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Effects of Vitamin D on Bone and Natural Selection of Skin Color: How Much Vitamin D Nutrition are We Talking About?

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1. Introduction

Until the 1990s, the criterion for appropriate vitamin D nutrition was simply the absence of overt rickets or osteomalacia (Blumberg *et al*., 1963). Now, circulating 25-hydroxyvitamin D [25(OH)D] concentrations are the appropriate measure of vitamin D nutritional status (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997). It is now possible to make more quantitative comparisons of vitamin D nutrition through primate and human evolution, and to draw inferences about how differences in vitamin D nutrition may have affected susceptibility to disease.

Authentic vitamin D comes in two forms, vitamin D_3 and D_2. Vitamin D_2, ergocalciferol, can be synthesized by exposing a fat extract of yeast to UV light. However, no metabolite of vitamin D_2 is normally detectable in the blood of humans or primates (Marx *et al*., 1989; Trang *et al*., 1998). The present discussion focuses on vitamin D_3, cholecalciferol, the natural, physiological form of vitamin D in mammals. Vitamin D_3 (from here on, vitamin D) is the natural, and more potent form of vitamin D in all primate species including humans (Marx *et al*., 1989; Trang *et al*., 1998). Vitamin D is the raw material for production of the hormone 1,25-dihydroxyvitamin D, synthesized and released by the kidney according to the needs of calcium homeostasis (Figure 9.1). For this, vitamin D itself plays a role as a structural substrate; similar to the way cholesterol is the structural raw material for other steroid hormones. For vitamin D, the intervening metabolite, 25(OH)D, is synthesized in liver mitochondria and liver microsomes. 25(OH)D has a biological half-life of about 2 months, and is thought to be relatively inactive. Because of these features,

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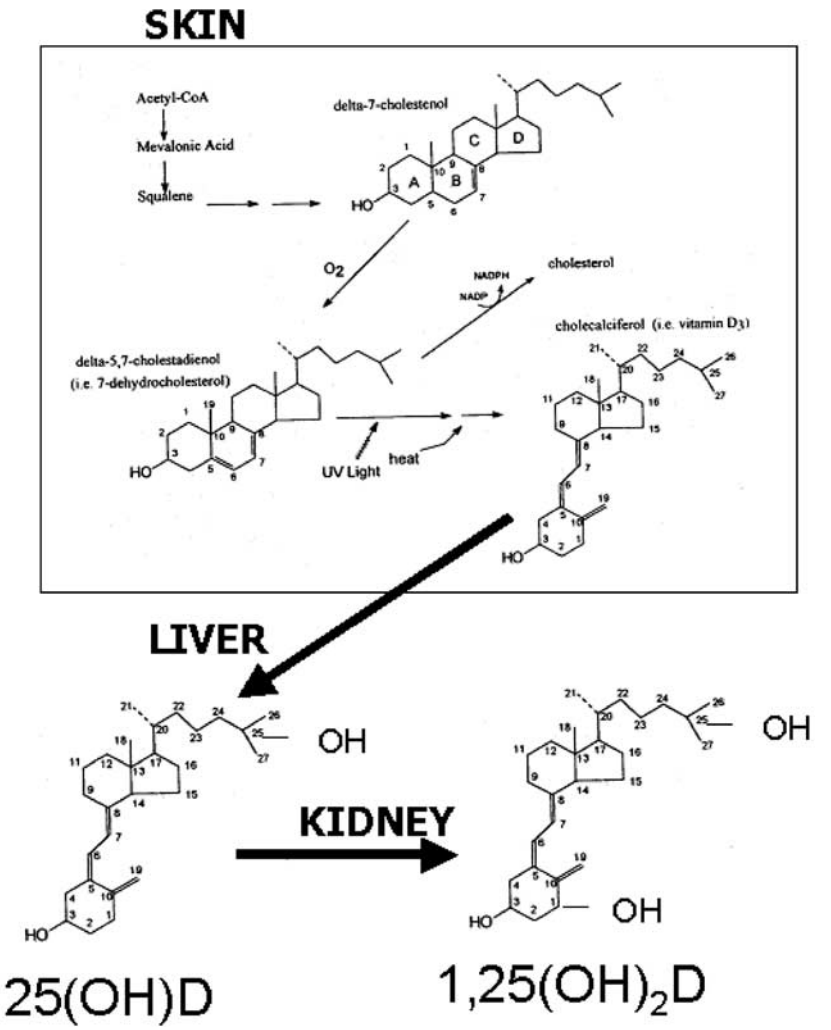

