Skin Color and Nutrient Photolysis: An Evolutionary Hypothesis

Abstract. *Human populations native to areas of intense sunlight tend to be heavily melanized. Previous explanations for this relationship have invoked only weak selective pressures. To test the hypothesis that dark pigmentation may protect against photolysis of crucial light-sensitive vitamins and metabolites by ultraviolet light, folate was used as a model. It was found that exposure of human plasma in vitro to simulated strong sunlight causes 30 to 50 percent loss of folate within 60 minutes. Furthermore, light-skinned patients exposed to ultraviolet light for dermatologic disorders have abnormally low serum folate concentrations, suggesting that photolysis may also occur in vivo. Deficiency of folate, which occurs in many marginally nourished populations, causes severe anemia, fetal wastage, frank infertility, and maternal mortality. Prevention of ultraviolet photolysis of folate and other light-sensitive nutrients by dark skin may be sufficient explanation for the maintenance of this characteristic in human groups indigenous to regions of intense solar radiation.*

In the majority of indigenous human populations, there is clinal covariation between the extent of skin pigmentation and the intensity of solar radiation (*1*, *2*). No fully satisfactory explanation of the selective forces involved in sustaining this relationship has yet been advanced. There is good evidence that the evolutionary maintenance of a genetic characteristic, particularly one such as skin color which is governed by at least three to five loci (*3*), requires continued positive selection (*4*). Therefore, some evolutionary pressures must act to favor retention of heavy pigmentation in areas of intense sunlight. Several hypotheses have been advanced to explain the selective advantage of dark pigmentation, including (i) protection against hypervitaminosis D, (ii) enhanced resistance to vectors or infections, (iii) improved visual acuity in bright light, and (iv) protection against the carcinogenic effects of ultraviolet (UV) radiation (*5*). Individually or in aggregate, these factors would appear to have relatively little impact on reproduction and consequently on the processes of selection. The limitations of current hypotheses have been summarized (*5*).

We suggest that dark skin color may protect critical metabolites in blood and dermal tissues from photodecomposition by solar UV radiation. Such photolysis would be of lesser importance in individuals exposed to the weaker solar radiation of temperate regions, and would therefore exert little or no positive selective pressure for retention of dark pigmentation. Although several vitamins—such as folic acid, vitamin E, and riboflavin—are clearly light-sensitive (*6*), we have confined our investigations to folate. Not only is folate particularly light-sensitive (*7*), but folate deficiency is frequent and is known to have adverse effects on survival and reproduction.

We confirmed the photosensitivity of folate by exposing normal plasma to UV light (360 nm). In briefly irradiated samples the folate concentration dropped 30 to 50 percent during light exposure (Table 1), whereas that in control samples shielded from light was unchanged (data not shown). Although this indicates that folate in unprotected plasma is very susceptible to photolytic degradation, it has little direct relevance to the situation in vivo. To partially test the latter circumstance, we measured serum folate levels in ten patients undergoing phototherapy for various dermatologic disorders. These light-skinned (primarily Scandinavian) patients were being treated with methoxsalen (*8*) and exposure to 360-nm UV light (4.5 to 9.5 J/cm^2) for 30 to 60 minutes once or twice per week for a minimum of 3 months. We found that the serum folate levels of these patients were significantly lower ($P < .005$) than those of 64 healthy light-skinned Caucasians (Fig. 1) (*9*). This was particularly striking in five individuals (Fig. 1) who had received phototherapy for prolonged periods, because their skin conditions had improved considerably with treatment so that it was unlikely that their low serum folate was due to the dermatologic condition alone (*10*). These limited observations demonstrate that long-wavelength UV light does cause rapid and extensive photolysis of folate in vitro, and may do so in vivo. Direct studies of humans exposed to intense sunlight are impossible in our location.

The hypothesis that dark pigmentation protects against UV-induced nutrient photolysis is attractive because it provides a strong positive selective pressure for retention of this phenotype. Folic acid, in its various forms, is a requisite cofactor in nucleic acid and protein synthesis and is indispensable to cell growth and replication. Tropical populations in particular are often in precarious folate balance, and in some periequatorial areas a majority of the population may suffer from folate deficiency [most often diagnosed as tropical macrocytic anemia, nutritional macrocytic anemia, or nutritional megaloblastic anemia (*11*)]. This deficiency may arise both from inadequate dietary folate (*12*) and from increased utilization of the vitamin during

Table 1. Folate concentrations in four samples of human plasma before and after exposure to UV light in vitro. Heparinized plasma (2 ml) was placed in open plastic petri dishes (35 by 10 mm) and exposed to 360-nm light for 1 hour (approximately 9.5 J/cm^2). Weights before and after exposure indicated that negligible evaporation had occurred (data not shown). Samples collected before and after irradiation were assayed for folate by radioassay (*16*) and by *Lactobacillus casei* growth (*17*). Statistical significance was tested by the paired *t*-test.

