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Research Article

CONGENITAL VITAMIN-D DEFICIENCY AND OVERDOSE

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ABSTRACT

Vitamin-D (vit-D) deficiency among pregnant women is frequent in many populations over the world and this is a preventable health problem. Research indicates that adequate vit-D intake in pregnancy should be optimal for both maternal and fetal health, because calcium demands increase in the third trimester of pregnancy that is why vit-D status becomes crucial for maternal health, fetal skeletal growth with good and optimal outcomes. Vit-D deficiency or overdose during pregnancy is the origin for a host of future perils for the child, especially the effect on neurodevelopment and the immune system. Therefore, prevention of vit-D deficiency or overdose among pregnant women is essential and demanding. The currently recommended supplementation amount of vit-D is not sufficient to maintain a value of 25 hydroxy vit-D during pregnancy. This review discusses vit-D metabolism, dietary requirements, recommendations and implications of vit-D deficiency during pregnancy and lactation.

INTRODUCTION

Vitamin-D (vit-D) refers to a group of fat-soluble secosteroids (Steroid with brocken ring). It helps in regulating the amount of calcium and phosphate in the body and keeps bones, teeth and muscles healthy. They are the organic compounds needed in small quantities for the body to sustain life. We get Vitamins from food or any other supplements because the human body either does not produce enough of them if produced it has to be triggered by an agent. Basically it is two types; fat soluble (stored in the fat tissues of the body, as well as the liver and can stay there as reserves for a long time) and water soluble (do not get stored in the body for a long time, they get expelled through urine) (http://www.medicalnewstoday.com/articles/161618.php). In humans, the most important compounds in this group are vit-D3 (also known as cholecalciferol) and vit-D2 (ergocalciferol) (Holick MF, 2006, Calvo MS *et al.*, 2005, Norman AW, 2008). Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements. Very few foods contain vit-D; synthesis of vit-D (specifically cholecalciferol) in the skin is the major natural source of the vitamin. Dermal synthesis of vit-D from cholesterol is dependent on sun exposure (specifically UVB radiation).

The major source of vit-D for humans is exposure to sunlight. The efficiency of the conversion of 7-dehydrocholesterol to vit-D3 is dependent on time of day, season of the year, latitude, skin color and age, however little bit of vit-D occurs naturally in the food supply too (Holick MF, 2007). The major naturally occurring food sources include fatty fish, beef liver and egg yolk. In the U.S. and Canada, the major dietary source of dietary vit-D is fortified foods, including cow's milk and, depending on country, other fortified foods and dietary supplements (DeLuca HF, 2006).

Adequate amount of vit-D prevents hypocalcemic tetany and it promotes calcium absorption in the gut, maintains adequate serum calcium, phosphate concentrations to enable normal mineralisation of bones. It takes a part in the modulation of cell growth, neuromuscular and immune function, and reduction of inflammation. An adequate amount of vit-D prevents osteoporosis in older adults. vit-D is a hormone-like Vitamin (precursor of a hormone) because of this the body is capable of producing its own vit-D through the action of sunlight on the skin. Many proteins that regulate cell proliferation, differentiation, and apoptosis (apoptosis is programmed cell death) are modulated in parts by vit-D. Other than the bone health vit-D may also have protection against cold and fighting depression and also increase the intestinal absorption of

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calcium, iron, magnesium, phosphate, and zinc (fig. 1) (http://naturallynicole.com/7-signs-you-may-be-lacking-vitamin-d/).