Figure 9.1. The skin of mammals actively synthesizes cholesterol. 7-dehydrocholesterol is an immediate precursor of cholesterol. 7-dehydrocholesterol present within the skin and in the oils secreted by skin is unstable. Part of the molecule breaks open during exposure to ultraviolet B light (285–310 nm), and this results in the nonenzymic generation of cholecalciferol. Within 1–3 days, the vitamin D is acted upon by 25-hydroxylase enzyme in the liver to produce 25(OH)D, the inactive, long-term storage form of vitamin D. The kidney uses some 25(OH)D to generate the hormone, $1,25(OH)_2D$, the levels of which are about 1,000 fold lower than those of 25(OH)D. The circulating level of hormone is regulated independently of vitamin D nutrition, and increases in response to the need for calcium. $1,25(OH)_2D$ stimulates the active transport of calcium through the intestinal mucosa. Recently, 25(OH)D-1-hydroxylase has been found in other tissues, and its presence may provide a mechanism through which the vitamin D nutrition can affect aspects of health beyond just calcium homeostasis.

25(OH)D has recently been acknowledged as the acceptable way to assess vitamin D nutritional status (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997).

Primates do not normally need vitamin D in their food, because sufficient sunlight makes it impossible to become vitamin D deficient. For humans, the "evolution" of vitamin D into a nutrient stems from the shift of humans away from the equator, from increased pollution, and from the cultures that avoid exposing skin surface to sunshine. This includes the use of clothing.

Vitamin D may have been a primordial steroid-like hormone in living things, and its effect was to signal exposure to ultraviolet light. Essentially all fungi, plants, and animals produce provitamin D, molecules that can become vitamin D (Holick, 1992). These are converted to previtamin D by exposure to sunlight (ultraviolet light B, 215–240 nm). Species of all vertebrate classes require vitamin D, and this must be metabolized to $1,25(OH)_2D$ before it exhibits biological activity (Henry and Norman, 1975; Holick, 1992).

2. Skin and Vitamin D Uptake

The skin is a major site of cholesterol synthesis. Cholesterol and its precursors are required for integrity of skin-cell membranes, and they are components of the oil secreted by skin into fur and hair. Vitamin D is generated in the skin by an unregulated process that involves only the dermal enzymes needed to synthesize cholesterol. Most of the vitamin D that is used for vitamin supplements and for milk fortification is derived from a form of fur—the lipid obtained from the defatting of lamb and sheep wool. This fat extract is exposed to UV, and the vitamin D is purified for nutritional use. When 7-dehydrocholesterol, a precursor in the synthetic path to cholesterol, is exposed to ultraviolet B light, the B-ring of the steroid molecule is split open between carbon 9 and carbon 10, to produce a secosteroid (a fractured steroid). It takes about 24 hr for this previtamin D to isomerize spontaneously into the mature vitamin D_3 that is useful for the body. If there is sustained exposure to ultraviolet light, the previtamin D and vitamin D in skin deteriorate to tachysterol and other compounds. This photodecomposition explains why excess sun exposure does not cause vitamin D intoxication. It takes 1–4 days after sun exposure before increases in vitamin D are apparent in the circulation (Haddad *et al*., 1993).

As humans age, the skin loses capacity for vitamin D production because its rate of cholesterol synthesis is less. In people over 70 years of age, a given amount of sun exposure may generate only a fourth of the vitamin D achieved in young individuals. Furthermore, the intensity of ultraviolet light from the sun diminishes during winter months. For example at the latitude of Boston (42°N), there is not enough outdoor ultraviolet intensity between November and February to generate any vitamin D in the skin, and this phenomenon is worse at higher latitudes (Webb *et al*., 1988).

