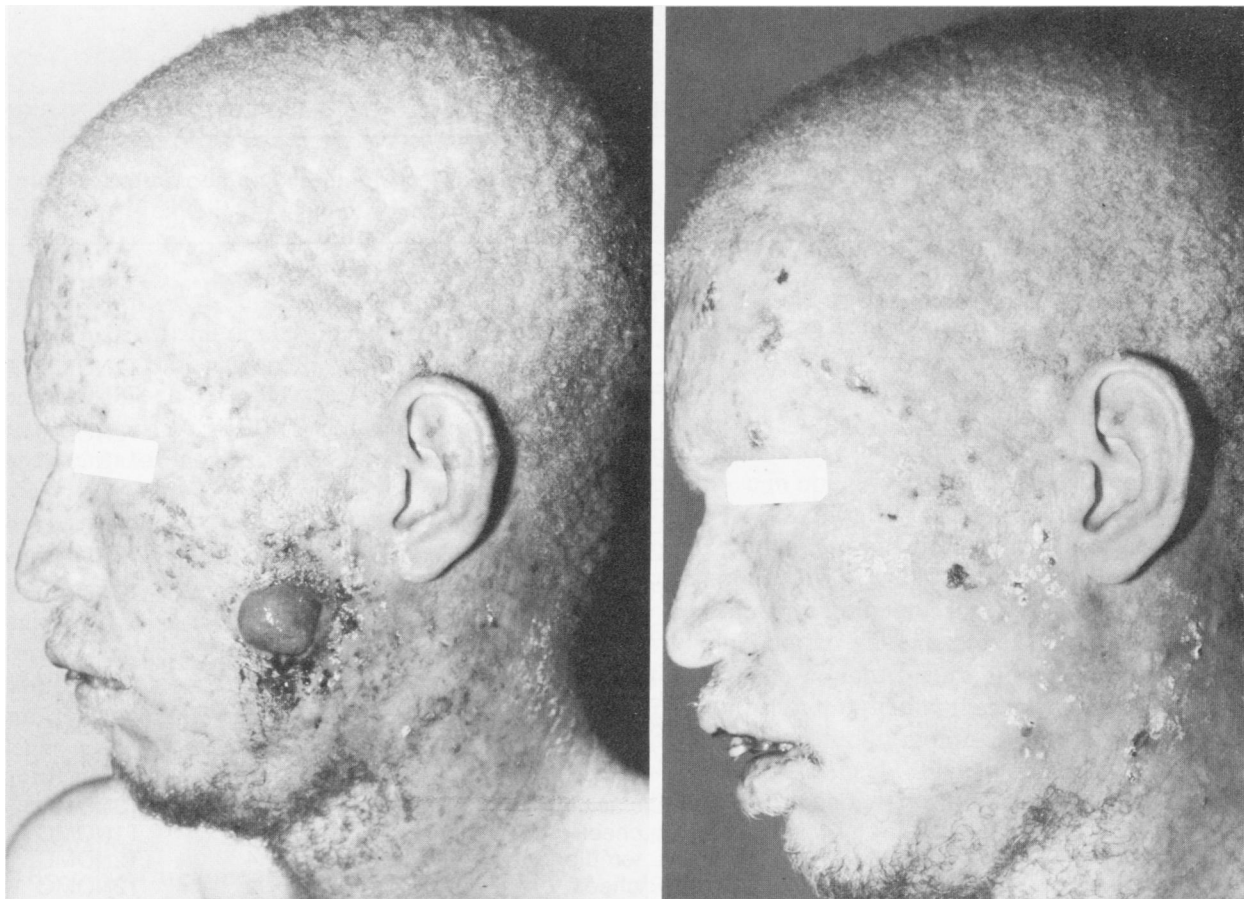
In pigmented peoples, melanin acts as a "light absorbing" filter which minimizes the impact of solar radiation on the vulnerable targets of the skin, such as, the dermis, epidermis, and the nuclei of cells. The skin of an albino has virtually no melanin pigment and the sun's ultraviolet radiation