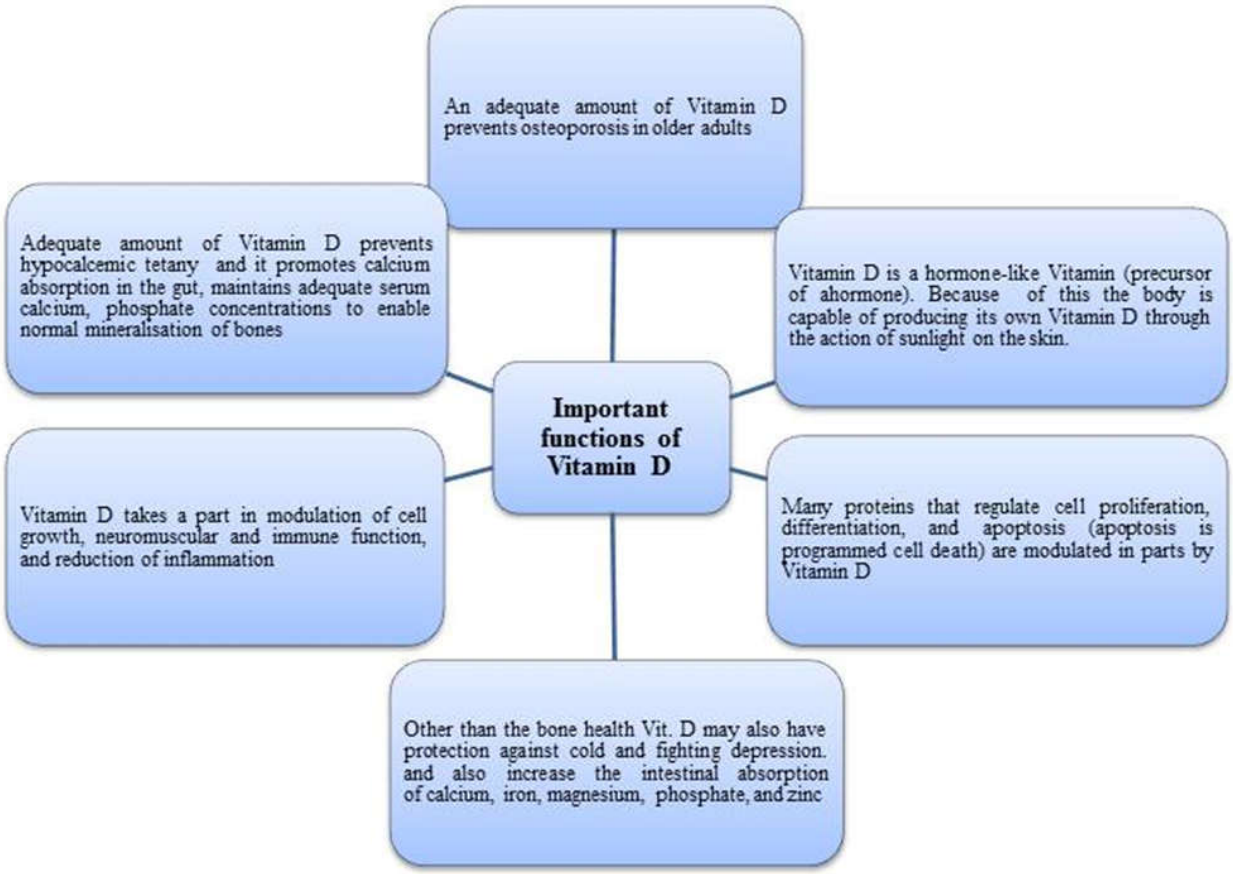

Figure 1 Shows important functions of vit-D

VIT-D Metabolism

Vit-D3 is produced in the skin in response to ultraviolet-B radiation from sunlight or can be obtained from the or from supplements. Both forms of vit-D undergo identical metabolism (Fig. 2). Some evidence indicates that vit-D2 may be metabolized more rapidly than vit-D3, (Armas LA *et al.* 2004, Trang HM *et al.,* 1998) but with regular daily intake they can be considered bioequivalent (Holick MF *et al.*, 2008, Thacher TD *et al.*, 2009, Plum LA and DeLuca HF, 2010). Both forms of vit-D is converted to 25-hydroxyvitamin [25(OH)D] in the liver, and the serum level of 25(OH) D is measured to determine the adequacy of vit-D status. In the kidney, 25(OH)D is hydroxylated to 1,25-dihydroxyvit-D [1,25(OH)2D], which is the only biologically active form of vit-D. Acting principally on the duodenum, 1,25(OH)2D increases calcium absorption.

The characteristics of 1,25(OH)2D are those of a hormone, and consequently vit-D is a prohormone rather than a true vitamin. The structure of 1,25(OH)2D is similar to that of other steroid hormones. As long as sunlight exposure is adequate, 1,25(OH)2D can be produced by the body without the requirement for ingestion in the diet. Based on the need for increased calcium absorption, the synthesis of 1,25(OH)2D is tightly regulated and stimulated primarily by serum parathyroid hormone (PTH), as well as low serum calcium or phosphorus levels, and inhibited by circulating FGF23 (Fibroblast Growth Factor-23) produced by osteocytes (Thacher TD *et al.*, 2009). Although produced in the kidney, 1,25(OH)2D acts at a distance in the intestinal cell to increase calcium absorption or in the bone to stimulate differentiation and activation of osteoblasts and osteoclasts (Holick MF, 2005).

VIT-D Status And Classification

Usually vit-D status is estimated by measuring the level of plasma 25(OH)D. Evidence of 25(OH)D concentrations of 44–70 ng/mL observed in healthy outdoor workers (such as farmers and lifeguards), it means an optimal healthy level that is far above the levels prevent from rickets and osteomalacia (Haddad JG and Chyu KJ, 1971, Hollis BW *et al.*, 2007). The correlation between vit-D levels and intestinal calcium absorption, maximal PTH suppression, bone loss prevention, and bone turnover have helped to develop a classification of stages for vit-D status in nonpregnant adults (Table 1) that indicate that levels of >32 ng/mL are required for adequacy (Zittermann A *et al.*, 2005, Hollis BW, 2005, Hollis BW and Wagner CL, 2006).