Absorption of vitamin D generated within the skin into the blood is facilitated by a concentration of a vitamin D-binding protein (DBP) that exists at remarkably high

concentration, compared to specific carriers for lipid-soluble hormones (Bikle and Pillai, 1993; Vieth, 1994). If vitamin D is consumed orally, it is absorbed as if it were cholesterol, in chylomicrons that deliver lipids to adipose tissue, and from which chylomicron remnants are cleared by the liver, making vitamin D available for metabolism (Haddad *et al*., 1993).

Eventually, all vitamin D and its metabolites circulate bound to DBP, a protein that can be taken up selectively by the kidney and probably some other tissues expressing megalin, which is a translocating protein and a member of the low density lipoprotein (LDL) receptor family (Nykjaer *et al*., 1999). Still, much of the 25(OH)D and $1,25(OH)_2D$ enters cells by diffusion of that small proportion of the seco-steroid present in the unbound, "free" form. This follows the classic model by which other fat-soluble hormones also enter target tissues (Vieth, 1994).

2.1. Metabolism of Vitamin D

Enzymes in human liver microsomes and mitochondria convert vitamin D to 25(OH)D. The concentration of this metabolite reflects vitamin D nutritional status. The kidney functions as an endocrine gland synthesizing and secreting the hormone, $1,25(OH)_2D$. Production of $1,25(OH)_2D$ is stimulated by low circulating calcium, low phosphate, and high parathyroid hormone (PTH). $1,25(OH)_2D$ stimulates the active transport of calcium through intestinal mucosa. Together with calcium, $1,25(OH)_2D_3$ suppresses the parathyroid gland. Together with PTH, $1,25(OH)_2D$ regulates both bone resorption and bone formation, thereby maintaining normal bone and mineral physiology.

Normal $1,25(OH)_2D$ production rates range between 0.2 and 2 μg per day. The RDA for vitamin D from infants to adults under 50 years is 2.5 μg per day (200 IU/day) (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997), but the evidence points to a far higher total need for vitamin D in adults, from both sun and diet (Vieth, 1999).

3. What is a Lack of Vitamin D?

The clinical decision level for poor vitamin D nutrition is a low 25(OH)D, less than 25 nmol/L (10 ng/mL). Levels below this are considered diagnostically causal of rickets and osteomalacia. The published 25(OH)D levels in children with frank nutritional rickets range as high as 20 nmol/L (8 ng/mL) (Chesney *et al*., 1981; Garabedian *et al*., 1983). However, milder forms of vitamin D "insufficiency" are starting to be recognized. In particular, the consequence of long-term vitamin D insufficiency is osteoporosis (Heaney, 1999), a long-term negative balance in the equilibrium of calcium with the skeleton.

It is wrong to assume that simply because individuals live at southern latitudes, they need less vitamin D supplementation—some people actively avoid exposing skin to the sun, and the supply of dermal vitamin D is a function of sun exposure and amount of skin surface exposed.

Calcium metabolism reflects only one aspect of vitamin D action. In cell culture systems *in vitro*, $1,25(OH)_2D$ acts on many tissues that are not related to calcium metabolism, including the hematopoietic and lymphatic systems, skeletal muscle, vascular smooth muscle, skin, reproductive tissues, the brain, and spinal cord

(McGrath, 2001; Walters *et al*., 1992). Several tissues possess 25(OH)D-1-hydroxylase; therefore, they have the ability to produce their own $1,25(OH)_2D$ (Hewison *et al*., 2000). This hormone production capability for local regulation of cellular activity is known as a paracrine control system (Dusso *et al*., 1990; Hewison *et al*., 2000). Such paracrine mechanisms can explain why vitamin D nutrition is related to various cellular mechanisms and their effects on many aspects of human health (Table 9.1). Walters *et al*. (1992) have concluded "vitamin D deficiency is a heterogeneous collection of physiologic conditions". In the most general sense, vitamin D deficiency is a state in which the supply of vitamin D is not sufficient for the optimal operation of at least one function that depends upon it.

