

# The Tanzanian Human Albino Skin

## Natural History

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Three hundred fifty albinos in the city of Dar-es-Salaam have been registered at the Tanzania Tumor Centre. Their skin changes were followed for at least 2 years. Chronic skin damage was evident in all albinos by the first year of life; by 20 years, the skin of every subject demonstrated subclinical malignant change, and some had clinical epitheliomas. Untreated, the latter tumors become intractable and disseminate, usually causing death in the third or fourth decade of life. Four clinical stages could be identified, each one associated with distinct pathologic changes: Stage 1, erythema; Stage 2, epidermal atrophy with dermal hypertrophy; Stage 3, solar keratosis; and Stage 4, clinical carcinoma (under 3 cm). It was found that clinical Stage 2 only occurs in those skin areas that show evidence of previous Stage 1 change. Similarly, Stage 3 occurs only in areas that have gone through Stages 1 and 2. Stage 4 cancers were only found in those areas that had gone through all of the three prior stages. During the 2-year period of this study, 104 skin cancers, both early and advanced, were recorded at the albino skin clinic. Thirty-three of the 104 cancers were advanced (over 4 cm in diameter). The median age of the latter group was 31.0 years. Whereas there was no sex bias in the distribution of clinical cancer, 28 of the 33 advanced cancers were in men. Histologically, the great majority of the advanced tumors were squamous cell carcinomas: 29 of 33. There was one melanoma and three basal cell tumors. The predominant site of advanced cancers in the study group was the head and neck region (30 patients); the other three occurred on the trunk, which is generally covered by clothes.

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**N**ONMELANOTIC skin cancers have been treated as a relatively insignificant subject in the medical literature, even though they constitute up to 50% of all cancers in western countries.<sup>1</sup> The fact that these tumors are so well controlled might explain the paradox; less than 5% of the individuals who develop such cancers ever succumb to them.<sup>2</sup> The major cause of the cancers is thought to be solar irradiation,<sup>3-5</sup> which could thus be the leading cause of cancer in the western countries. In less than two decades, the incidence of skin cancer has doubled in certain localities for no obvious reason.<sup>1</sup> The continuous impact of supersonic transport planes and fluorocarbon aerosols on the stratospheric ozone and the increasing incidence of skin cancer might cause renewed interest or concern about further study of ultraviolet (UV) light carcinogenesis.

Skin cancer among albinos in the equatorial regions of the world has a higher incidence and a more ominous

course, perhaps due to neglect. Most albinos in these areas who contract the disease die as a consequence. Okoro<sup>6</sup> noted that no Nigerian albinos older than 20 years were free from either frank or premalignant skin cancer. The same author also noted that only 6.3% of albinos were older than 30 years, as compared to the expected 20% of the general population. Thus, whereas skin cancer may not be a major cause of mortality in the western world, it is indeed an important killer among the tropical albino population.

This study, instituted at the Tanzania Tumor Centre, was performed to chart out the natural history of albino solar skin damage and to develop a program for skin cancer prevention within that population.

### Patients and Methods

This study is based in Dar-es-Salaam, the capital of Tanzania, a city that lies south of the equator and is exposed throughout the year to a high degree of UV light. Dar-es-Salaam, a coastal city, is warm and humid for most of the year, making it necessary for most town dwellers to dress lightly. The head and neck regions, the arms below mid upper arm, and the legs below the knees are generally exposed.

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TABLE 1. Distribution of Lesions by Age in 350 Albinos (Clinical Staging)

Age group (yr)	Total no.	Epidermal atrophy	Focal benign lesions	Clinical cancer
Younger than 1	26	14	0	0
2-10	149	149	30	0
11-20	52	52	52	28
21-30	70	70	70	51
31-40	45	45	45	38
41-50	3	3	3	4
51-60	3	3	3	3
Older than 60	2	2	2	1
Total	350	338	205	125

Early in their lives, *i.e.*, in the first and second decades, albinos complain of inability to sweat as well as their black counterparts. This forces them to dress more lightly, in turn promoting more intense exposure to UV light.