Time	Folate (ng/ml) in sample				
	1	2	3	4	Mean
Radioassay					
Before exposure	6.0	6.7	3.2	6.1	5.5*
After exposure	3.6	4.6	1.5	4.3	3.5*
Lactobacillus casei assay					
Before exposure	6.3	8.8	5.3		6.8†
After exposure	4.5	6.2	2.0		4.2†

*Significantly different at $P < .005$. †Significantly different at $P < .05$.

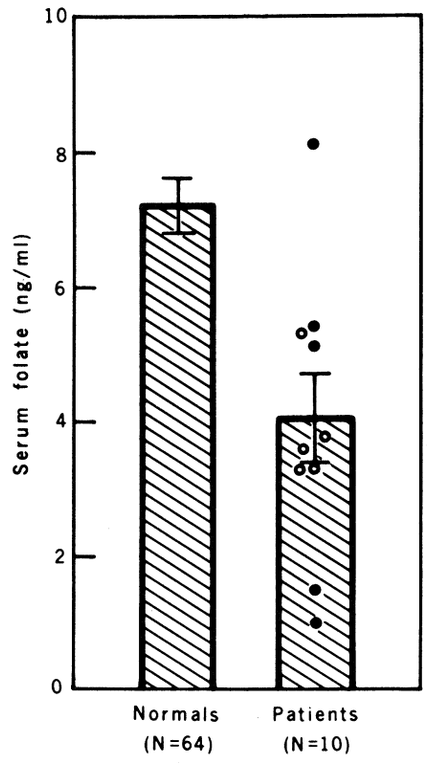

Fig. 1. Serum folate concentrations measured by radioassay (*17*) in ten patients receiving phototherapy (see text) and in 64 healthy individuals. All patients had received phototherapy for at least 3 months, and five patients had been exposed to UV light 9.5 to 13.5 months (open circles). The difference between the two groups was statistically significant ($P < .005$). Brackets represent the standard error of the mean.

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pregnancy, childhood, and hemolysis (such as that caused by malaria) (*11*). For example, the World Health Organization recommends a daily folate intake of 400 μg for adults and 800 μg during pregnancy, while nutritional surveys in several tropical areas indicate daily folate intakes of only 40 to 138 μg (*12*).

Individuals with marginal or low folate levels might be particularly susceptible to severe deficiency if photolysis of the vitamin were also to occur. Deficiency of folic acid may greatly diminish reproductive capacity. It has been estimated that 10 to 60 percent of pregnant women are deficient in folate (*11*). If severe enough, this deficiency may be fatal, and it is said to cause significant maternal mortality in tropical countries (*11*). Less severe deficiencies have been associated with major obstetric complications (abruptio placentae and placenta previa), congenital abnormalities, perinatal mortality, premature delivery, and repeated miscarriages (*11*). Folate deficiency in infancy and early childhood results in growth retardation, hematologic abnormalities, and failure to thrive (*13*). Thus, severe folate deficiency may have a profound influence on reproductive capacity and therefore on the process of natural selection.

The possibility that dark skin color protects against nutrient photolysis also fits well with the solar spectral distribution and with the light transmission spectra of human stratum corneum and epidermis (*14*). Analysis of the midday UV spectrum shows that the greatest intensity of light occurs at wavelengths longer than 330 nm. At shorter wavelengths intensity declines very rapidly, becoming only 0.01 percent of peak relative energy at 300 nm (*14*), and almost no solar radiation shorter than 295 nm reaches the earth's surface (*15*). Skin from both Negroes and Caucasians is highly effective in screening UV wavelengths below 280 nm. Between 280 and 320 nm, melanized skin is more effective in blocking transmission of light, but the difference in transmission between white and black skin is most marked at wavelengths greater than 320 nm (*14*), which are known to cause rapid photolysis of folate (*7*). In contrast, the carcinogenic and antirachitic effects of light are observed for wavelengths between 280 and 320 nm (*15*). Thus, melanized skin provides much more relative protection against the nutrient-destroying, intense, longer wavelengths of sunlight than from the shorter, less intense, mutagenic, and vitamin D–forming wavelengths.

These observations provide support for the idea that heavily pigmented skin may protect against extensive photolysis of certain crucial metabolites, such as folate. The protection of light-sensitive vitamins and other nutrients against UV-induced photodecomposition provides an alternative explanation for the maintenance of dark skin color among members of human groups indigenous to areas of intense solar radiation.