Prevalence of Congenital Vit-D Deficiency

On the basis of several studies (Dawodu A and Wagner CL, 2007, Van der Meer IM *et al.*, 2006, Bassir M *et al.*, 2001, Markestad T *et al.*, 1984, Sachan A *et al.*, 2005) Vit-D deficiency during pregnancy is 18–84% worldwide epidemic. In the United States, vit-D deficiency is estimated to occur in 5–50% of pregnant women (Lee JM, *et al.*, 2007, Hillman LS *et al.*, 1976).

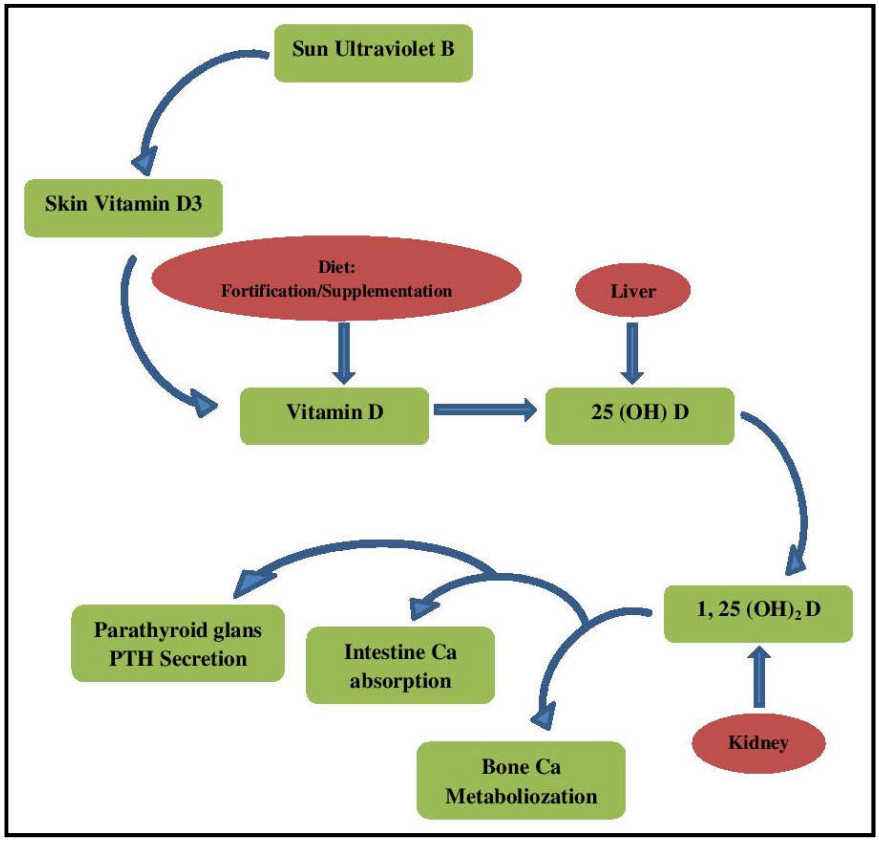

Figure 2 Diagram representing Vit-D Metabolism

African American women have a much higher risk of vit-D deficiency compared with other women because of increased skin pigmentation and low dietary intake (Nesby-O'Dell S, *et al.*, 2002). Bodnar *et al.* (Bodnar LM *et al.*, 2007) reported the prevalence of vit-D deficiency and insufficiency in 200 white and 200 black pregnant women, they found in African American pregnant women, vit-D deficiency and insufficiency occurred in 29.2% and 54.1%, respectively, compared with 5% and 42.1% of white pregnant women. Interestingly, 90% of study participants reported that they were taking prenatal vitamins.

Recent studies with larger patient samples suggest that both milk consumption and vit-D intake are predictors of infant size. One study showed that, for every cup of milk consumed per day by the mother, there is an associated increase in infant birth weight of 41 g, and that every microgram of daily vit-D intake correlates with an increased birth-weight of 11 g (Brooke OG and Wood C, 1980, Brooke OG *et al.*, 1981, Brooke OG *et al.*, 1981, Mallet E *et al.*, 1986, Mannion CA *et al.*, 2006). A study of >50,000 women showed that those women who drank a significant amount of milk (≥6 glasses per day) had a large-for-gestational age baby.