The city of Dar-es-Salaam has one million residents, with an estimated population of 700 albinos. Three hundred fifty albinos within the confines of the city were registered at the Tanzania Tumor Centre. A detailed questionnaire was presented to each of these individuals in order to ascertain their basic demographic characteristics (*e.g.*, age, education, employment, family responsibility), family background (including any incidence of Albinism), and their educational and occupational characteristics.

Each of these albinos was seen at regular intervals at a special clinic over a period of 2 years, beginning in October 1980. At each visit, the occupational and educational status of each subject was updated; in addition, any skin changes were thoroughly examined. When lesions were detected, biopsies were made of the affected areas.

## Results

### Demographic Characteristics

The age range of the albino study group was from birth to 70 years (median age, 10 years). Less than 10% of the population were 30 years or older. This study group is young, even when compared with the Tanzania mainland census figure of 1978 which has only 34.11% of the population less than 10 years of age.<sup>7</sup> At the other end of the age spectrum, there are also fewer albinos than expected; the Tanzania mainland figure shows that 23.53% of the general population is older than 35 years, as contrasted with 10% of the albino study group.

Virtually all albinos have eyesight impairment, partially due to deficient iris pigment, which starts early in

childhood. This affects their performance in school, and the majority of the children can benefit only from schools in which special visual aids are provided.

Only 12 of the 350 adults studied had occupations as full-time indoor workers. The others had outdoor occupations. Suffering from poor vision and often poorly educated, Albinos rarely have the opportunity to work indoors where sight and at least some education are prerequisites. One of the two oldest albinos, age 60 years, received financial support from his community and thus had not had to work outside in the sun throughout his life. This patient did not have any evidence of clinical skin malignancy.

### Skin Changes

Evidence of field skin damage was already manifest in the exposed areas in all children by the first year of life. They had a shiny, leathery and erythematous skin. Focal lesions generally started on the maximally exposed areas of neck, arms and legs as early as 5 years of age; these took the form of tiny, raised nodules. These nodules are circumscribed areas of multilayered epithelium with large, nucleated cells spanning the entire thickness of the epidermis. No dermal tissue is involved. The earliest case of skin cancer was documented clinically when the patient was 9 years of age.

The incidence of early focal lesions increased with age (Table 1). Frequently, these lesions regressed spontaneously. When they persisted, they ulcerated, bled, and occasionally became infected and tender. At this point, electric fulguration or surgical excision proved curative. By ages 15 to 18 years, most albinos had evidence of multiple, hyperkeratotic skin nodules (Table 1). Many albinos remembered skin nodules which had formed and later disappeared without treatment. This suggests spontaneous regression for such lesions.

Advanced, symptomatic cancers with necrotic beds and raised edges were common among patients in their late 20s and early 30s (Table 1). Such cancers result from untended smaller lesions and force the patient to come to hospital due to bleeding, intense pain, or foul-smelling discharge.

There is a subset of the albino population consisting predominantly of females who have minimal or no history of development of symptomatic focal skin lesions, although they have the same evidence of generalized solar skin damage. The sun exposure pattern of these albinos was no different than their more affected counterparts. Histologically, their skin shows dermal hypertrophy and epidermal atrophy. To date no distinguishing clinical characteristics have become apparent. Close study of this subset is underway.



FIGS. 1A AND 1B. (A, left) One-year-old Albino with erythema (Stage 1). (B, right) Three-year-old with severe erythema and second-degree burns (Stage 1).

### Clinical Stages

After following the skin changes in our study group for more than 2 years and documenting the corresponding pathologic findings, four distinct clinical stages could be identified, each with associated pathologic patterns. It was found that clinical Stage 2 occurs only in those skin areas that showed evidence of previous damage from Stage 1. Similarly, Stage 3 followed only in those areas that had gone through the Stages 1 and 2. Clinical cancers, Stage 4, were only found in those areas that had gone through all of the three prior stages, never in those which had only advanced to Stage 1 or 2.