Table 9.1. Diseases Known to be, or Implicated as being Prevented by Greater Vitamin D Nutrition or Skin UV Exposure

Disease	Type of evidence supporting the association	Reference
Rickets	Long established, causal, and preventive	
Osteomalacia	Long established, causal, and preventive	
Osteoporosis	Direct, controlled studies that vitamin D prevents loss of bone density and lessens fracture risk	Chapuy *et al*., 1992; Dawson-Hughes *et al*., 1991; Dawson-Hughes *et al*., 1997
Blood-pressure regulation	Epidemiological and interventional data	Krause *et al*., 1998; Pfeifer *et al*., 2000; Rostand, 1997
Risk of diabetes	Epidemiological and case-control data	Eva, 1999; Stene *et al*., 2000
Progression osteoarthritis	Epidemiological, cross-sectional studies	Lane *et al*., 1999; McAlindon *et al*., 1996
Diminished intra-uterine growth	Presumed effect	Fuller, 2000
Resistance to pneumonia	Epidemiological association with rickets	Muhe *et al*., 1997
Multiple sclerosis, occurrence and progression	Epidemiological data and lab effects on tissue	Embry *et al*., 2000; Hayes *et al*., 1997; Mahon *et al*., 2001
Prevention of tuberculosis,	Epidemiological data and lab effects on tissue	Chan, 2000; Douglas *et al*., 1998
Protection against cancers		
Breast	Epidemiological data and lab effects on tissue	Garland *et al*., 1999
Prostate	Epidemiological and lab effects on tissue	Hsu *et al*., 2001; Schwartz *et al*., 1997; Schwartz *et al*., 1998
Large bowel	Epidemiological and cross-sectional data based on latitude and serum 25(OH)D	Garland *et al*., 1999

There is growing epidemiological evidence, which amounts only to circumstantial evidence at this time, that vitamin D nutrition affects many diseases not previously associated with this nutrient. These diseases are summarized in Table 9.1. The list is so long that it is probably hard for some readers to believe that one nutrient could have so much attributed to it. However, vitamin D is a very unusual nutrient. It's most abundant form in the circulation, 25(OH)D, serves as the raw material that many tissues need for paracrine hormone control of their own cellular functions. Furthermore, the capacity for $1,25(OH)_2D$ production by the kidney and other tissues is not just a function of the amount of 1-hydroxylase enzyme. *In vivo* $1,25(OH)_2D$ production is determined by mass action. For example, a doubling in the concentration of 25(OH)D results in double the rate at which a given amount of 1-hydroxylase produces the hormone (Vieth *et al*., 1990). I am not aware of any other hormone-generating system so severely limited by the supply of substrate, except in the case of severe iodine deficiency, and its effect on thyroid hormone production. The situation where vitamin D supply became limiting to production of the hormone made from it did not exist during early human development. Sunshine was never lacking, and it is certain that humans were not designed through evolution to wear clothes. Exposure of the face and hands exposes a mere 5% of our skin surface area, and many modern humans avoid exposing even that to the sun. If the sun provides a nutrient, most of us are depriving ourselves of it. Because this is so prevalent, we assume this to be our normal state of vitamin D nutrition.

4. "Normal" Requirements for Calcium and Vitamin D

Vitamin D and calcium are the key nutrients favoring bone growth and preservation throughout life. Calcium alone has never been shown to prevent fractures. However, calcium combined with 17.5–20 μg/d vitamin D, results in lower fracture risk in the elderly (Chapuy *et al*., 1992; Dawson-Hughes *et al*., 1997). When elderly people previously deficient in vitamin D are given an annual injection of vitamin D, they have fewer fractures (Heikinheimo *et al*., 1992). Aside from benefits to bone density, the reduction in fractures with vitamin D supplementation is attributed to improved neuromuscular function, better balance, and fewer falls (Pfeifer *et al*., 2000). The latter actions of vitamin D have no direct connection with calcium or bone.

Higher vitamin D supplies than what prevails in modern times are probably normal for our species. Consensus holds that modern humans originated in equatorial Africa, were exposed to abundant sunshine and wore no clothing. The calcium intakes of prehistoric humans have been estimated by Eaton and Nelson to be over 1,500 mg/day, who contend that such calcium supplies represent the natural paradigm for humans (Eaton and Nelson, 1991). However, these Paleolithic calcium intakes are difficult to maintain in the modern world. Adults must consume dairy products, or take calcium supplements merely to maintain the kinds of calcium intakes now regarded as "adequate," based on dietary recommendations (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997). However, the practice of milk consumption into adulthood is unusual for any species, and for humans it is a relatively recent phenomenon. It would seem more likely that like any other nutrient throughout human history, calcium nutrition was highly variable, affected by region, seasonal food supply, and dietary and cultural preferences

(Nestle, 2000). Perhaps such high dietary intakes would not be necessary if the supply of vitamin D were greater. I propose that the high requirements that modern adults have for calcium are because of the need to compensate for a severe lack of vitamin D compared to their evolutionary paradigm.