**TABLE 2. CLINICAL SUMMARY OF ALBINO PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE SKIN**

Case	Age/Sex	Duration of Symptoms (months)	Site	Size (cm)	Stage
1	50/M	12	R forearm	15 × 5	T4NOMO
			R leg	12 × 8	T4NOMO
2	38/M	36	L posterior shoulder	6.5 × 5	T4NOMO
			L neck	0.5	T1NOMO
			R scapular	1.5	T1NOMO
3	25/F	5	L temple	5 × 4	T2NOMO
			L scapular	15 × 12	T4NOMO
4	35/M	72	R nose	6 × 4.5	T4NOMO
			L temple	4 × 3.5	T2NOMO
			L temple	5 × 4.3	T2NOMO
5	35/M	12	R upper eyelid	6 × 5.5	T3NOMO
6	60/M	12	R lower back	16 × 14	T4N2aMO
7	16/M	12	L temple	5 × 4	T2NOMO
			L preauricular	8 × 6	T4NOMO
			R postauricular	5 × 3	T2NOMO
8	28/M	15	L postauricular	9 × 2	T4N2bMO
9	30/M	12	L clavicle	6 × 8	T3NOMO
			L cheek	2	T1NOMO
			L temple	5 × 4	T2NOMO
			R cheek	3 × 2	T2NOMO
10	28/M	2	R forehead	2	T1NOMO
			L cheek	2.5 × 2.5	T2NOMO



**Figure 3. Advanced squamous cell carcinoma of the forearm showing infiltration of deep muscle**



**Figure 4. Squamous cell carcinoma of the cheek before initiation of radiotherapy. Multiple premalignant solar keratoses are seen involving the entire face (Case 10), (left). Complete regression of squamous cell carcinoma, two months following radiation, (right)**

can penetrate it readily.<sup>17</sup> Early in life, the epidermis of an albino develops abnormal changes secondary to actinic radiation. These changes include sunburn, blisters, solar elastosis, ephelides, centrofacial lentiginosis, solar keratoses, chronic superficial ulcers, and squamous and basal cell carcinomas.<sup>10</sup> Shapiro et al<sup>16</sup> observed that pigmentation was the most important factor in determining the incidence and distribution of skin carcinoma in South African Bantu.

In Tanzania the frequency of albinism has been estimated to be approximately 1 in 2,500. Traditionally, a newborn child with albinism was considered to be evil and disfigured. Many tribes practiced infanticide and these children, therefore, were sacrificed.<sup>18</sup> In Swahili, the national language of Tanzania, albinos or *zeruzeru* are "thought by some to be substituted for the proper children by

**TABLE 3. ANATOMICAL DISTRIBUTION OF SQUAMOUS CELL CARCINOMAS OF SKIN IN TEN ALBINO PATIENTS**

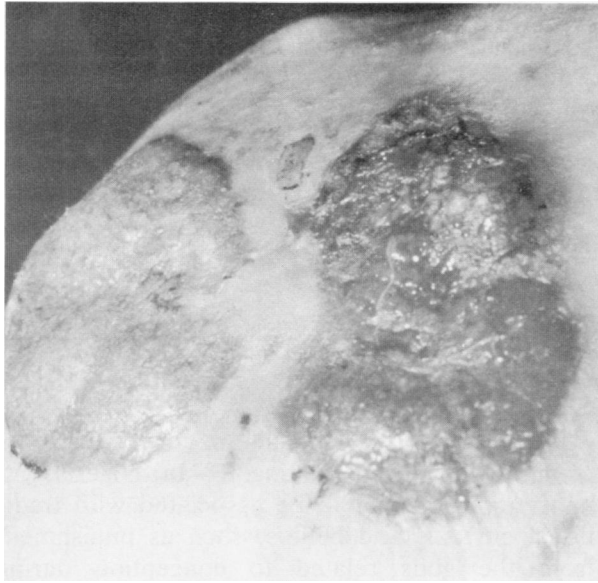
Area	Number of Lesions
Head and neck	15
Trunk	4
Upper limb	1
Lower limb	1
<b>Total</b>	<b>21</b>

evil spirits, or to be children conceived by a woman while menstruating."<sup>19</sup> In Nigeria, albinism was thought to be associated with traditional customs and beliefs, such as punishment from the gods related to conception during

**TABLE 4. TREATMENT SUMMARY AND RESULTS IN ALBINOS WITH SQUAMOUS CELL CARCINOMA OF SKIN**

Case	Irradiated Site	Dose Co-60 (rads)	Response	Follow-Up
1	R forearm R leg	700 700	Unknown RT incomplete	Lost at completion
2	L posterior shoulder L neck R scapular	6,000 5,000 5,000	Excellent	28 months, skin necrosis, NED*
3	L temple L scapular	4,500 5,000	Improved	13 months, recurrence
4	R nose L temple	7,000 7,000	Excellent	Lost at completion
5	R eye and orbit	6,000	Improved	Lost at completion
6	R lower back R inguinal area	3,800 1,600	Improved	Lost at completion 4 months, recurrence
7	L lateral face R postauricular	6,500 6,000	Excellent	4 months, recurrence
8	L postauricular and submandibular node	5,000	Improved	16 months, dead from disease
9	L clavicle L cheek L temple R cheek	4,800 4,800 4,800 5,000	Excellent	Lost at completion
10	R forehead L cheek	4,400 6,000	Excellent	5 months, NED* 2 months, NED*