*Stage 1, erythema:* This is the first observable reaction of the albino skin when exposed to sun rays. The change is manifest after as short an exposure as 1 to 2 hours in direct sunlight between 9 and 4 o'clock in Dar-es-Salaam. Usually first exposures occur during or after the second month of life. The traditional habit of strapping babies with a cotton cloth on the mother's back leaves the baby's head and neck, arms, and distal one third of the lower limbs exposed (Fig. 1A). The pattern of erythema reproduces the distribution of UV intensity to the skin surface. It is most intense on the second day,

at which time a noninfectious febrile episode may be experienced. In the case of single short exposures, the erythema subsides within 2 to 3 days. It is not unusual for albino children to experience overt skin burns, especially during the hotter months between late July and December. Some patients who incurred second-degree burns during these exposures have had to be admitted to the Centre for treatment (Fig. 1B). Recovery from such burns with just rest and exposure to the indoor environment of the wards is rapid and remarkable.

*Stage 2, epidermal atrophy with dermal hypertrophy:* Albino children usually enjoy the same developmental milestones as their counterparts with normal skin. They crawl at about 6 months and walk at just over 1 year. Repeated UV exposures lead to permanent clinical and morphologic skin changes, typical of what is described in textbooks as "sailors' skin." The skin feels firm and coarse to palpation, hair is sparse in the majority of cases, and sweating is diminished (Fig. 2). Erythema is nonexistent in areas where these advanced, permanent skin changes have taken place.

The distribution of these skin changes faithfully follows that of the preceding erythema. Because of integumental destruction, discomfort from the tropical heat is partic-

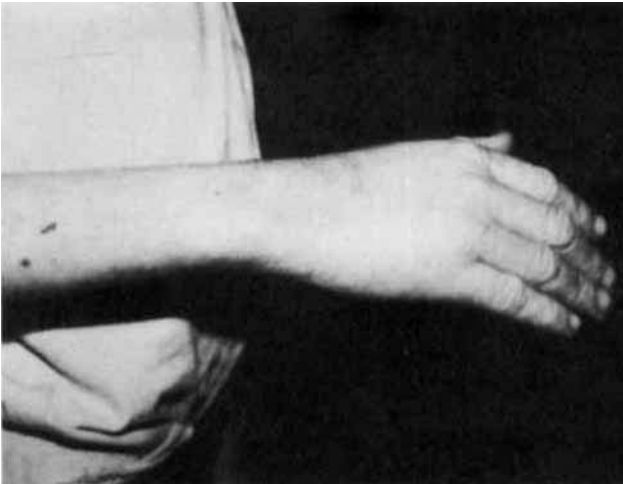


FIG. 2. Albino with epidermal atrophy and dermal hypertrophy (Stage 2).

ularly pronounced in this group. By the time most of the children are 1 year old, varying degrees of these changes are already noticeable.

It is worth mentioning here that a few albinos demonstrate a paradoxical overgrowth of body hair in the exposed parts. The distribution and amount of the hair is clearly different from that found in their black counterparts in the same geographical setting. The phenom-

enon suggests some desperate attempt by the skin to furnish a hair cover. It is during the first decade of life that pigment formation and hair growth are attempted and tyrosine-positive individuals form the typical patchy distribution of skin melanization.

*Stage 3, solar keratosis:* As early as the first decade of life, children start developing raised domes of skin that may be initially as small as 1 mm. These are normally smooth-surfaced and noninflamed. They may look erythematous. Later they become scaly and rough (Fig. 3A), and a few eventually break down and bleed. Pain is not a significant complaint. Keratotic lesions are found only where epidermal atrophy and dermal hypertrophy have already altered the skin. Histochemically, glycogen is demonstrated in the earliest lesions, which can appear in crops of hundreds in any one individual (Fig. 3B). Apparently they are reversible; some will recede whereas new ones appear in other areas. Response to 5-fluorouracil (5-FU) (5% ointment) and BCG is excellent.

*Stage 4, clinically symptomatic cancer:* (a) early ( $\leq 3$  cm diameter) and (b) advanced ( $>4$  cm in diameter): Clinically, the change from keratotic lesions to ulcerating cancer is not as clear-cut as one might expect. As already pointed out, patients hardly ever complain about the former, whereas they do complain about the large ulcerated and symptomatic lesions. One very remarkable aspect of the larger lesions which eventually ulcerate



FIGS. 3A AND 3B. (A, left) Seven-year-old girl with skin atrophy and keratosis. (Stages 2 and 3). (B, right) Example of multiple keratoses.



