bulb exhibited severe atrophy and decreased pigmentation. The atrophied bulbs ranged from 0.025 to 0.075 mm in maximum diameter compared with a range of 0.250 to 0.550 mm before protein deprivation. (This measurement did not include the root sheaths.) The atrophied bulbs manifested distal constriction which extended for a short distance along the shaft. (ii) The external root sheath was consistently absent in atrophied bulbs (Figs. 1 and 2). (iii) The internal root sheath was frequently absent as well.

The marked atrophy of the bulb was observed in one-half of the total sample in the anagen phase for each subject after protein deprivation (range 48 to 65 percent). Care was taken to differentiate between twisted and atrophied bulbs by rotating specimens. Many of the bulbs in the anagen phase which did not atrophy after the subject was deprived of protein had a distinct pinch constriction distal to the bulb. Intrafollicular hair shaft breakage at epilation was considerably more frequent after protein deprivation [before deprivation (mean) $\bar{X}$, 41 percent; after deprivation $\bar{X}$, 77 percent]. Hair samples were taken for chemical analysis 25 days after the root samples in order to obtain hair produced during the deprivation period. Some shaft constriction was noted as a result of the short-term protein deprivation of the subjects but less than that which we have observed with children suffering from acute protein-calorie malnutrition (*13*) or that which has been reported by Van Scott (*11*) with the use of cancer chemotherapeutic drugs.

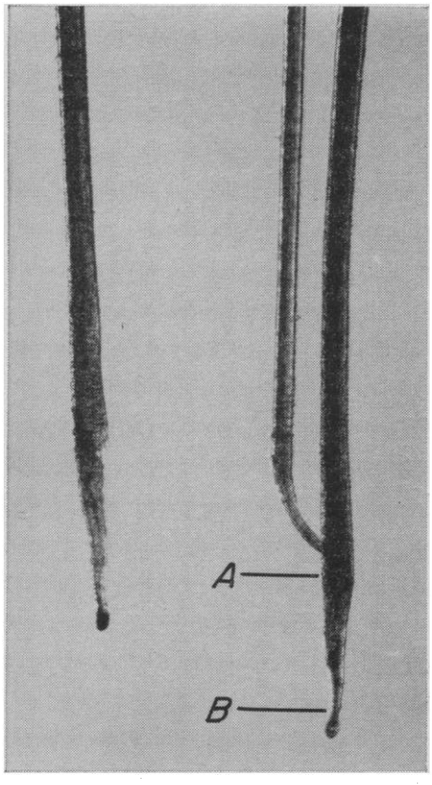

Fig. 2. Hair root of the same subject after 15-day protein deprivation (× 75). (*A*) atrophy of external root sheath; (*B*) marked atrophy and loss of pigment of the bulb.

The morphological changes between the samples taken before and after protein deprivation were consistent in all subjects, although the amount of change varied with the individual. These changes occurred in short-term protein deprivation of normal healthy subjects in the absence of decreases of serum protein, hemoglobin, and hematocrit, and were reversible to some degree when protein was again added to the diet.

Hair root examination may prove to be a useful tool in public health programs as an inexpensive and simple diagnostic aid in protein-calorie malnutrition, particularly in developing areas where more sophisticated equipment is not readily available and where tissue samples must be transported under adverse conditions of temperature and humidity.

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Langerhans Cells: Uptake of Tritiated Thymidine

Abstract. *After irradiation of the skin of the rhesus monkey with ultraviolet light, there is temporary suppression of the proliferating activity of the epidermal cells, followed by some hyperplasia and a striking increase in synthesis of DNA by Langerhans cells. Since Langerhans cells can proliferate, they can no longer be considered to be worn-out melanocytes.*

In spite of the many varied approaches of studies, the function and genealogy of a population of dendritic cells interspersed in the higher level of the epidermis still remain unknown. Discovered by Langerhans (*1*) in 1868 and named after him, these cells were first demonstrated by treating the skin with an acid solution of gold chloride. Since this stain has a particular affinity for nervous tissue, the impregnated cells were considered to be nervous receptors (*2*) derived from cells located in the dermis (*3*). Assuming that they represent terminal stages of previously mature melanocytes or desquamating, effete, pigment cells, investigators have generally included the elusive Langerhans cells with the melanocytes (*4*). No one, however, has conclusively shown activities in Langerhans cells, and evidence for the thesis that they are wornout epidermal melanocyte is circumstantial.

