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The Uncertain Significance of Low Vitamin D Levels in African Descent Populations: A Review of the Bone and Cardiometabolic Literature

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ABSTRACT

Vitamin D levels in people of African descent are often described as inadequate or deficient. Whether low vitamin D levels in people of African descent lead to compromised bone or cardiometabolic health is unknown. Clarity on this issue is essential because if clinically significant vitamin D deficiency is present, vitamin D supplementation is necessary. However, if vitamin D is metabolically sufficient, vitamin D supplementation could be wasteful of scarce resources and even harmful. In this review vitamin D physiology is described with a focus on issues specific to populations of African descent such as the influence of melanin on endogenous vitamin D production and lactose intolerance on the willingness of people to ingest vitamin D fortified foods. Then data on the relationship of vitamin D to bone and cardiometabolic health in people of African descent are evaluated.

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In populations throughout the African diaspora low vitamin D levels are anticipated. However, there is a paucity of data and hence uncertainty about vitamin D status in people living in Africa. Nonetheless, the most critical gap in existing knowledge is whether low levels of vitamin D are healthy and appropriate for African descent populations or whether levels of vitamin D considered to be low by the Institute of Medicine (IOM) and the Endocrine Society represent a health issue.[1,2]

Historically, vitamin D research has focused on bone metabolism and calcium balance. Our understanding of the contribution of vitamin D to health now extends from skeletal integrity to cardiometabolic health and beyond. The essential discovery was the identification in many cell types that there is a vitamin D receptor (VDR) within both the nucleus and plasma membrane caveolae.[3] In the nucleus, vitamin D in the form of 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) acts as a steroid hormone, joining with the nuclear VDR to form a transcription-factor complex that controls the expression of over 200 genes.[3,4] Beyond its genomic activity $1,25(OH)_2D$ interacts with the VDR on the plasma membrane and thereby influences a host of intracellular actions.[3–5]

In this review we focus on the effect of vitamin D on bone and cardiometabolic conditions specifically: obesity, diabetes, hypertension and cardiovascular disease. To understand the relationship of vitamin D to bone health, we examined data in three groups: sub-Saharan Africans, African-Americans and the African diaspora beyond the United States. Due to the depth of the literature, the cardiometabolic health section is

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Abbreviations and Acronyms

BMD = bone mineral density

FDA = Federal Drug Administration

IOM = Institute of Medicine

NHANES = National Health and Nutrition Examination Survey

PTH = parathyroid hormone

VDR = vitamin D receptor

UVB = ultraviolet B

WHI-OS = Women's Health Initiative–Observational Study

focused on African-Americans but has important implications for sub-Saharan Africa and the African diaspora.

Vitamin D

Vitamin D sources and pathway

Vitamin D has two forms, D_2 and D_3. But vitamin D is not a classic vitamin.[5,6] By definition, a vitamin is a nutrient that cannot be produced endogenously but is essential for good health and must be ingested. Yet one of the two forms, D_3, can be produced in the epidermal layer of sun-exposed skin by conversion from 7-dehydrocholesterol (Fig 1). However, sun exposure is rarely sufficient to meet vitamin D requirements. Therefore vitamin D must be obtained from either dietary sources or supplements.[4] Vitamin D_2 is found in fungi such as mushrooms, while vitamin D_3 is available in oily fish (e.g. salmon, sardines, herring, anchovies, trout, cod). Vitamin D supplements may provide either D_2 or D_3. Because of greater potency and a longer duration of action most supplements contain D_3.[7,8] In the United States, all forms of milk (fluid, concentrated, dry, evaporated), calcium-fortified juice drinks (orange juice) and ready-to-eat cereals are fortified with vitamin D_3.[9–11]

In the liver D_2 and D_3 become hydroxlyated at the 25-carbon position leading to the formation of the biochemically stable compound, 25-hydroxyvitamin D (25(OH)D) (Fig 1).[6] Even though 25(OH)D is used clinically as a marker of vitamin D sufficiency, it is not biologically active. To become biologically active, 25(OH)D must undergo a second hydroxylation by 1α-hydroxylase to form 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) (Fig 1). This enzyme was first identified in the kidney which is the most important physiological source of $1,25(OH)_2D$, but has subsequently been found in adipose tissue and in a myriad of other tissues including bone and pancreatic cells, vascular tissue and cardiac muscle.[12–14] Both 25(OH)D and $1,25(OH)_2D$, are deactivated by hydroxylation at the 24-carbon position, to ultimately form calcitroic acid, which is excreted in the urine.[15]

Vitamin D production and ingestion in people of African descent

Melanin pigmentation

Irradiation of 7-dehydrocholesterol in the epidermal layer of sun-exposed skin leads to the production of vitamin D_3. The amount of vitamin D_3 produced depends on the balance between the availability of ultraviolet B (UVB) light and the amount of melanin in the epidermis. UVB refers to ultraviolet light with wavelengths between 280 and 315 nm and is the specific form of ultraviolet light necessary for the conversion of 7-dehydrocholesterol to vitamin D_3. UVB exposure is greatest at the equator and declines at higher and lower latitudes. Therefore residents of countries in equatorial Africa receive more UVB than their counterparts in North America, Europe, Australia and even North and South Africa.[6,16]

Due to high exposure to UVB, Africans living in equatorial countries should have high endogenous production of vitamin D_3. However, melanin in the epidermis competes with 7-dehydrocholesterol for UVB absorption.[16] Therefore, when skin melanin content is high, longer periods of sun exposure are necessary for vitamin D_3 synthesis. Overall the endogenous production of vitamin D_3 depends on both latitudinal position and melanin content. As equatorial Africans move to

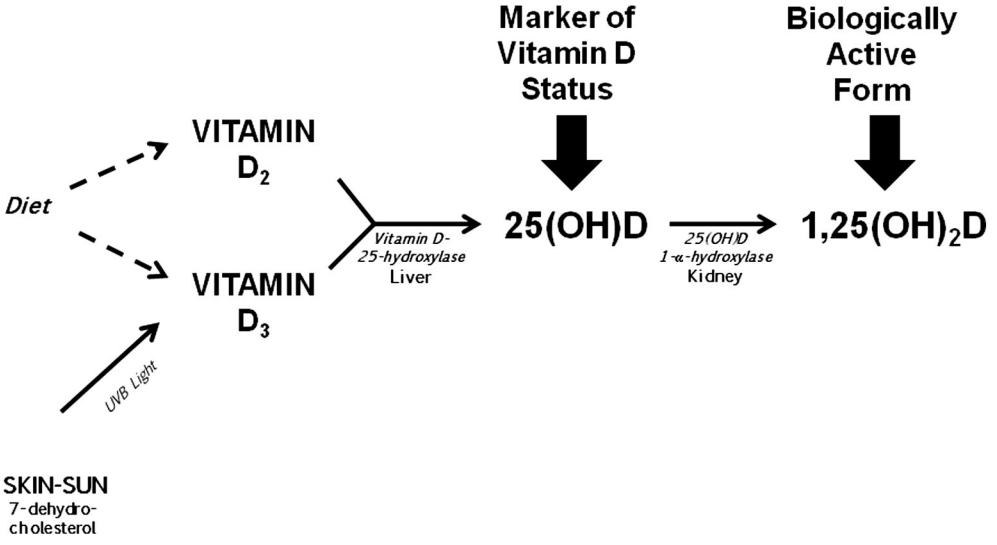

Fig 1 – Vitamin D pathway from precursors to active form.