Table 1 Representing status of vit-D in pregnant adult women and newborn infants

Stage	Serum 25(OH)D, ng/mL	Maternal adverse effects	Newborn infant adverse effects
Severe deficiency	<10	Increased risk of preeclampsia, calcium malabsorption, bone loss, poor weight gain, myopathy, higher parathyroid hormone levels	Small for gestational age, neonatal hypocalcemia, hypocalcemic seizures, infantile heart failure, enamel defects, large fontanelle, congenital rickets, rickets of infancy if breastfed
Insufficiency	11–32	Bone loss, subclinical myopathy	Neonatal hypocalcemia, reduced bone mineral density, rickets of infancy if breastfed
Adequacy	32–100	Adequatecalcium balance, parathyroid hormone levels	None, unless exclusively breastfed
Toxicity	>100	Hypercalcemia, increased urine calcium loss	Infantile idiopathic hypercalcemia

Effects of Gestational Vit-D Deficiency Fetal Development

Infant size

In a study on few pregnant women, who received recommended dietary allowance of calcium and vit-D, occurs in result in lower incidence of birth weight was significantly lower in newborn infants (Sabour H *et al.*, 2006). In addition, pregnant women with vit-D intakes <200 IU/d had infants with birth weights that were 60 g below from those who takes 200 IU/d and above intake (Scholl TO and Chen X. Vit-D, 2009).

Inversely, women who consumed no milk during their pregnancy had a significantly increased risk of having a small-for-gestational-age baby (Olsen SF *et al.*, 2007).

Skeletal development

Poor skeletal mineralization in utero that is induced by vit-D deficiency may manifest as congenital rickets, craniotabes, or osteopenia in newborn infants. Congenital rickets is rare, typically occurring only in infants born to mothers with severe vit-D deficiency and osteomalacia (Russell JG and Hill LF,

1976, Orbak Z *et al.*, 2007, Specker BL *et al.*, 1992, Weiler H *et al.*, 2005). Interestingly, reduced concentrations of 25(OH)D in mothers during late pregnancy was associated with reduced whole-body and lumbar-spine bone-mineral content in their children at age 9 years (Javaid MK *et al.*, 2006). Maternal vit-D deficiency has also been associated with craniotabes or larger fontanelles which is consistent with impaired ossification of the skull (Reif S *et al.*, 1988, Congdon P *et al.*, 1983).

Vit-D deficiency during lactation

In the first 6–8 weeks of postnatal life, the vit-D status of a neonate is dependent largely on vit-D that is acquired through placental transfer in utero, as evidenced by the direct linear relationship between maternal and cord blood levels of 25(OH)D (Hillman LS and Haddad JG, 1974, Ala-Houhala M, 1985). In contrast, babies who are exclusively breastfed are at higher risk for vit-D deficiency (Salle BL *et al.*, 1998). Human milk contains a very low concentration of vit-D (approximately 20–60 IU/L), which represents 1.5–3% of the maternal level (Hollis BW *et al.*, 1981). This concentration is not sufficient to maintain an optimal vit-D level in the baby if exposure to sunlight is limited.

Breast-fed infants of vit-D deficient mothers occasionally manifest life-threatening conditions such as hypocalcemic seizures and dilated cardiomyopathy (Orbak Z *et al.*, 2007, Camadoo L *et al.*, 2007, Oki J *et al.*, 1991, Maiya S *et al.*, 2008, Kosecik M and Ertas T, 2007). Recent reports of rickets in breast-fed infants with a lack of sun exposure are concerned (Ward LM *et al.*, 2007, Ladhani S *et al.*, 2004, Dawodu A and Tsang R, 2007, Hollis BW and Wagner CL, 2004). According to American Academy of Pediatrics breast-fed infants should receive supplements that contain 400 IU of vit-D daily, beginning shortly after birth and continuing throughout childhood and adolescence. Recent studies show that maternal vit-D intake of 4000 IU daily during lactation in vit-D–in-sufficient mothers enhances it's levels in breast milk which may prevent vit-D deficiency–related complications in both women and their breast-fed infants (Hollis BW and Wagner CL, 2004).

Recommendations For Monitoring

Vit-D is important to maternal health, fetal development, and postnatal life. Current prenatal care does not include the monitoring of vit-D levels, which is an unfortunate oversight because the deficiency is easily treated. Women with ≥1 risk factors for vit-D deficiency (Table 1) should have a plasma 25(OH)D level drawn at the beginning of gestation and at mid pregnancy. The recommended target range for nonpregnant adults is 32–100 ng/mL (80–250 nmol/L), which appears to be a safe range during pregnancy. However, the studies have shown that prenatal supplements that contain 400 IU of vit-D are not adequate to achieve normal vit-D levels in pregnant women or their infants. Therefore, supplemental vit-D in doses that exceed 1000 IU per day (2000–10,000 IU/ d) may be required to achieve a normal concentration of circulating vit-D in severely deficient patients (Mallet E *et al.*, 1986, Cockburn F *et al.*, 1980, Brooke OG *et al.*, 1980, Vieth R et aal., 2001, Heaney RP *et al.*, 2003).