We now show that, after irradiation of the skin with ultraviolet light, Langerhans cells incorporate tritiated thymidine. This fact suggests that Langerhans cells synthesize DNA and that probably they are not effete melanocytes.

Three areas of the chests of three rhesus monkeys were irradiated (*5*) for 3 seconds with a flux of 7×10^5 erg sec^{-1} cm^{-2}; 1, 2, and 3 days later, 1.5 microcuries of tritiated thymidine (^{3}HT; specific activity, 6.7 c/m*M*; New England Nuclear Corp.) was injected intradermally at each site irradiated. For a control, a similar amount of ^{3}HT was injected intradermally in adjacent unirradiated skin of the chest. Biopsy specimens obtained from the irradiated and control areas 1 hour after the injections were fixed in 10-percent formalin and stained by the gold chloride technique of Gairns (*6*). After embedment in paraffin the sections were cut at 6 μ, freed of paraffin, rehydrated, and dipped in NTB_2 Kodak emulsion. The dipped slides were ex-

posed for 1 month at 4°C in light-proof plastic boxes containing Drierite, and developed by the technique of Messier and Leblond (*7*).

After ultraviolet irradiation both gross and microscopic changes occur in the epidermis. In general, erythema develops approximately 3 hours after exposure, reaching a maximum after 9 hours; then it gradually fades. The earliest histologic change, a degeneration of scattered prickle cells in the epidermis, first appears 24 hours after exposure; these cells reveal shrunken cytoplasm and pyknotic nuclei. Thirty to 40 hours after exposure an intercellular edema occurs around these altered epidermal cells. The morphology of the Langerhans cells remains remarkably unaffected.

On the 1st and 2nd day after irradiation no uptake of ^{3}HT by either epidermal or Langerhans cells was observed. At the end of the 3rd day, when a new granular layer appeared below the desquamating prickle cells, ^{3}HT was seen incorporated in the basal epidermal cells and in Langerhans cells.

