Vitamin D in cutaneous carcinogenesis

Part I

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3. Achievement of a 70% or higher on the online Case-based Post Test
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Learning Objectives
After completing this learning activity, participants should be able to identify the correct laboratory test to check vitamin D status; recognize the factors that affect cutaneous vitamin D_3 synthesis; and identify the recommended dietary allowance (RDA) for vitamin D in children and adults.

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Skin cancer is the most common cancer in the United States. Exposure to ultraviolet radiation is a known risk factor for skin cancer but is also the principal means by which the body obtains vitamin D. Several studies have suggested that vitamin D plays a protective role in a variety of internal malignancies. With regard to skin cancer, epidemiologic and laboratory studies suggest that vitamin D and its metabolites may have a similar protective effect. These noncalcemic actions of vitamin D have called into question whether the current recommended intake of vitamin D is too low for optimal health and cancer prevention. Part I will review the role of vitamin D in the epidermis; part II will review the role of vitamin D in keratinocyte-derived tumors to help frame the discussion on the possible role of vitamin D in the prevention of skin cancer. (J Am Acad Dermatol 2012;67:803.e1-12.)

Key words: 25(OH)D levels; cholecalciferol; supplements; vitamin D; ultraviolet radiation.

CAPSULE SUMMARY

- 25-hydroxyvitamin D, or 25(OH)D, is the circulating form of vitamin D used to determine vitamin D status and for screening for vitamin deficiency.
- The Institute of Medicine recommends 600 International Units of vitamin D daily for most children and adults.
- Both vitamin D_2 and vitamin D_3 are effective at correcting vitamin D deficiency.
- Cutaneous production of vitamin D_3 is affected by age, skin pigmentation, latitude, and sun avoidance behaviors

Vitamin D is a fat-soluble prohormone whose major biologic function is to maintain serum calcium and phosphorous homeostasis. It promotes calcium absorption in the gut and reabsorption from the kidneys and inhibits the secretion of parathyroid hormone. Vitamin D therefore enables the normal mineralization of bone by regulating bone growth and remodeling the activity of osteoblasts and osteoclasts.[1] Vitamin D deficiency has significant musculoskeletal consequences, causing rickets in children and osteomalacia and osteoporosis in adults.[2] In addition to its functions in the endocrine and skeletal systems, vitamin D has roles in modulating the immune, cardiovascular, and inflammatory systems; among other actions, it regulates macrophage phagocytosis[3,4] and inhibits macrophage activation.[5,6] Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated, in part, by vitamin D.[7]

Many (but not all) epidemiologic studies have found an association between low levels of vitamin D and all-cause mortality,[8-11] cancer mortality,[12,13] and cancer survival.[14-18] Others have linked lower rates of prostate and ovarian cancer[19-25] to residency at lower latitudes. Some studies have shown that cancer patients who undergo treatment in summer have better survival rates than those who undergo treatment in winter, suggesting that variation in cancer survival may be associated with seasonal factors, including vitamin D levels.[26-30]

While the role of vitamin D in visceral cancers is under intensive research, the role of vitamin D in skin cancer is even more controversial. This is because the same spectrum of ultraviolet (UV) light necessary for vitamin D synthesis (290-320 nm) is also the most important environmental risk factor for the development of many skin cancer types. Nevertheless, laboratory studies suggest that vitamin D and its metabolites may reduce the risk of skin cancer by inhibiting the hedgehog signaling pathway,[31,32] the pathway underlying the development of basal cell carcinomas and upregulating DNA nucleotide excision repair enzymes.[33-35] Mice lacking the vitamin D receptor develop increased numbers of nonmelanoma skin cancers,[36] and the addition of vitamin D decreases the growth of nonmelanoma skin cancer and melanoma cells in vitro and in mouse models.[31,37-39] In humans, epidemiologic studies have reported mixed findings, with some reporting an association between higher vitamin D levels and increased skin cancer risk,[40,41] others showing a decreased skin cancer risk,[42,43] and still others showing no

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