Clinical Implications of Vitamin D and Calcium

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Dr. Ron Grabowski is a practicing Doctor of Chiropractic in Houston, Texas. He has presented over 500 seminars and lectures on nutrition throughout the United States and in Europe, publishing several articles and a textbook in clinical nutrition.

Receiving his Bachelor of Science degree in Nutrition from North Dakota State University, he went on to be awarded his Doctor of Chiropractic degree from Texas Chiropractic College in Pasadena, Texas in 1989 where he became a professor and postgraduate diplomate lecturer. His dietitian experience includes tenure at some of the leading hospitals in the nation - The New York Hospital, Memorial Sloan Kettering in New York City (affiliated with Cornell Medical Center), Memorial Care System and the University of Texas M.D. Anderson Cancer Center in Houston, Texas.

Dr. Grabowski has served on the State of Texas Governor’s Childhood Obesity Taskforce and is a member of the American Dietetic Association, American Chiropractic Association and the Endocrine Society. In addition to his chiropractic practice, he has developed numerous vitamin and mineral formulas for supplement companies. Professional athletes, including those of Olympic standing, seek his expertise in nutrition consultation.

His research interests include nutritional support of the athlete and the use of supplements in clinical practice for the prevention and treatment of chronic diseases such as diabetes, heart disease, arthritis, fibromyalgia and gastrointestinal disorders.
Cardiology and Vitamin D

- Heart myocytes (Receptor & Production)
- Vascular smooth muscle
- Vascular endothelia (Receptor & Production)
Vitamin D and Hypertension

- Epidemiological studies suggest vitamin D insufficiency is associated with a higher risk for hypertension.  
  
  J Hypertens 2009
1. The renin angiotensin system (RAS) is a regulatory cascade that plays a critical role in the regulation of blood pressure, electrolyte, and plasma volume homeostasis.

2. Inappropriate stimulation of the RAS has been associated with hypertension.

3. Li et al. demonstrated that vitamin D is a potent endocrine suppressor of renin biosynthesis to regulate the RAS.

(Int J Endocrinol. 2010; 2010:579640)
Heart Disease and Childhood

- In early childhood, vitamin D deficiency is associated with cardiomyopathy and congestive heart failure. *Pediatr Cardiol – 1999*
- Vitamin D deficiency has been linked to life-threatening heart failure in infants. *Heart - 2008*
Vitamin D Mechanisms Associated with Cardiology

- Cardiac muscle cells and Vascular endothelial cells.
  - Contain the 1alpha-hydroxylase enzyme that converts circulating 25D₃ to 1,25D₃.
- Vitamin D Receptors are distributed in muscle cells, vascular endothelial cells and vascular smooth muscle.

Eur J Clin Nutr – 2009
Am J Geriatr Pharmacother - 2010
Dermatology and Vitamin D

- Keratinocytes (Receptor & Production)
- Hair follicles
Vitamin D Synthesis

- The amount of 7-dehydrocholesterol in the epidermis is relatively constant until later in life, when it begins to decline.
  
  *J Clin Invest 1985 and Lancet 1989*

- A person 70 years of age exposed to the same amount of sunlight as a 20-year-old person makes 25% of the vitamin D$_3$ that the 20-year-old person can make.
  
  *AJCN – 12/2004*
Sunscreens and Vitamin D

• Sunscreens efficiently absorb UVB radiation and thus markedly diminish the total number of UVB photons that reach the 7-dehydrocholesterol in the skin’s cells.

• A sunscreen with an sun protection factor of 8 reduces cutaneous production of previtamin D₃ by > 95%.

• The proper use of a sunscreen with a sun protection factor of 15 reduces the capacity > 99%.

J Clin Endocrinol Metab 1987 and Am J Clin Nutr 1994
Psoriasis and Vitamin D

- Normal and cancer cells that have a vitamin D receptor often respond to 1,25(OH)$_2$D by decreasing their proliferation and enhancing their maturation.

- This is the rationale for using 1,25(OH)$_2$D$_3$ and its analogs to treat the common hyperproliferative skin disorder psoriasis.

  - Retinoids 1998 and Br J Dermatol 1988

- Chronic plaque psoriasis is frequently associated with obesity.