5. Fur-Bearing Primates Obtain Vitamin D by Mouth

In contrast to the unreliable supply of just about any other nutrient during primate evolution, there can be no doubt that the state of vitamin D "nutrition" must have been far greater than what prevails in modern times. This kind of statement could not have been made until recently, because there was no widely acknowledged way to characterize the status of vitamin D nutrition. However, the consensus is now established that the circulating concentration of 25(OH)D is the primary measure of vitamin D nutritional status (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997). Because of this, we can use modern data to infer what the 25(OH)D concentrations would have been in early humans. From this, we can estimate what the effective daily supply of vitamin D would have been during early human evolution.

At the low latitudes natural to all primates, sunlight penetrates the atmosphere with enough UVB light all year to disrupt 7-dehydrocholesterol molecules in the skin, and produce cholecalciferol (vitamin D) (Holick *et al*., 1981). In all studies of healthy non-human primates, circulating 25(OH)D concentrations exceed 80 nmol/L (Ott *et al*., 1999) (Table 9.2) (Vieth *et al*., 1987; Marx *et al*., 1989; Gacad and Adams, 1992; Kewenig *et al*., 1999). New World primates given sun exposure attain circulating 25(OH)D in excess of 500 nmol/L (Gacad and Adams, 1992). Similarly, Rhesus macaques, from the Old World, and raised outdoors in Puerto Rico have average 25(OH)D concentrations of more than 500 nmol/L (Vieth *et al*., 1987). I do not mean to imply that the data on monkeys should apply to humans, but to highlight the earlier trend of high 25(OH)D levels toward the evolution of humans. There have been severe difficulties with rickets in captive apes and monkeys, and to overcome the problem, commercial diets for captive primates contain far more vitamin D than do human diets (Fiennes, 1974; Vieth *et al*., 1987).

The high 25(OH)D concentrations, and relatively high vitamin D requirements of apes and monkeys are understandable in light of their biology—their body surface area relative to mass is generally greater than for humans, and they are inveterate groomers, consuming by mouth the vitamin D generated from the oils secreted by skin into fur. Although much of the vitamin D produced within human skin is absorbed directly, birds and fur-bearing animals acquire most of their vitamin D orally, as they groom themselves (Bicknell and Prescott, 1946; Carpenter and Zhao, 1999). Vitamin D is generated from the oily secretions of skin into fur. The oral consumption of UV-exposed dermal excretion is the way many animals acquire the "nutrient," vitamin D. Although Fraser (1983) has argued that dermal absorption of vitamin D may be more natural, what we know from animals indicates that oral consumption is equally physiological. Since vitamin D can be extracted from UV-exposed human sweat and skin secretions (Bicknell and Prescott, 1946), it is also reasonable to think that early humans obtained some of their vitamin D by mouth as well, by licking the skin.

Table 9.2. Circulating Concentrations of 25(OH)D in Non-human Primates and in Modern Adults with Abundant Sun Exposure

	25(OH)D Mean values nmol/L	Reference
Non-human primates		
Rhesus Macaques, outdoor	500	Vieth *et al*., 1987
Rhesus Macaque	322.5	Ott *et al*., 1999
Rhesus Macaque	362.5	Kewenig *et al*., 1999
Old World, No UV	110	Marx *et al*., 1989
Old World, No UV	170	Marx *et al*., 1989
New World, No UV	140	Marx *et al*., 1989
New World, No UV	150	Marx *et al*., 1989
New World, pre-UV	87.5	Gacad and Adams, 1992
New World, post-UV	575	Gacad and Adams, 1992
New World	335	Adams *et al*., 1985
Old World (gorilla, orangutang)	82.5	Adams *et al*., 1985
Humans under sunny conditions		
Puerto Rico, hospital personnel	105	Haddock *et al*., 1982
Puerto Rico farmers	135	Haddock *et al*., 1982
St. Louis, USA, lifeguards	163	Haddad and Kyung, 1971
Israel lifeguards	148	Better *et al*., 1980

