Vitamin D Deficiency in Allergic Disorders and Immune Mechanisms

Marianne Frieri, M.D., Ph.D, FAAAAAI, FACAAI
Chief of Allergy & Immunology, Department of Medicine, Nassau University Medical Center,
Attending in Pediatrics & Medicine
North Shore Long Island Jewish Health Care System
Private Practice North Shore Allergy & Asthma Institute
Professor of Medicine & Pathology, State University of NY, Stony Brook
Vitamin D has been reported in very high rates in US population, implicated in various diseases such as diabetes, high blood pressure, cardiovascular disease, and many cancers.\textsuperscript{1,2} It has also been implicated in immune system dysregulation\textsuperscript{2}. Our hypothesis is that low vitamin D has been implicated with increased incidence of various types of allergic conditions. NHANES 2005-2006 as a cross sectional survey done on the non-institutionalized population of the US by the CDC and Prevention and National Centre for Health Statistics consists of an extensive interview done at home and an examination done at a mobile center.

An allergy questionnaire provided interview data on self-reported allergic diseases including hay fever, allergies and eczema, using the question “Has the doctor or other health professional ever told that you have allergies and using the lab parameter vitamin D, < 10ng/ml, analyzed by logistic regression with SAS version 9.1 (Cary, NC) and using the proc survey. Out of 10,348 who participated our final sample consisted of 4,979 after deleting those < 20 years and those with missing values.

Vitamin D deficiency was positively correlated with prevalence of allergies (odds ratio of 1.37, 95% CI of 1.14 to 69). After adjusting the model for age, gender, race, smoking, alcohol, and educational status odds ratio still remained significant (OR of 1.34, 95% CI of 1.10 to 1.63). *There was also a positive correlation with prevalence of rashes, sneezing; sinus infections with low vitamin D.
Conclusion

- Our study showed a positive association between vitamin D deficiency and prevalence of allergies. Based on the magnitude of deficiency and its association with other diseases a careful consideration has to be given in educating the general population about the vitamin D intake. 5

- 1,25(OH)(2)D(3) has been shown to potentiate the efficacy of allergen immunotherapy used for allergic rhinitis therapy which effects regulatory cytokines IL-10 and TGF. 3 Supplementation of oral vitamin D can result in correction of defects in cathelicidins in the innate immune system of atopic subjects related to eczema. 4

- More research is needed to confirm this relationship and to further elucidate its effects on the immune system, whether it is due to impaired white blood cell or anti-inflammatory function.

The Role of Vitamin D in Asthmatic Children


- The authors investigated disease variables associated with vitamin D insufficiency in patients with childhood asthma and interaction of vitamin D with corticosteroid mediated anti-inflammatory responses.

- This excellent article provided very important data on vitamin D deficiency in pediatric asthmatics’ disease severity, along with a correlation between atopic markers and pulmonary function. The relationship found between perennial aeroallergen sensitivity to house dust mite, dog allergens, and lower vitamin D level was of interest.
Steroid Requirements and Immune Associations with Vitamin D are Stronger in Children than Adult Asthmatics.

• Serum vitamin D levels were examined in a prospective study of adults and children and healthy control subjects. PBMCs were cultured for 3 hours with or without 100 nmol/L dexamethasone.

• The expression of corticosteroid-regulated genes was detected by using real-time PCR. Serum IgE levels were measured, and information about asthmatic patients' steroid requirements was collected.

• Serum vitamin D level as well as PBMC cyp24a expression demonstrated a significant inverse relationship with daily inhaled corticosteroid dose in the pediatric asthma group only. Cyp24a expression in PBMCs correlated positively with in vitro suppression of TNF-α by dexamethasone (P = .05) and IL-13 (P = .0094) in PBMCs in the pediatric asthma group only.
Bacterial components plus vitamin D: The ultimate solution to the asthma (autoimmune disease) epidemic?

**Weiss ST Editorial J Allergy Clin Immunol 127;1128-1130, 2011**

- The microbiome/vitamin D hypothesis to explain the origins of the autoimmune disease epidemic fits better than the hygiene hypothesis that never could explain the increase in TH1 autoimmune disease, high rates of asthma, allergy. Both are easily explained by VDD.

- The strong link between the microbiome and vitamin D closes the loop, providing a plausible immunologic substrate for vitamin D’s effects on normal tolerization. There is evidence for dramatic changes in vitamin D levels over the 50-year period with a dramatic increase in autoimmune disease. We do not know what has happened to the gut microbiome during that period.

Vitamin D might determine how the gut flora interacts with the immune system.
Vitamin D deficiency has been associated with epidemiologic patterns in the asthma epidemic, more common with obesity, African American ethnicity, and westernization with higher asthma.

Evidence suggests that VDD is associated with increased airway hyper-responsiveness, lower pulmonary functions, worse asthma control, and possibly steroid resistance.

Lung epithelial cells express high baseline levels of 1-hydroxylase, allowing the conversion of inactive calcidiol to active calcitriol locally within the lung inhibiting the synthesis and release of certain cytokines, such as RANTES, PDGF and MMP from bronchial SMC, leading to decreased lung inflammation and SMC proliferation.

The Role of Vitamin D in Asthma
Vitamin D metabolites contribute to defenses at epithelial surfaces by stimulating production of antimicrobial peptides, such as defensins and cathelicidin. 1,25(OH)2D influences integration of host-microbe signaling pathways by modulating microbial pattern-recognition molecules, such as NOD2, CD14, and Toll-like receptors.

VDD appears to predispose to a wide variety of infections, including tuberculosis and respiratory tract viruses.

VDD might predispose to more frequent infections, more severe infections, or both caused by common gastrointestinal pathogens.

VDD (through altered production of antimicrobial peptides) and intestinal infections might promote persistent abnormal microbial ecology or "dysbiosis."

Does vitamin D in infancy promote development of atopic allergy?


Vitamin D3 intake during infancy was recorded in a previous study and the relationship between lower or higher vitamin D3 intake and atopic illness later in childhood was assessed.

Atopic manifestations were more prevalent in the group with higher intake of vitamin D3.
Vitamin D3 targets skin DC subsets to promote distinct Treg cell populations. Vitamin D3–activated epidermal LCs generate Foxp3^IL-10^low Treg cells in a TGF-β–dependent fashion, whereas vitamin D3–activated DDCs promote Foxp3^IL-10^high TR1 cell development through IL-10.