  - AJCN-11/2008
Endocrinology and Vitamin D

- Adrenal
- Pancreatic β-cells (Receptors & Production)
- Parathyroid (Receptor & Production)
- Parotid
- Pituitary
- Thyroid C Cells
Diabetes and Vitamin D

- When nonobese diabetic mice, who typically develop type 1 diabetes, received 1,25(OH)$_2$D$_3$ throughout their life, their risk of developing type 1 diabetes was reduced by 80%.

  *Diabetes – 2002 and Diabetologia -1994*

- Observation by Hypponen et al that children receiving 2000 IU vitamin D from age 1 y on decreased their risk of getting type 1 diabetes by 80%.

  *Lancet - 2001*
Insulin and Vitamin D

- Low vitamin D levels have been correlated with insulin resistance. *J Pediatr Endocrinol Metab.* 2011

- Vitamin D not only facilitates the biosynthetic capacity of ß cells but also accelerates the conversion of proinsulin to insulin. *J Endocrinol* 1999

- Vitamin D supplementation has been reported to improve insulin secretion in vitamin D–deficient and nondiabetic subjects and in patients with type 2 diabetes. *Diabetologia 1986* and *Bone Miner 1986*

- Research suggests that vitamin D deficiency affects ß cell function and that vitamin D supplementation improves ß cell function.
Thyroid and Vitamin D

- Significantly low levels of vitamin D have been documented in patients with Autoimmune Thyroid Diseases (AITDs) that were related to the presence of anti-thyroid antibodies and abnormal thyroid function tests, suggesting the involvement of vitamin D in the pathogenesis of AITDs.

Cell Mol Immunol. 2011 May
Gastroenterology and Vitamin D

- Colon mucosal, immune cells (Receptor & Production)
- Esophagus
- Intestine
- Stomach
- Liver parenchymal cells
Gastroenterology and Vitamin D

- The active form of vitamin D, 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃], has been shown to inhibit the development of autoimmune diseases, including inflammatory bowel disease (IBD).
- Vitamin D-deficient mice on low-calcium diets developed the most severe IBD, and 1,25(OH)₂D₃ treatment of mice on low-calcium diets improved IBD symptoms.

AJCN – 12/2004
Immunology and Pulmonology

- **Immunology**
  - Dendritic cells (Receptors & Production)
  - Lymphocytes (activated B and T) (Receptors & Production)
  - Macrophages/monocytes (Receptors & Production)
  - Thymus

- **Respiratory**
  - Lung; Alveolar tissue
A number of studies have established that vitamin D is a principal controller of innate immunity, with the production of antimicrobial peptides able to kill viruses, bacteria and fungi and that it exerts a inhibitory effect on the inflammatory response to viral infections.

Asthma and Vitamin D

- Recent data suggest that vitamin D deficiency could be related to the onset of asthma, as well as be a marker of disease severity in children with asthma.
- A significant relationship (with an apparent dose-response effect) between higher percent-predicted forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) values and the increased circulating concentrations of 25-hydroxyvitamin D has been demonstrated in a large study of approximately 14,000 subjects in the United States.

(Am J Respir Crit Care Med 2009, Chest 2005)
Vitamin D Deficiency and URI’s

Vitamin D deficiency has been shown to predispose children to respiratory infections, and this predisposition is much stronger in children with asthma.

Vitamin D Supplementation

It has been shown that vitamin D supplementation decreases the incidence of respiratory infections, which are a major trigger of asthma exacerbation.

Steroids and Vitamin D

- In vitro studies have shown that 1,25 (OH)2D3 has a direct inhibitory effect on passively sensitized airway smooth muscle cells and that it increases glucocorticoid bioavailability in bronchial smooth muscle cells.

- Decreased serum vitamin D levels in children with asthma have been observed to be associated with increased corticosteroid use and an investigation with T cells from patients with steroid-resistant asthma showed that vitamin D supplementation could potentially increase the therapeutic response to glucocorticoids by restoring the impaired steroid-induced interleukin-10 response.