FIGS. 4A-4C. (A, left) Twenty-eight-year-old woman with ulcers for 3 months (Stage 4). (B, center) Overt skin cancer (Stage 4) in a 35-year-old. The patient died 4 months later. (C, right) Thirty-five-year-old after surgery: full-thickness skin graft.

and become large tumors is the frequency with which they tend to favor the head and neck region, as opposed to the wider distribution of the keratotic lesions (Figs. 4A-4C).

If not treated promptly and carefully, the cancers continue to grow to a very large size, over 4 cm; only later do they develop regional lymph node metastases. Distribution of metastasis beyond the nodes is currently under study. In our experience, erosion of bone—especially skull, in the case of head tumors—is not uncommon. Later progression to metastatic liver and bone disease have also been documented.

The time from the development or irreversible symptomatic skin lesions to the appearance of metastases and finally to the patient's death is usually 4 years. On the other hand, control of the keratotic and small cancerous lesions will prevent the development of clinically overt cancers.

### Discussion

Although skin cancer can be readily produced by UV radiation in experimental animal models, evidence for such an effect in man remains epidemiologic. Members of pigmented races, who sunburn much less readily than do people with white skin, also have much less skin cancer; when the disease does occur, it is not predominantly found on light-exposed areas.

Like many other cancers, skin cancer has many causes. In albinos, the lack of skin pigment—melanin—predisposes their skin to the damaging effect of UV light, and their presence in periequatorial areas exposes them to maximal UV light. This combination of circumstances makes albinos extremely vulnerable to skin cancer.

Previous studies have suggested that the incidence, age of onset, and severity of skin cancer vary in different albino populations. Nigeria, which is sandwiched between the 4° and 14° latitude north of the equator, presumably has UV light of equal intensity to that of Tanzania, which is between the 1° and 11° latitudes south of the equator. In Nigeria, the progression of skin changes leading to cancer formation in albinos is very similar. Thus, in Nigeria,<sup>7</sup> all albinos older than 10 years were reported to have maximal benign chronic changes of the skin, and none older than 20 years were free of subclinical malignant skin changes. This experience is exactly the same as ours in Dar-es-Salaam, where the severity of the skin problem is measured by the survival of the particular albino population under study.

Less than 10% of the Dar-es-Salaam albinos survive beyond 30 years: the same percentage as reported by Okoro for his 1000 collected cases.<sup>6</sup> This fact is the more intriguing if one considers that whereas the Nigerian albinos are predominantly of Negroid stock, those of Tanzania are overwhelmingly Bantu. Of the Bantu albinos in South Africa, 32.7% live beyond 30 years: a percentage three times as high as that of their Tanzanian counterparts.<sup>7</sup> This is a higher survival rate than even nonalbino Africans in the other two localities (20% of the population in Nigeria and 23.53% in Tanzania lives beyond 30 years). The figures suggest that racial differences in these groups are probably not a factor in their development of skin cancer. At the same time, the data suggest that the common proximity of Nigeria and Tanzania to the equator and hence to UV light intensity, might be responsible for the observed similarities. South Africa Bantu albinos who live between latitudes 20° to 25° south have less skin cancer and a much longer life

span. Urbach<sup>8</sup> estimates that the incidence of skin cancer doubles for every 10 degrees of latitude from the equator. From such data a theoretical tripling of albino skin cancer might be expected between Dar-es-Salaam (7° latitude) and South Africa (22° latitude), corroborating the observed figures.

Other environmental influences might include dress, diet, occupation, and patterns of exposure. These certainly differ among these African localities; for example, the staple palm oil in Nigeria contains a high level of carotenoids not consumed in Tanzania. Whereas experience elsewhere has suggested that carotenoids might protect the skin from the carcinogenic effect of UV light,<sup>9-11</sup> the high intensity of the light around the equator might offset the expected beneficial effect.<sup>12</sup> Such possibilities raise several issues of scientific and medical interest which are being pursued by our Centre.

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