AQ: Pls check the entries Old world, No UV; New World, No UV have same reference but different values

To estimate the circulating 25(OH)D concentrations prevalent in humans of the late Paleolithic period, we need to focus on people in sun-rich environments who regularly expose most of their skin surface to the sun. Lifeguards in the United States and in Israel, as well as farmers in the Caribbean all exhibit serum 25(OH)D concentrations greater than 100 nmol/L (Haddock *et al*., 1982) (Table 9.2) (Haddad and Kyung, 1971; Better *et al*., 1980). Furthermore, even regular short periods in sun-tan parlors consistently raise serum 25(OH)D to beyond 80 nmol/L (Dent *et al*., 1973; Stamp *et al*., 1977; Mawer *et al*., 1984; Varghese *et al*., 1989; Matsuoka *et al*., 1990; Falkenbach *et al*., 1993; Krause *et al*., 1998). The synthesis of vitamin D is a self-limiting chemical reaction whereby equilibrium is achieved between production of precursors that will become vitamin D, and the photocatalytic breakdown of these precursors and vitamin D into inactive molecules (Webb *et al*., 1989). Skin color does not affect the amount of vitamin D that can be generated. However, darker skin requires longer exposure. Very black skin requires about 1.5 hr, or six times longer than white skin, to reach the equilibrium for vitamin D production (Holick *et al*., 1981). At least four studies show that UV exposure of the full skin surface of an adult is equivalent to a vitamin D consumption of about 250 ug (10,000 IU/d) (Stamp, 1975; Davie *et al*., 1982; Holick, 1995; Chel *et al*., 1998).

At latitudes beyond 40°, the angle of the sun is so low for much of the year, that UVB light penetration to the earth's surface is minimal. For much of the rest of the year UV intensity is much lower than at tropical latitudes (Webb *et al*., 1988). At high latitudes,

black skin would need substantially more than 1.5 hr to achieve the yield of vitamin D they could attain more readily at lower latitudes. Even if modern humans do live in sunny climates, they are not ensured of a desirable serum 25(OH)D concentration. Culture, clothing, and shelter minimize the natural production of vitamin D by skin. Consequently 25(OH)D concentrations for populations in the Middle East tend to be even lower than they are for people living in America or Europe (Sedrani *et al*., 1983; Al Arabi *et al*., 1984; Fonseca *et al*., 1984; Fuleihan and Deeb, 1999; Alagol *et al*., 2000). These differences in vitamin D nutrition are not attributable to fortification of milk, because this is not permitted in most European countries.

Since early human evolution occurred under UV-rich conditions, typical 25(OH)D concentrations were surely higher than 100 nmol/L. Levels like this are now seen only in lifeguards and farmers. This range of 25(OH)D concentration reflects an adult vitamin D input of 200–500 μg/day (Vieth, 1999). Since our genome was selected through evolution under these conditions, it should be evident that our biology was optimized for a vitamin D supply far high than what we currently regard as normal. The question of whether such high levels of vitamin D nutrition actually make a difference to human health needs to be addressed with further research involving controlled prospective studies of vitamin D supplementation.

6. Vitamin D Deficiency Affecting Genetic Selection for Lighter Skin Color

In a biological sense, all modern humans belong to a species designed by evolution and natural selection to be native to the environment of the Horn of Africa. Deeply pigmented skin is probably the natural, default color (Sturm *et al*., 1998; Jablonski and Chaplin, 2000). Dark skin protects against skin cancer, and preserves the function of sweat glands needed for thermoregulation. Moreover, dark skin protects circulating micronutrients, especially folic acid, from photodegradation. Folic acid is needed to ensure an intact fetal neural tube (Jablonski and Chaplin, 2000), and thus dark skin would have been prevalent because natural selection favored it for survival and reproduction.