RICHARD F. BRANDA, JOHN W. EATON
Department of Medicine, University of Minnesota, Minneapolis 55455

References and Notes

1. C. L. Brace and M. F. A. Montague, *Man's Evolution: An Introduction to Physical Anthropology* (Macmillan, New York, 1965), pp. 271–293.
2. The amount of UV radiation reaching the earth's surface at sea level varies from more than 450 J/cm²-year in some periequatorial areas, to about 200 J/cm²-year at the 45th parallel, to less than 50 J/cm²-year at the poles (measured at 307.5 nm) [R. Schulze and K. Grafe, in *The Biologic Effects of Ultraviolet Radiation*, F. Urbach, Ed. (Pergamon, Oxford, 1969), p. 367].
3. L. L. Cavalli-Sforza and W. F. Bodmer, *The Genetics of Human Populations* (Freeman, San Francisco, 1971).
4. C. L. Brace, *Am. Nat.* **97**, 39 (1963).
5. F. Daniels, Jr., P. W. Post, B. E. Johnson, in *Pigmentation: Its Genesis and Biologic Control*, V. Riley, Ed. (Appleton-Century-Crofts, New York, 1972), pp. 13–22.
6. L. S. Goodman and A. Gilman, *The Pharmacological Basis of Therapeutics* (Macmillan, New York, ed. 5, 1975).
7. E. L. R. Stokstad, D. Fordham, A. DeGrunigen, *J. Biol. Chem.* **167**, 877 (1947).
8. J. A. Parrish *et al.*, *N. Engl. J. Med.* **291**, 1207 (1974).
9. Folate levels were also measured in four patients before and immediately after exposure to UV light. Mean serum folate dropped from 4.1 to 3.7 ng/ml for the group. This decrement was not statistically significant. It may be that the small amounts of folate photolyzed during each exposure are partially replaced from storage sites in individuals with adequate reserves.
10. S. Shuster, J. Marks, I. Chanarin, *Br. J. Dermatol.* **79**, 398 (1967).
11. R. L. Blakely, *The Biochemistry of Folic Acid and Related Pteridines* (North-Holland, Amsterdam, 1969), pp. 411–424.
12. H. E. Saubelich, in *Folic Acid: Biochemistry and Physiology in Relation to the Human Nutrition Requirement* (National Academy of Sciences, Washington, D.C., 1977), pp. 213–231.
13. C. I. Waslien, in *ibid.*, pp. 232–246.
14. D. S. Berger, *J. Invest. Dermatol.* **53**, 192 (1969); M. A. Pathak and T. B. Fitzpatrick, in *Proceedings of the International Conference on Photosensitization and Photoprotection*, T. B. Fitzpatrick, M. A. Pathak, L. C. Harber, M. Seiji, A. Kukita, Eds. (Univ. of Tokyo Press, Tokyo, 1974), pp. 725–750.
15. R. G. Freeman, D. W. Owens, J. M. Knox, H. I. Hudson, *J. Invest. Dermatol.* **47**, 586 (1966).
16. R. T. Dunn and L. B. Foster, *Clin. Chem.* **19**, 1101 (1973); J. K. Givas and S. Gutcho, *ibid.* **21**, 427 (1975).
17. A. H. Waters and D. L. Mollin, *J. Clin. Pathol.* **14**, 335 (1961).
18. We thank R. King, C. L. Brace, D. Haldane, W. Gentry, and M. Dahl for helpful discussions. Supported in part by NIH grants CA20251 and HL 16833, by an NIH Career Development Award (J.W.E.), and by the National Leukemia Association, Inc. R.F.B. is a special fellow of the Leukemia Society of America, Inc.

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Tentaculites: Evidence for a Brachiopod Affinity?

Abstract. *Transmission electron microscope studies of fractured surfaces reveal that the shells of* Tentaculites *are constructed of calcite with a ridge and groove structure and cross-bladed fabric heretofore unique to some articulate brachiopods. A possible affinity with brachiopods or phoronids is suggested for* Tentaculites.

Tentaculites is a genus of annulate cone-shaped fossils (Fig. 1a) that are found in rocks ranging in age from Ordovician to Devonian. The systematic position of this problematic group is unknown and has been the subject of much speculation since they were first described by E. F. von Schlotheim in 1820. Tentaculitids have been variously placed among the annelids, mollusks, crinoids, coelenterates, foraminifera, brachiopods, and trilobites (*1*, *2*). Currently, *Tentaculites* is precariously classified with the cephalopods in the phylum Mollusca (*3*, *4*). The purpose of this report is to present new evidence suggesting that some tentaculitids may instead be related to articulate brachiopods.

The conical shells of *Tentaculites* are made of calcite arranged in a concentrically laminated fashion and sometimes penetrated by pores, canals, or pseudopores. The preservation of the microstructure and the general absence of recrystallization indicate that the calcite is original rather than an alteration product of aragonite or magnesium calcite. In spite of the excellent preservation of many specimens of *Tentaculites*, there have been surprisingly few attempts at examining the fine structure of the shell with the electron microscope. Only the work of Blind (*3*) is noteworthy in this regard, although Hurst and Hewitt (*5*) described but did not figure their scanning electron microscope results. Blind examined the laminated shell in the scanning electron microscope, figuring the microscopic layers of calcite in his plate 12, figure 7 (*3*). He compared this structure to that of the "brick-wall" aragonite typical of molluscan nacre (mother-of-pearl). Although the morphological similarity may be appropriate (in cross section) the difference in mineralogy makes the comparison awkward for taxonomic purposes. Such fidelity of morphological preservation in any calcite transformed from aragonite is without precedent.

With this difficulty in mind, a reexamination of the fine structure of *Tentaculites* was undertaken with the transmission electron microscope. Using a single-

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