Musculoskeletal and Vitamin D

- Cartilage chondrocytes (Receptor & Production)
- Bone osteoblasts (Receptor & Production)
- Skeletal muscle fibers
- Bone marrow
Musculoskeletal Conditions and Vitamin D

- It is estimated that 40-60% of patients with fibromyalgia may have some component of vitamin D deficiency and osteomalacia. *Calcif Tissue Int 2000, J Bone Miner Res 2003, Bone Miner Res 2000*

- Glerup et al reported that 88% of Danish Arab women with muscle weakness and pain were vitamin D deficient. *J Intern Med 2000*

- More than 90% of 150 children and adults 10–65 y of age who presented with nonspecific muscle aches and bone aches and pains at a Minnesota hospital were found to be vitamin D deficient. *Mayo Clin Proc 2003*
Vitamin D and Neurology

- Brain neurons, glia (Receptor & Production)
- Patients who live at higher latitudes and are at risk of vitamin D deficiency are also more prone to developing schizophrenia.
- Vitamin D deficiency has been associated with depression.

*Schizophr Res 2002 and J Nutr Health Aging 1999*
Male and Female Reproductive Organs

- Breast (Receptor & Production)
- Ovary
- Placenta, decidua (Receptor & Production)
- Prostate (Receptor & Production)
- Testis
- Uterus
Ophthalmology and Vitamin D

- **Retina** - Receptor
- Fish contain vitamin D and retinol, which may represent alternative or additional potentially protective agents for Age-related Macular Degeneration (AMD).
- It has been postulated that vitamin D per se may reduce the risk of AMD because of its antiinflammatory properties, and several putative mechanisms support an antiinflammatory role for vitamin D.

*Arch Ophthalmol 2003*
Nephrology and Vitamin D

Kidney tubules, other (Receptor & Production)

WHO Classifications of Obesity

If your BMI is:

• 18.5–24.9 kg/m²  
  A healthy adult
• 25.0–29.9 kg/m²  
  Overweight
• 30.0–34.9 kg/m²  
  Class I obesity
• 35.0–39.9 kg/m²  
  Class II obesity
  – 40 kg/m²  
  Class III obesity
Obesity and Vitamin D

- **Adipose tissue (Vitamin D Receptor)**
- Serum 25(OH) D has been positively correlated with insulin sensitivity, but negatively correlated with HbA(1c), implying that obese children and adolescents with low vitamin D status may be at increased risk of developing impaired glucose metabolism independent of body adiposity.

*Metabolism - 2008 Feb*
Obesity and Vitamin D (continued)

• Obese individuals, as a group, have low plasma concentrations of 25-hydroxyvitamin D [25(OH)D], which are associated with increased plasma concentrations of immunoreactive parathyroid hormone.

• It has been postulated that obese individuals may avoid exposure to solar ultraviolet (UV) radiation, which is indispensable for the cutaneous synthesis of vitamin D$_3$.

• It has been proposed that production of the active vitamin D metabolite 1,25-dihydroxyvitamin D [1,25(OH)$_2$D] is enhanced and thus, its higher concentrations exert negative feedback control on the hepatic synthesis of 25(OH)D.

• It has also been suggested that the metabolic clearance of vitamin D may increase in obesity, possibly with enhanced uptake by adipose tissue.

Bariatric Surgery and Vitamin D Deficiency

- Compared with gastric bypass, duodenal switch was associated with lower postoperative concentrations of vitamin A and 25-hydroxyvitamin D and a steeper decline in thiamine concentrations. *AJCN – 5/2009*
A low vitamin D status and inadequate calcium intake are important risk factors for various types of cancer.

Colon, rectal, breast, gastric, endometrial, renal and ovarian cancer exhibit a significant inverse relationship between incidence and oral intake of calcium.

Lung and endometrial cancer as well as multiple myeloma are considered calcium and vitamin D sensitive.

Studies on tissue-specific expression of the CYP27B1-encoded 25-hydroxyvitamin D-1alpha-hydroxylase and of the extracellular calcium-sensing receptor (CaR) have led to an understanding how locally produced 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) and extracellular Ca2+ act jointly as key regulators of cellular proliferation, differentiation and function.

Anticancer Res. 2009 Sep
Summary

Previtamin D₃

Skin

Milk
Orange Juice

Diet

Salmon

Supplements

Vitamin D

Liver

25(OH)D

Kidney

Prostate Gland, Breast, Colon

Immune Cells

1,25(OH)₂D

Calcium, Muscle
Bone Health
&
Regulation of Blood Pressure
Insulin Production
(heart disease and diabetes prevention)

Regulation of Cell Growth (cancer prevention)

Regulation of Immune Function (diabetes type 1 and autoimmune disease prevention)