As the first human populations migrated out of Africa, the vitamin D supplies declined because of less ultraviolet light exposure. Among populations across the Old World, there is a striking correlation between skin reflectivity (whiteness of skin) and latitude (Relethford, 1997; Jablonski and Chaplin, 2000). Among White children living in Great Britain, rickets was observed in at least one third of children tested by all large public health studies reported between 1868 and 1935 (Harris, 1956). If it had been children with dark skin in Great Britain or northern Europe prior to the last century, there is no doubt that the prevalence of rickets would have been greater and its form more severe. We know this both from older reports about people with dark skin in Great Britain (Harris, 1935; Bicknell and Prescott, 1946), and from the 25(OH)D concentrations reported for non-White children and adults in northern countries now (Meulmeester *et al*., 1990; Koch and Burmeister, 1993; Gessner *et al*., 1997; Lawson *et al*., 1999). The natural history of untreated rickets is one of severe anatomical

Figure 9.2. The consequence of vitamin D deficiency is rickets in the child, and osteomalacia in the adult. This is one of the numerous cases of osteomalacia seen in Central Europe after World War I, illustrating "marmalade legs." (Harris, 1935) © reprinted with permission of Cambridge University Press.

deformity (Figure 9.2). Normal childbirth would be impossible for women or girls with unresolved rickets, and for nutritionally marginal women delivery would have become progressively more difficult. More often than not, it was during pregnancy that asymptomatic vitamin D deficiency manifest itself in adulthood, as osteomalacia (Harris, 1935; Bicknell and Prescott, 1946). With poor vitamin D nutrition, pelvic deformity became worse with each pregnancy. The contracted pelvic opening made a vaginal delivery impossible (Figure 9.3).

The improved vitamin D nutrition facilitated by a whiter skin or diets of ocean fish (the only meaningful nutritional source of vitamin D) would have been essential for human reproduction at northern latitudes. However, depigmented skin by itself may not have been enough of an adaptation to prevent rickets at northern latitudes. It has been argued that high calcium intakes were needed. To achieve this, human populations in northern Europe adapted to permit consumption of milk into adulthood, by the process of natural selection favoring high intestinal lactase activity beyond childhood (Fuller, 2000).

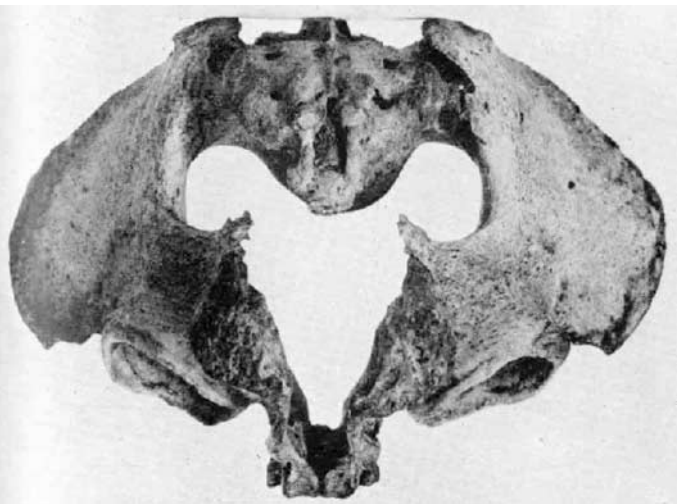

Figure 9.3. Women with osteomalacia exhibit a contracted pelvis, which is a progressive condition. It was said that the earliest symptom of vitamin D deficiency in younger women is pain and deformation around the pelvic area. The diminished size of the pelvic outlet made a vaginal delivery impossible, and older medical texts advised simply that these women be "forbidden" from becoming pregnant (Bicknell and Prescott, 1946) reprinted with permission ©.

7. Nutritional Implications of Vitamin D in Human Biology

Senile osteoporosis has long been thought to be a consequence of prolonged, mild vitamin D deficiency (Bicknell and Prescott, 1946; Parfitt, 1990; Heaney, 1999). In terms of severity of vitamin D deficiency, rickets is the most severe stage of the resulting bone disease. Less severe is the adult onset of osteomalacia during nutritionally stressed periods. The consequence for bone of still milder vitamin D insufficiency would be osteoporosis. This view is supported by the modern clinical evidence of fracture prevention with vitamin D in the elderly (Chapuy *et al*., 1992; Dawson-Hughes *et al*., 1997).