Overdose of VIT-D

Hypervitaminosis D is a serious and a very rare condition. It is said that serum 25 hydroxyvit-D concentrations above 75 nmol/L (30 ng/mL) are "not consistently associated with increased benefit". For vit-D, there are still underlying questions: How much is the daily requirement and How much is too much ? (GannagéYared MH *et al.*, 2000). New research suggests that women who takes high doses of vit-D during pregnancy have a greatly reduced risk of complications (Heaney RP *et al.*, 2003), including gestational diabetes, preterm birth, and infection.

Epidemiological analyses implicated high dietary vit-D intake during pregnancy results in the birth of syndrome babies. In the early 1960s, Williams, *et al.* (Friedman WF and Mills LF, 1969, Williams JC *et al.*, 1961), described a syndrome of supravalvular aortic stenosis, peripheral pulmonic stenosis, and body features indistinguishable from those in survivors of the syndrome of idiopathic hypercalcemia of infancy. A study in human subjects involved the administration of 100,000 IU vit-D per day (2.5 mg/day) throughout pregnancy to hypoparathyroid women to maintain serum calcium with no fatal outcome (Hollis BW and Wagner CL, 2006). Most prenatal vitamins have around 400 IU of vit-D, and most health groups recommend taking no more than 2,000 IU of the vitamin in supplement form daily. Eventually, as circulating 25(OH)D increases to toxic concentrations, the classic situation of hypercalciuria, hypercalcemia, and finally extraskeletal calcification becomes evident. Hypercalciuria due to excessive vit-D intakes is always accompanied by circulating 25(OH)D concentrations >250nmol/L (100 ng/mL).

Testing And Treatment For Vit-D Deficiency

The recommendations not to made untill possible measure of the circulating concentration of 25-hydroxyvitamin-D [25(OH) D], which is the indicator of nutritional vit-D status (Haddad JG and Stamp TC, 1974, Hollis BW, 1996). The testing would be appropriate in adults or children with bone pain, elevated serum alkaline phosphatase or PTH levels, and low serum calcium or phosphorus levels and, the persons with advanced age, those with osteoporosis, or those at increased risk of falls or fractures may also benefit from measurement of 25(OH)D levels (Holick MF *et al.*, 2011, McCarty CA, 2008, Brooke OG *et al.*, 1981).

Those identified as at risk include: Women from black and ethnic minorities who are socially excluded, women with limited exposure to sunlight, especially those who are housebound and obese women with prepregnancy BMI > 30. Current U.S. guidelines call for pregnant women to get 400-600 IU vitamins remains the recommended daily intake for pregnant women. However, getting 25(OH) D levels consistently above 75 nmol/L (30 ng/mL) may require at least 1500-2000 IU/day of vit-D. If a mother is vit-D deficient, breast milk is not a good source of vit-D, so infants need to be given vit-D supplementation until they are weaned. Also, women are encouraged to continue to take vit-D supplements after pregnancy to help protect against health problems such as osteoporosis.

The Dietary Recommended Intake (DRI) OF VIT-D

The DRIs for vit-D are based on maintaining skeletal health and have been set using the assumption that sun exposure is minimal (Langlois K *et al.*, 2010, Whiting SJ, 2011).

The DRIs for vit-D, which can also be found in the DRI tables, are as follows:

Age group	Recommended Dietary Allowance (RDA) per day	Tolerable Upper Intake Level (UL) per day
Infants 0-6 months	400 IU (10 mcg)*	1000 IU (25 mcg)
Infants 7-12 months	400 IU (10 mcg)*	1500 IU (38 mcg)
Children 1-3 years	600 IU (15 mcg)	2500 IU (63 mcg)
Children 4-8 years	600 IU (15 mcg)	3000 IU (75 mcg)
Children and Adults 9-70 years	600 IU (15 mcg)	4000 IU (100 mcg)
Adults > 70 years	800 IU (20 mcg)	4000 IU (100 mcg)
Pregnancy & Lactation	600 IU (15 mcg)	4000 IU (100 mcg)
Infants 0-6 months	400 IU (10 mcg)*	1000 IU (25 mcg)

* Adequate Intake rather than Recommended Dietary Allowance.