\*NED—No evidence of disease



**Figure 5. Skin necrosis, 28 months after radiation (Case 2)**

menstruation, or seeing frightening sights during pregnancy.<sup>10</sup> There appears to have been no social stigma traditionally attached to albinism among the Caribe Cuna Indians. In fact, the Cuna Moon-child albinos had a special culturally defined role in that only they were allowed to view eclipses of the moon or sun—important events in Cuna cosmology.<sup>20</sup> This explains the perpetuation of albinism among the Cuna.

Traditionally, albinos in Africa have been looked down upon by society. Thus, their problems of vision, employment, and skin cancer often have been neglected and their social life correspondingly is extremely difficult. With the abandonment of such traditional tribal customs as infanticide, the albino population is becoming larger. Skin carcinoma, therefore, is being seen with greater frequency. It is now common to observe six-month-old albino infants with severe blistering, sunburn, and other stigmata at the Albino Skin Cancer Prevention Clinic of the Tanzanian Tumor Center in Dar-es-Salaam. These preliminary manifestations, if uncontrolled, may later progress into more serious skin aberrations.

Of 50 cases of skin carcinoma reported by Sha-

piro et al,<sup>16</sup> 12 were among albinos. Histologically, nine of these had squamous cell carcinomas and three had basal cell carcinomas. Higgenson and Oettlé<sup>8</sup> observed nine cases of skin cancers occurring in albinos among 125 South African Bantu (7.2 percent) with skin cancer. Six patients had squamous cell carcinomas, two had basal cell carcinomas, and one had a malignant melanoma. More recently, Iversen and Iversen<sup>9</sup> have reported four cases of squamous cell carcinoma of the skin of albinos in Uganda: three basal cell carcinomas and one trichoepithelioma among 663 patients with histologically confirmed tumors. In this present small series, basal cell carcinoma was not recorded in any patient. A possible explanation is that the majority of patients had multiple pre-malignant and malignant lesions and an early basal cell cancer may have been overlooked because of the more symptomatic and advanced squamous carcinomas.

The occurrence of melanomas in albinos is rare.<sup>21</sup> Kennedy et al<sup>22</sup> reviewed five cases of melanomas in albinos in the literature and reported another case in a 38-year-old male in which the primary tumor arose in a nevus which had been present since birth. These authors suggested that removal of all birthmarks in albinos should be considered, since three out of six patients had lesions which arose from nevi.

Most skin cancer in African albinos occurs after 20 years of age.<sup>10</sup> In the present series the average age was 34 years with a male to female ratio of 9:1.

The location in exposed areas of the body of the majority of skin carcinomas in these patients suggested a high correlation with exposure to sunlight. Moreover, 15 out of 21 lesions were confined to the head and neck. Urbach's study of skin malignancies in US whites has shown that squamous cell carcinomas of the head and neck occur almost exclusively in those areas which have been found to receive the greatest amount of solar ultraviolet (UV) radiation.<sup>23</sup> These are the nose, malar region, vermilion border of lower lip, rim of the ear, forehead, and back of neck (in order of decreasing UV absorption). In the present series, the temple region was the most frequent site of involvement. This observation can be explained in part by the photophobia characteristic of albinism which might cause the albino to avoid direct sunlight into the eyes or the central region of the face by turning the head 45 degrees or more away from

the sun's primary beam. In this situation, the temple regions would receive greater amounts of ultraviolet radiation and could explain the higher frequency of involvement of these areas. The same reasoning explains the increased involvement of the cheeks.

The ultraviolet spectrum is characterized by three distinct portions, UV-A (400-315 nm), UV-B (315-280 nm), and UV-C (<280 nm).<sup>24</sup> The cancer-producing segment of UV radiation in experimental animals lies between 290 nm and 320 nm. This coincides with the spectral range that produces sunburn in human skin.<sup>25</sup> Great variations exist in the amount of biologically effective ultraviolet radiation reaching various areas of the earth's surface. The highest levels are found near the equator.<sup>26</sup> Tanzania borders on the equator and is located in low geographic latitudes (1-11 degrees South). The ultraviolet radiation reaching the ground is more intense in lower latitudes due to the greater sun angle. At higher sun angles, less UV radiation of the sun is absorbed by the ozone atmosphere of the earth. Sunlight, therefore, is exceedingly harsh to the albino in East Africa. The susceptibility of the skin and the amount of sunlight exposure are the two main factors involved in squamous cell carcinomas of skin in albinos.