Osteoporosis and most of the other conditions listed in Table 9.1 are unlikely to have contributed to natural selection, because only rickets and osteomalacia would have affected reproductive capacity. Therefore, there is no reason to assume that natural selection for skin color and greater dietary calcium were sufficient to eliminate the predisposition to the other vitamin D deficiency related diseases listed in Table 9.1.

The amounts of vitamin D needed to bring about the kinds of 25(OH)D concentrations associated with abundant sunshine exposure exceed the current official safety limit of 50 μg/d (2,000 IU/day) (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997; Vieth, 2001). Figure 9.4 compares circulating 25(OH)D concentrations as they would have been through primate and early human evolution, against levels that are now common for adults, and levels attained with vitamin D intakes far higher than current RDA's for the nutrient. In the broader context of this comparison, modern humans are relatively deprived of vitamin D, and even the most recently revised dietary

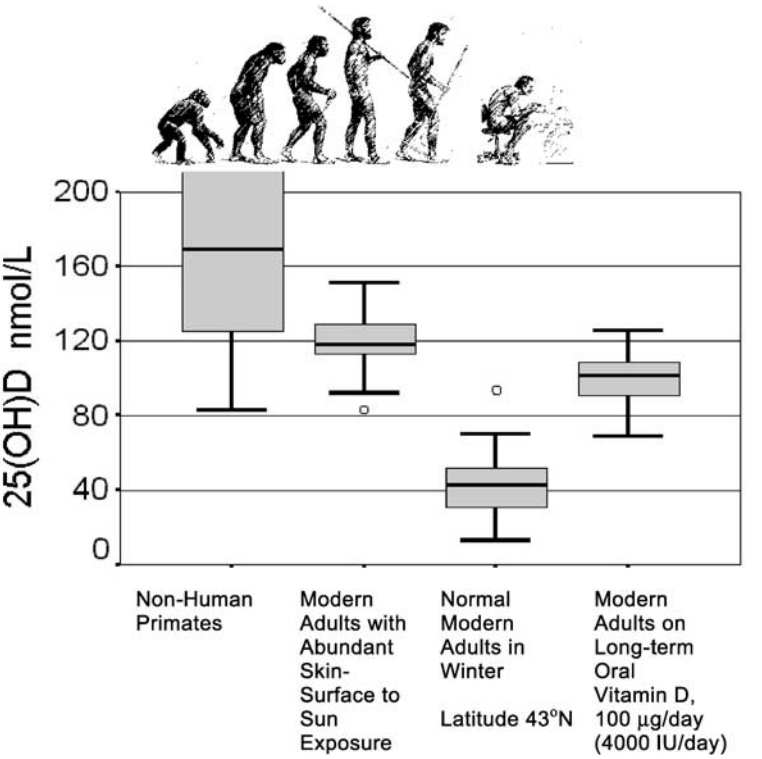

Figure 9.4. Summary of what is known about circulating 25(OH)D concentrations in non-human primates and in modern adults. The cartoon along the top serves only to provide symbolic reference points for the corresponding parts of the graph below. It is assumed here that since modern humans evolved in tropical regions and without clothing, early vitamin D nutrition was similar to that of modern humans living under similar conditions. Results for non-human primates and for sun-rich adults are from Table 9.2, with additional data for adults given artificial tanning sessions (Vieth, 1999). Data for modern adults in winter and their responses to vitamin D are from a recent study involving hospital workers in Toronto, Canada (Vieth, 2001). These plots include whiskers that show the lowest and highest values, the boxes show the range of the central 50% of the sample group, with a line indicating the median value of the group.

guidelines for this nutrient (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997) are probably still woefully inadequate for adults.

The reason contemporary older adults require calcium intakes at levels attainable only with dairy foods or mineral supplements, may be because they are relatively vitamin D deprived. Because current nutrient recommendations provide far less vitamin D than is attainable through sunshine, modern medical thinking effectively maintains adults in a state of relative vitamin D insufficiency, compensated for by high requirements for calcium. In contrast, early humans living in sun-rich environments were relatively vitamin D rich—probably at least 100 μg/day (4,000 IU/day). Therefore, early humans may not have required as much calcium to prevent osteoporosis or rickets. Moreover, maintenance of higher vitamin D supplies may have optimized cellular control mechanisms that prevented many diseases that have not been classically associated with vitamin D nutrition.

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