CONCLUSION

Vitamin D has emerged as something of a wonder supplement, according to the claims of dozens of studies published in the past few years. In the present review, we summarised the effect of vit-D status of mothers during pregnancy, correlated with the morphology of the developing fetus skeleton. That is why vit-D intake in pregnancy should be optimal for both maternal and fetal health, because calcium demands increase during pregnancy and lactation that is why vit-D status becomes crucial for maternal health, fetal skeletal growth with good and optimal outcomes. Intake of vit-D during the gestational period may reduce risk of complications, including gestational diabetes, preterm birth, and infection, however high doses of vit-D has also shown harmful effect includes the syndrome of supravalvular aortic stenosis, peripheral pulmonic stenosis, and body features indistinguishable from those in survivors of the syndrome of idiopathic hypercalcemia of infancy. Furthermore, the authors recommends future studies to determine the accurate vit-D requirement during pregnancy not only for maternal skeletal preservation and fetal skeletal formation, but also for fetal “imprinting" that may affect neurodevelopment, immune function and chronic disease susceptibility soon after birth as well as later in their life spain.

References

1. http://www.medicalnewstoday.com/articles/161618.php
2. Holick MF, (2006): "High prevalence of vit-D inadequacy and implications for health". Mayo Clin. Proc. 81 (3): 353–373.
3. Calvo MS, Whiting SJ, Barton CN; Whiting; Barton, (2005): Vit-D intake: a global perspective of current status. *J. Nutr*. 135 (2): 310–316
4. Norman AW, (2008): From vit-D to hormone D: fundamentals of the vit-D endocrine system essential for good health. *Am. J. Clin. Nutr*. 88 (2): 491S–499S
5. Holick MF, (2007): Vit-D deficiency. *N Engl J Med*. 357:266-281.
6. DeLuca HF, (2004): Overview of general physiologic features and functions of vit-D. *Am J Clin Nutr*. 80:1689S-1696S.
7. http://naturallynicole.com/7-signs-you-may-be-lacking-vitamin-d
8. Armas LA, Hollis BW, Heaney RP, (2004): Vit-D2 is much less effective than vit-D3 in humans. *J Clin Endocrinol Metab*. 89(11):5387-5391.
9. Trang HM, Cole DE, Rubin LA, Pierratos A, Siu S, Vieth R, (1998): Evidence that vit-D3 increases serum 25-hydroxyvit-D more efficiently than does vit-D2. *Am J Clin Nutr*. 1998; 68(4):854-858.
10. Holick MF, Biancuzzo RM, Chen TC, Ellen K. Klein, Azzie Young, Douglass Bibuld, Richard Reitz, Wael Salameh, Allen Ameri, and Andrew D. Tannenbaum, (2008): Vit-D2 is as effective as vit-D3 in maintaining circulating concentrations of 25-hydroxyvit-D. J Clin Endocrinol Metab. 93(3):677-681.
11. Thacher TD, Obadofin MO, O’Brien KO, Abrams SA, (2009): The effect of vit-D2 and vit-D3 on intestinal calcium absorption in Nigerian children with rickets. *J Clin Endocrinol Metab*. 94(9):3314-3321.
12. Plum LA, DeLuca HF, (2010): The functional metabolism and molecular biology of vit-D action. In: Holick MF, ed. Vit-D: Physiology, Molecular Biology, and Clinical Applications. 2nd ed. New York, NY: Humana Press; 61-97.
13. Haddad JG, Chyu KJ, (1971): Competitive protein-binding radioassay for 25-hydroxycholecalciferol. *J Clin Endocrinol Metab*. 33:992–995.
14. Hollis BW, Wagner CL, Drezner MK, Binkley NC, (2007): Circulating vit-D3 and 25-hydroxyvit-D in humans: an important tool to define adequate nutritional vit-D status. *J Steroid Biochem Mol Biol*. 103 (3-5):631–634.
15. Zittermann A, Schleithoff SS, Koerfer R. Putting cardiovascular disease and vit-D insufficiency into perspective. *Br J Nutr*. 2005; 94:483–492.
16. Hollis BW, (2007): Circulating 25-hydroxyvit-D levels indicative of vit-D sufficiency: implications for establishing a new effective dietary intake recommendation for vit-D. *J Nutr*. 135:317–322.
17. Hollis BW, Wagner CL, (2006): Vit-D deficiency during pregnancy: an ongoing epidemic. *Am J Clin Nutr*. 84 (2):273.
18. Dawodu A, Wagner CL, (2007): Mother-child vit-D deficiency: an international perspective. Arch Dis Child. 92:737–740.
19. Van der Meer IM, Karamali NS, Boeke AJ, (2006): High prevalence of vit-D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr*. 84:350–359.
20. Bassir M, Laborie S, Lapillonne A, Claris O, Chappuis MC, Salle BL, (2001): Vit-D deficiency in Iranian mothers and their neonates: a pilot study. Acta Paediatr. 90 (5):577–579.
21. Markestad T, Elzouki A, Legnain M, Ulstein M, Aksnes L, (1984): Serum concentrations of vit-D metabolites in maternal and umbilical cord blood of Libyan and Norwegian women. Hum Nutr Clin Nutr. 38 (1):55–62.
22. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V, (2005): High prevalence of vit-D deficiency