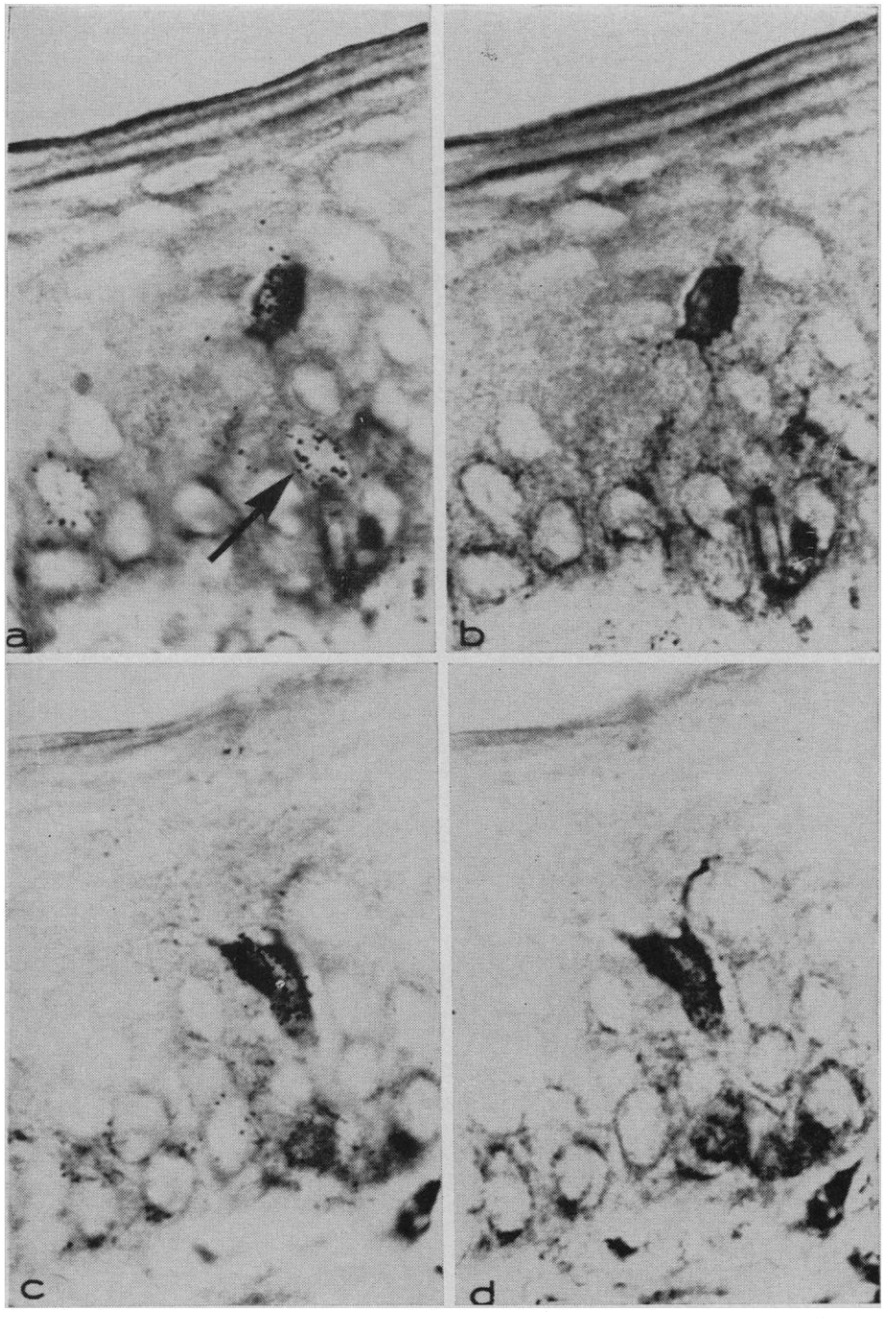

Fig. 1. (a) A labeled Langerhans cell; note also a labeled basal epidermal cell (arrow) (× 1200). (b) The same Langerhans cell photographed at a different level of focus to show one of the dendritic processes. (c) Another labeled Langerhans cell showing heavy concentration of silver grains (× 1200). (d) The same Langerhans cell photographed at a different level of focus to show one of the dendritic processes.

In typical labeled Langerhans cells (Fig. 1, a–d) the grains of reduced silver produced by tritium were easily distinguished from the grains of precipitated metallic gold that impregnated the Langerhans cells. Silver grains, larger than the finely precipitated gold, were localized over the perikarya of the Langerhans cells about 1 μ above the nuclei.

Approximately 1 percent of the Langerhans cells were labeled in irradiated skin after 3 days; however, because of the vagaries of histologic preparation, one cannot obtain a precise count. Autoradiographs of normal, unirradiated skin also showed an occasional labeled Langerhans cell.

These observations demonstrate that a single dose of ultraviolet irradiation results in temporary suppression of proliferation of epidermal cells; this suppression is followed by hyperplasia and an increase in synthesis of DNA by Langerhans cells. The uptake of ^{3}HT by the occasional Langerhans cell in unirradiated skin and by approximately 1 percent of the cells in irradiated skin indicates that they are capable of proliferating. Whatever may be the nature of the stimulation by ultraviolet light, Langerhans cells do not remain indifferent to the changes in the surrounding Malpighian cells described herein.

Thus Langerhans cells do not seem to be wornout epidermal melanocytes; on the contrary, they appear to be viable cells. This information should lead to a fresh approach in further studies of this system of cells.

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