Vitamin D, Sunlight, and Natural Selection

Most readers will agree with Loomis (*1*) that there is generally a latitude influence on the distribution of human skin pigmentation, that melanin pigment absorbs light, and that the epidermal production of vitamin D requires ultraviolet radiation. I suspect, however, that only a few will agree, on the basis of the data given, with his thesis that the control of vitamin D synthesis is the primary role of human skin pigmentation.

First, the evolutionary implication does not support this view: the melanin pigments are widely distributed from fungi to man, and tyrosinase, the enzyme associated with melanin synthesis, occurs in bacteria as well. On the other hand, only mammals and birds are subject to rickets, and vitamin D is not found to occur regularly, or to play a physiological role, in forms more primitive than the bony fishes. In view of the wide distribution of the melanins, and the narrow distribution of vitamin D, it may be assumed that the former arose earlier in evolutionary development. It seems improbable, then, that a control system would evolve in advance of the thing to be controlled.

Second, the quantitative considerations which form the basis of Loomis's argument may be viewed somewhat differently from the way he views them. Starting with Bekemeier's data (*2*), one may prefer to take the average of the six experimental determinations, rather than the extreme value [particularly since Bekemeier reports (*3*) analytical variations of up to 300 percent from sample to sample]. One may also prefer not to assume that the total skin surface is maximally illuminated at a given instant (at least half the skin is on the side of the body *away* from the sun), or to assume that light incident at low angles to the skin is as effective as light incident normally. One may also wish to assume that people sit, walk, or stand during the day, exposing in each instance still less than half their total skin surface to the overhead sun. Finally, one may wish to assume that even primitive man did not dwell continually in direct sunlight, but sought the shade of the tropical rain forest for at least a part of the day. If a reader uses these assumptions in making the calculation for vitamin D synthesis, the daily yield of vitamin D (for either white or dark skin) turns out to be in the physiological range as defined by Loomis.

Third, the normal range of vitamin D intake is given in the argument as 400 to 100,000 international units, a range of variation of 1:250. Yet the hypothetical control system, if we use Loomis's data for the transmittances of the stratum corneum of dark and light skin, can control the input light over a range of variation of only 1:3. An excess or deficiency of light could lead to hyper- or hypovitaminosis only if the individual's daily synthesis of vitamin D were near one of the extremes of the physiological range, and even then could produce only one or the other, and not both, as proposed.

Fourth, if cutaneous pigmentation were of major importance in regulating vitamin D metabolism, one would expect to find hypervitaminosis D reported in albinos who had undergone exposure to the sun. I am unaware of any such reports.

The hypothesis that Loomis presents is quite interesting, and obviously skin pigmentation affects to some extent cutaneous synthesis of vitamin D; the thesis that this is the primary control mechanism is not proved by the data given.

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In a recent article (*1*) and subsequent letter (*2*), W. Farnsworth Loomis cites a paper of mine (*3*) in support of his argument that the melanin pigment of Negro skin has evolved as a protection against excess vitamin D by modulating the effective amount of ultraviolet radiation in the skin. Loomis seems to have neglected a good part of the argument in my paper. I point out there that ultraviolet light has at least three effects which could conceivably exert selection pressure leading to genetic modification: sunburn, induction of skin cancer, and production of vitamin D. All three effects are elicited by wavelengths ranging from about 0.3 μ to the lower limit of sunlight at 0.29 μ; all may be expected to be greater in skins with little melanin, although we do not know how closely this generalization may hold. On the other hand, a high melanin content in the skin increases the absorption of total sunlight and so imposes a greater heat load upon the body. The selective pressure exerted by sunlight should thus be reckoned in terms of an algebraic summation of these four effects and probably others, and without much more information than is available the pressure of any one of them cannot be evaluated.

In his evolutionary argument Loomis invokes the distribution of ultraviolet light with latitude. This differs markedly from the distribution of total sunlight and, because of intense scattering back from the sky, different methods of measurement may give different results. A greater factor than latitude may be reflection from the terrain, most components of which absorb strongly, although snow is a good reflector. In addition, we have much to learn about the actual amount of absorption by melanin in different types of skin, the complicated optics of that organ making this very difficult to measure. All these things are discussed in my paper (*4*).

As regards Loomis's suggestion that darkly pigmented men moved from Africa to northern climates and there became lighter, it may be pointed out that the paleontological record gives us no evidence as to the time when the races of men were differentiated with respect to color, or as to where this occurred. Men moving from forested tropical Africa to northerly latitudes during one of the periods of glaciation might have received more ultraviolet radiation, because of reflection from snow, than they received in the tropics.

All such speculation seems to little purpose, however, in light of the complexity of the problem and our lack of knowledge. We should, in any event, be cautions about introducing teleology and undue determinism into our thinking about natural selection and the evolution of man.