among pregnant women and their newborns in northern India. *Am J Clin Nutr*. 81 (5):1060–1064.
23. Joyce M. Lee, MD, MPH Jessica R. Smith, MD Barbara L. Philipp, MD Tai C. Chen, PhD Jeffrey Mathieu, (2007): Vit-D deficiency in a healthy group of mothers and newborn infants. Clin Pediatr (Phila). 46:42–44.
24. Hillman LS, Haddad JG, (1976): Perinatal vit-D metabolism. III. Factors influencing late gestational human serum 25-hydroxyvit-D. Am J Obstet Gynecol. 125(2):196–200.
25. Shanna Nesby-O'Dell, Kelley S Scanlon, Mary E Cogswell, Cathleen Gillespie, Bruce W Hollis, Anne C Looker, Chris Allen, Cindy Doughertly, Elaine W Gunter, and Barbara A Bowman, (2002): Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: third National Health and Nutrition Examination Survey, 1988–1994. *Am J Clin Nutr*. 76(1):187–192.
26. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM, (2007): High prevalence of vit-D insufficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr. 137 (2):447–452.
27. Sabour H, Hossein-Nezhad A, Maghbooli Z, Madani F, Mir E, Larijani B, (2006): Relationship between pregnancy outcomes and maternal vit-D and calcium intake: a cross-sectional study. Gynecol Endocrinol. 22(10):585–589.
28. Scholl TO, Chen X, (2009): Vit-D. intake during pregnancy: association with maternal characteristics and infant birth weight. Early Hum Dev. 85(4):231–234.
29. Brooke OG, Wood C, (1980): Growth in British Asians: longitudinal data in the first year. J Hum Nutr. 34(5):355–9
30. Brooke OG, Brown IR, Cleeve HJ, Sood A, (1981): Observations on the vit-D state of pregnant Asian women in London. BJOG. 88(1):18–26.
31. Brooke OG, Butters F, Wood C. Intrauterine vit-D nutrition and postnatal growth in Asian infants. BMJ (Clin Res Ed). 1981; 283(6298):1024.
32. Mallet E, Gügi B, Brunelle P, Hénocq A, Basuyau JP, Lemeur H, (1986): Vit-D supplementation in pregnancy: a controlled trial of two methods. Obstet Gynecol. 68(3):300–304.
33. Mannion CA, Gray-Donald K, Koski KG, (2006): Association of low intake of milk and vit-D during pregnancy with decreased birth weight. CMAJ. 174(9):1273–7.
34. Sjurdur F Olsen, Thorhallur I Halldorsson, Walter C Willett, Vibeke K Knudsen, Matthew W Gillman, Tina B Mikkelsen, Jørn Olsen, and and The NUTRIX Consortium, (2007): Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study. *Am J Clin Nutr*. 86 (4):1104–1110.
35. Russell JG, Hill LF, (1974): True fetal rickets. Br J Radiol. 47:732–734.
36. Orbak Z, Karacan M, Doneray H, Karakel-leoglu C, (2007): Congenital rickets presenting with hypocalcaemic seizures. *West Indian Med J*. 56(4):364–367.
37. Specker BL, Ho ML, Oestreich A, (1992): Prospective study of vit-D supplementation and rickets in China. *J Pediatr*. 120(5):733–739.
38. Weiler H, Fitzpatrick-Wong S, Veitch R, (2005): Vit-D deficiency and whole-body and femur bone mass relative to weight in healthy newborns. CMAJ. 172(6):757–61.
39. MK Javaid, SR Crozier, NC Harvey, CR Gale, EM Dennison, BJ Boucher, NK Arden, KM Godfrey, C Cooper, FMedScia, (2004): The Princess Anne Hospital Study Group‡,. Maternal vit-D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. Lancet. 367 (9504):36–43.
40. Reif S, Katzir Y, Eisenberg Z, Weisman Y, (1998): Serum 25-hydroxyvit-D levels in congenital craniotabes. Acta Paediatr Scand. 77:167–168.
41. Congdon P, Horsman A, Kirby PA, Dibble J, Bashir T, (1983): Mineral content of the forearms of babies born to Asian and white mothers. BMJ (Clin Res Ed). 286:1233–1235.
42. Hillman LS, Haddad JG, (1974): Human perinatal vit-D metabolism: I, 25-hydroxyvit-D in maternal and cord blood. *J Pediatr*. 84(5):742–749.
43. Ala-Houhala M, (1985): 25-Hydroxyvit-D levels during breast-feeding with or without maternal or infantile supplementation of vit-D. *J Pediatr Gastroenterol Nutr*. 4(2):220–226.
44. Salle BL, Glorieux FH, Lapillone A. Vit-D status in breastfed term babies. Acta Paediatr.1998; 87(7):726–727.
45. Hollis BW, Roos BA, Draper HH, Lambert PW, (1981): Vit-D and its metabolites in human and bovine milk. *J Nutr.* 111(7):1240–1248.
46. Camadoo L, Tibbott R, Isaza F, (2007): Maternal vit-D deficiency associated with neonatalh ypocalcaemic convulsions. *Nutr J*. 6:23.
47. Oki J, Takedatsu M, Itoh J, Yano K, Cho K, Okuno A, (1991): Hypocalcemic focal seizures in a onemonth-old infant of a mother with a low circulating level of vit-D. Brain Dev. 13(2):132–134.
48. S Maiya, I Sullivan, J Allgrove, R Yates, M Malone, C Brain, N Archer, Q Mok, P Daubeney, R Tulloh, M Burch, (2008): Hypocalcaemia and vit-D deficiency: an important, but preventable, cause of life-threatening infant heart failure. Heart. 2008; 94 (4):581–584.
49. Kosecik M, Ertas T, (2007): Dilated cardiomyopathy due to nutritional vit-D deficiency rickets. Pediatr Int. 49(3):397–399.
50. Ward LM, Gaboury I, Ladhani M, Zlotkin S, (2007): Vit-D-deficiency rickets among children in Canada. CMAJ. 177(2):161–166.
51. Ladhani S, Srinivasan L, Buchanan C, All-grove J, (2004): Presentation of vit-D deficiency. Arch Dis Child. 89:781–784.