The majority of patients in this series had advanced lesions involving muscle or cartilage. Distant metastasis was not observed in any patient. This finding is explained in part by the fact that squamous cell carcinomas arising in sun damaged areas have a lower incidence of metastasis than do carcinomas arising from chronic ulcerations or *de novo*.<sup>27</sup> The average duration of symptoms of 17.9 months among these patients and the advanced nature of the presenting lesions suggest serious delays in seeking proper medical attention. Many albinos particularly in the rural regions of Tanzania are unaware that these devastating skin changes are due to exposure to sunlight.

All patients in the present series were referred for radiation therapy due to a lack of an alternative form of treatment. Without treatment these patients most certainly would have had miserable existences because of the advanced nature of their disease. Radiation therapy for skin carcinoma in albinos is recommended in the following conditions: (1) inoperable lesions, or those for which an effective operation is unreasonable, (2) multiple lesions, and (3) in patients with medical contrain-

dications to surgery. In this series, all patients fulfilled one or two of these criteria for treatment.

Five patients had excellent immediate responses to radiotherapy. Four were improved. Bleeding from lesions was controlled effectively with radiation in the majority of patients. Relief of painful symptoms was achieved. Only five out of ten patients treated have been followed adequately. In two of these (Cases 3 and 7) recurrent disease was observed at 4 and 13 months after radiotherapy. Necrosis of skin over the scapula with failure to heal some 28 months after treatment was noted in one patient (Case 2). Skin grafting was recommended.

Of the squamous cell carcinomas of skin which arise from exposed parts of the body, ear lesions have been reported to exhibit the greatest tendency to metastasize.<sup>28</sup> The only patient (Case 8), who died with disease 16 months after diagnosis, had a primary lesion in the post-auricular region involving the external ear. It eventually encompassed the middle ear with regional lymph node involvement. The major problem in this patient probably was not the aggressive biology of the tumor, but more probably, the inadequacy of the multiple limited surgical excisions performed.

Long-term control is difficult to assess in the present series of squamous cell carcinomas in albinos due to a significant portion of patients being lost to follow-up. Transportation is a major factor influencing poor follow-up. As many patients travel long distances to receive radiotherapy at the Muhimbili Medical Center, it is often a physical and financial burden for them to return for follow-up. The pressures of family separation and loss of earned income on patients while under treatment also affect patient compliance and follow-up. However, the majority of patients benefited from radiotherapy and continuation of such treatment appears to be justified.

The single most important prophylactic safeguard against the development of premalignant or malignant lesions in albinos is to avoid excessive exposure to the sun's ultraviolet radiation. The most practical method is to educate the albino community about the harmful effects of the sun. This can best be implemented by establishing screening clinics at which albinos can receive instruction in appropriate protective measures against the sun. This approach has been found to be extremely effective in Dar-es-Salaam. Such

protective measures include staying out of the sun during hours of peak intensity (10:00 to 15:00 hrs); wearing protective clothing such as wide-brimmed hats, long sleeves, conservative dresses and trousers; and using sunscreens, such as zinc oxide paste, aminobenzoic acid, and titanium dioxide, which block sunlight in the erythemogenic and cancerogenic ultraviolet band of 290 to 320 nm. In addition, employment of albinos in indoor occupations should be an effective safeguard against skin cancer.

Since inbreeding has been recognized as a major factor in populations with high incidence of albinism, Okoro has recommended considering genetic counseling as an alternative solution to this skin cancer problem.<sup>10</sup> Counseling could theoretically decrease the prevalence of the autosomal recessive trait (the most frequent form) resulting in less albinism and ultimately less skin cancer in albinos. Counseling, therefore, should be incorporated in every screening program.

In summary, ultraviolet radiation of the sun, particularly in tropical and subtropical latitudes, is extremely harmful to the melanin-deficient albinotic skin. Premalignant and malignant lesions are seen most frequently in the head and neck regions. Radiotherapy can produce acceptable results in albino patients who present with multiple, inoperable, and/or advanced skin cancers. Adequate follow-up is needed in order to assess long-term control rates. Education concerning prophylactic measures to prevent excessive exposure to sunlight is perhaps the most practical method for prevention of skin cancer in albinos.

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