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References and Notes

1. W. F. Loomis, *Science* **157**, 501 (1967).
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4. For further information on the ultraviolet of sunlight, see P. Bener, *Strahlentherapie* **123**, 306 (1964); R. Schulze, *Arch. Meteorol. Geophys. Bioklimatol.* **12**, 185 (1963); P. T. Baker, *Headquarters Quartermaster Res. Eng. Command, U.S. Army, Tech. Rept. EP-75* (1958).

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I would like to answer Blois's interesting points first.

1) Phylogenetically older substances are sometimes used in phylogenetically newer control systems: (i) CO_2 is a metabolite found even in bacteria, yet it is used to control the rate of mammalian respiration; (ii) melanin is found even in fungi, as Blois points out, yet it is used to control the amount of light reaching the retina by rendering the mammalian iris opaque; (iii) protoporphyrin is present as cytochrome *c* in protista, yet it is used to control the oxygen- and CO_2-carrying power of the blood in the form of hemoglobin in animals that later evolved a circulatory system.

2) In my article I calculated the maximum daily amount of vitamin D that would be synthesized by an untanned Caucasian exposed all day long to an equatorial sun without protection from clothing, trees, or shelters. I agree with Blois that, in fact, equatorial people could well be exposed to much less ultraviolet radiation; this lesser amount is probably still toxic in terms of hypervitaminosis D, as discussed in the next paragraph.

3) No general agreement has been reached on (i) the minimum toxic dose of vitamin D in short-term experiments or (ii) the least amount of the vitamin needed to produce chronic hypervitaminosis D, especially in children. Jeans and Stearns (*1*), for example, found that the linear growth of infants was retarded by the administration of as little as 1800 I.U. per day. Most estimates of the minimum toxic dose vary from 10,000 I.U. per day upward; a standard physiological textbook (*2*) reports that "the minimal toxic overdose does not appear to be far from the optimum curative dose." Wanting to be on the safe side, I stated in my article that daily ingestion of 100,000 I.U. per day could produce hypervitaminosis. This is undoubtedly true, but should not be interpreted as the actual toxicity threshold, which could easily be 1/10 this amount, or less. Thresholds for chronic toxicity must be lower than those for acute toxicity; yet any degree of toxicity could act overtime as a genetic selection factor for black skin in the tropics. Certainly more experimental work must be done to determine these thresholds with exactitude.

4) Blum is correct in stating that his paper provides no direct support for my theory; it does not even mention the disease hypervitaminosis D at all. I used his paper for indirect support as regards (i) the equatorial force of summer ultraviolet in the temperate zones and (ii) the difficulties in viewing either sunburn or skin cancer as effective genetic selection factors responsible for the black skins of equatorial primates. Since heat-load adaptation would lead one to expect Negroes in the north and white men in the south, it appears that adaptation to *ultraviolet penetration* was the major factor in the epidermal differentiation of man. As far as "teleology" is concerned, I look on the development of rickets-resistant strains of white men in northern latitudes and of hypervitaminosis D–resistant strains of black men in the tropics as no more teleological than the development of streptomycin-resistant strains in a culture of *Escherichia coli.*

5) I would like to mention here that Charles E. Bills of Johns Hopkins Hospital informs me that my figure of 3.8 percent provitamin D in the skin should have referred to this percentage of the total sterol in the skin; he adds, "Fortunately, this does not invalidate to any appreciable degree your thesis on the origin of blondes."

6) In a like vein, Peter Flesch of the University of Pennsylvania Hospital corrected the dermatological facts I abstracted from an anthropological textbook (*3*) by pointing out (*4*) that (i) "vitamin D synthesis does not take place solely in the stratum granulosum, but throughout the entire epidermis . . . and most probably also in the sebaceous glands or ducts"; (ii) keratohyaline is a hard keratinous structure without granular layers; and (iii) since keratin is essentially colorless, "the yellowish skin color of Mongoloids is caused by decomposed pigment 'excreted' with the horny layer."

In conclusion, I would like to mention two papers that have recently come to my attention. In the first (*5*), Pathak reports that over twice as much (290 to 320 $m\mu$) ultraviolet passes through white stratum corneum as passes through Negro stratum corneum, this 2 : 1 difference in ultraviolet-light transmission being increased to 3 : 1 for whole epidermis. According to the second paper (*6*), significantly higher concentrations of serum calcium (10.9 as compared with 9.6 mg per 100 ml) and phosphorous (3.8 as compared with 3.1 mg per 100 ml), as well as higher levels of "serum antirachitic activity" (4.4 as compared with 2.6 units per milliliter), were found in comparable groups of 65 women living at latitude 18°N in Puerto Rico and 116 women living at latitude 43°N in Michigan. If the solubility product of these two minerals is viewed as a rough measure of calcification potential, then these two groups are already separated by a 25-percent difference (39.5 as against 29.8) in calcification. Further and probably toxic increases would be expected, from these findings, in people living on the equator at 0° latitude, especially if, unlike the Puerto Rican group studied, they wore little clothing, had outdoor occupations, and did not have partially pigmented skin.

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