52. Dawodu A, Tsang R, (2007): Vit-D deficiency and rickets: possible role of maternal vit-Ddeficiency. Ann Trop Paediatr. 27:319.
53. Hollis BW, Wagner CL, (2004): Vit-D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr*. 80:1752S–1758S.
54. F Cockburn, N R Belton, R J Purvis, M M Giles, J K Brown, T L Turner, E M Wilkinson, J O Forfar, W J Barrie, G S McKay, S J Pocock, (1980): Maternal vit-D intake and mineral metabolism in mothers and their newborn infants. BMJ. 281:11–14
55. O G Brooke, I R Brown, C D Bone, N D Carter, H J Cleeve, J D Maxwell, V P Robinson, S M Winder, (1980): Vit-D supplements in pregnant Asian women: effects on calcium status and fetal growth. BMJ. 280:751–754.
56. Vieth R, Chan PC, MacFarlane GD, (2001): Efficacy and safety of vit-D3 intake exceeding the lowest observed adverse effect level. *Am J Clin Nutr*. 73(2):288–294
57. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ, (2003): Human serum 25 hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr*. 77(1):204–210
58. GannagéYared MH, Chemali R, Yaacoub N, Halaby G, (2000): Hypovitaminosis D in a sunny country: Relation to lifestyle and bone markers. *J Bone Miner Res*. 15(9):1856–1862
59. Friedman WF, Mills LF, (1969): The relationship between vit-D and the craniofacial and dental anomalies of the supravalvular aortic stenosis syndrome. Pediatrics. 43(1):12–18
60. Williams JC, BarrattBoyes BG, Lowe JB, (1961): Supravalvular aortic stenosis. Circulation. 24(6):1311–1318.
61. Hollis BW, Wagner CL, (2006): Vit-D deficiency during pregnancy: An ongoing epidemic. *Am J Clin Nutr*. 84(2):273
62. Haddad JG, Stamp TC, (1974): Circulating 25hydroxyvit-D in man. Am J Med. 57:57–62.
63. Hollis BW, (1996): Assessment of vit-D nutritional and hormonal status: What to measure and how to do it. Calcif Tissue Int. 58(4):4–55
64. Holick MF, Binkley NC, BischoffFerrari HA, Gordon CM, Hanley DA, Heaney RP, (2011): Evaluation, treatment, and prevention of vit-D deficiency: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 96(7):1911–30
65. McCarty CA, (2008): Sunlight exposure assessment: Can we accurately assess vit-D exposure from sunlight questionnaires? *Am J Clin Nutr*. 87(4):S1097–1101
66. Brooke OG, Brown IR, Cleeve HJ, Sood A, (1981): Observations on the vit-D state of pregnant Asian women in London. Br J Obstet Gynaecol. 88(1):18–26
67. Langlois K, Greene-Finestone L, Little J, Hidiroglou N, Whiting S, (2010): Vit-D status of Canadians as measured in the 2007 to 2009 Canadian Health Measures Survey. Health Reports, Catalogue no 82-003]
68. Whiting SJ, Langlois KA, Vatanparast H, Greene-Finestone LS, (2011): The vit-D status of Canadians relative to the 2011 Dietary Reference Intakes: An examination in children and adults with and without supplement use. *Am J Clin Nutr* 94(1): 128-35

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