

# Vitamin D in cutaneous carcinogenesis

## Part II

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1. Reading of the CME Information (delineated below)
2. Reading of the Source Article
3. Achievement of a 70% or higher on the online Case-based Post Test
4. Completion of the Journal CME Evaluation

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###### Learning Objectives

After completing this learning activity, participants should be able to assess possible associations between vitamin D and the risk of skin cancer and define what constitutes adequate vitamin D supplementation and goal serum vitamin D levels.

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The role of vitamin D in health maintenance and disease prevention in fields ranging from bone metabolism to cancer is currently under intensive investigation. A number of epidemiologic studies have suggested that vitamin D may have a protective effect on cancer risk and cancer-associated mortality. With regard to skin cancer, epidemiologic and laboratory studies suggest that vitamin D and its metabolites may have a similar risk reducing effect. Potential mechanisms of action include inhibition of the hedgehog signaling pathway and upregulation of nucleotide excision repair enzymes. The key factor complicating the association between vitamin D and skin cancer is ultraviolet B radiation. The same spectrum of ultraviolet B radiation that catalyzes the production of vitamin D in the skin also causes DNA damage that can lead to epidermal malignancies. Part II of this continuing medical education article will summarize the literature on vitamin D and skin cancer to identify evidence-based optimal serum levels of vitamin D and to recommend ways of achieving those levels while minimizing the risk of skin cancer. (J Am Acad Dermatol 2012;67:817.e1-11.)

**Key words:** 25(OH)D levels; basal cell carcinoma; melanoma; nonmelanoma skin cancer; vitamin D; vitamin D receptor; squamous cell carcinoma; sunlight.

Overall, there is some evidence that vitamin D may play a role in nonmelanoma skin cancer (NMSC) and melanoma prevention, although as of yet there is no direct evidence to show a protective effect. The relative contributions of diet, supplementation, and cutaneous vitamin D synthesis to serum vitamin D levels need additional study. While some in vitro and animal data suggest that vitamin D may have protective effects against skin cancer, additional studies in humans are needed. Several laboratory studies suggest that vitamin D and its metabolites may reduce the risk of skin cancer by inhibiting the hedgehog signaling pathway, the pathway underlying development of basal cell carcinomas (BCCs), and upregulating DNA nucleotide excision repair enzymes. Mice lacking the vitamin D receptor (VDR) develop increased numbers of NMSCs, and the addition of vitamin D decreases the

### CAPSULE SUMMARY

- Vitamin D deficiency is defined as serum 25(OH)D levels below 20 ng/mL.
- Vitamin D in vitro inhibits keratinocyte growth and promotes differentiation—factors that are important for skin cancer prevention.
- Mice lacking the vitamin D receptor have increased basal cell and squamous cell carcinoma tumors, suggesting a role of vitamin D in keratinocytic carcinoma.
- However, epidemiologic studies do not show a clear relationship between vitamin D levels and the risk of nonmelanoma skin cancer.
- Some, but not all, epidemiologic studies show that higher levels of vitamin D are correlated with reduced melanoma risk and improved survival.
- There is no current consensus on clinical recommendations for vitamin D intake and optimal vitamin D levels for skin cancer prevention.

growth of NMSC and melanoma cells in vitro and in mouse models. In humans, epidemiologic studies have reported mixed findings, with some reporting an association between higher vitamin D levels and increased skin cancer risk, others showing a decreased skin cancer risk, and still others showing no association.

However, because ultraviolet (UV) rays are known to be carcinogenic, and because it is very difficult to discern when small amounts of sun exposure cross the line from potential benefit to harm, the American Academy of Dermatology recommends that an adequate amount of vitamin D should be obtained from a healthy diet that includes foods and beverages that are naturally rich in or fortified with vitamin D and/or vitamin D supplements; it

should not be obtained from unprotected exposure to UV radiation. Therefore, given the current

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