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VITAMIN D DEFICIENCY IN CHILDREN AND ITS MANAGEMENT

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Abstract:
Vitamin D IS a prohormone that is essential for normal absorption of calcium from the gut, and deficiency of vitamin D is associated with rickets in growing children and osteomalacia in adults. Rickets is the lack of mineralization ability of growing bone and cartilage. At the turn of the 20th century, with industrialization, this disease became endemic until it was discovered that exposure to sunlight and cod liver oil could both prevent and treat rickets. Once vitamin D was identified and easy ways to supplement foods were developed, nutritional rickets almost disappeared from industrialized countries. However, there has been a reappearance of rickets from vitamin D deficiency in recent decades as a result of multiple factors. Dark-skinned infants who are exclusively breastfed and infants born to mothers who were vitamin D deficient through pregnancy seem to be at particularly high risk. However, rickets is also being reported in older children. The increasing numbers of reports of rickets in Western industrialized nations are related to the practice of exclusive breastfeeding without concomitant vitamin D supplementation in northern latitudes, decreased UV-B exposure (particularly in dark-skinned people), and the excessive use of sunscreen. Recommendations for fortification of commonly used foods with vitamin D are necessary in keeping with various cultural norms of food intake and geography. Current recommendations of sun exposure and vitamin D supplementation are limited because of a paucity of studies in children A low threshold for assessing vitamin D sufficiency in infants, children, and adolescents is recommended given the growing knowledge about effects of vitamin D not only on bone mineral metabolism but also on the immune system and in preventing various kinds of cancer.

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INTRODUCTION:

Vitamin D IS a prohormone that is essential for normal absorption of calcium from the gut, and deficiency of vitamin D is associated with rickets in growing children and osteomalacia in adults. Rickets is the lack of mineralization ability of growing bone and cartilage. At the turn of the 20th century, with industrialization, this disease became endemic until it was discovered that exposure to sunlight and cod liver oil could both prevent and treat rickets.[1, 2] Once vitamin D was identified and easy ways to supplement foods were developed, nutritional rickets almost disappeared from industrialized countries.[1–3] However, there has been a reappearance of rickets from vitamin D deficiency in recent decades as a result of multiple factors. Dark-skinned infants who are exclusively breastfed and infants born to mothers who were vitamin D deficient through pregnancy seem to be at particularly high risk. However, rickets is also being reported in older children.

American Academy of Pediatrics (AAP) recommended a vitamin D supplement for [1] breastfed infants who do not consume at least 500 mL of a vitamin D–fortified formula/beverage14 and [2] no breastfed infants who do not consume 500 mL of vitamin D–fortified beverages. The supplementation should start during the first 2 months of life and continue throughout childhood and adolescence. The rationale for this timing is that vitamin D stores in the newborn, which are obtained through trans placental passage from the vitamin D–replete mother, should last for at least 8 weeks after delivery given that the half-life of serum 25(OH)-vitamin D [25(OH)-D] is 2 to 3 weeks. In a term infant born to a vitamin D–replete mother, the supply of vitamin D may last even longer (8 –12 weeks) given the storage of vitamin D in fat. Daily intake of at least 500 mL of vitamin D–fortified formula would ensure the required minimum daily intake of vitamin D of 200 IU/day. However, despite current guidelines for vitamin D supplementation, rickets continues to be reported.

Sources and Metabolism of Vitamin D: Humans get vitamin D from exposure to sunlight, from their diet, and from dietary supplements (Table 1).[4-8] A diet high in oily fish prevents vitamin D deficiency.[3] Solar ultraviolet B radiation (wavelength, 290 to 315 nm) penetrates the skin and converts 7-dehydrocholesterol to pre vitamin D3, which is rapidly converted to vitamin D3.[4] Because any excess pre vitamin D3 or vitamin D3 is destroyed by sunlight, excessive exposure to sunlight does not cause vitamin D3 intoxication.

Table 1. Dietary, Supplemental, and Pharmaceutical Sources of Vitamins D_2 and D_3

Source	Vitamin D Content
Natural sources	
Salmon	
Fresh, wild (3.5 oz)	About 600–1000 IU of vitamin D_3
Fresh, farmed (3.5 oz)	About 100–250 IU of vitamin D_3 or D_2
Canned (3.5 oz)	About 300–600 IU of vitamin D_3
Sardines, canned (3.5 oz)	About 300 IU of vitamin D_3
Mackerel, canned (3.5 oz)	About 250 IU of vitamin D_3
Tuna, canned (3.6 oz)	About 230 IU of vitamin D_3
Cod liver oil (1 tsp)	About 400–1000 IU of vitamin D_3
Shiitake mushrooms	
Fresh (3.5 oz)	About 100 IU of vitamin D_2
Sun-dried (3.5 oz)	About 1600 IU of vitamin D_2
Egg yolk	About 20 IU of vitamin D_3 or D_2
Exposure to sunlight, ultraviolet B radiation (0.5 minimal erythemal dose)†	About 3000 IU of vitamin D_3
Fortified foods:	
Fortified milk	About 100 IU/8 oz, usually vitamin D_3
Fortified orange juice	About 100 IU/8 oz vitamin D_3
Infant formulas	About 100 IU/8 oz vitamin D_3
Fortified yogurts	About 100 IU/8 oz, usually vitamin D_3
Fortified butter	About 50 IU/3.5 oz, usually vitamin D_3
Fortified margarine	About 430 IU/3.5 oz, usually vitamin D_3
Fortified cheeses	About 100 IU/3 oz, usually vitamin D_3
Fortified breakfast cereals	About 100 IU/serving, usually vitamin D_3
Supplements:	
Prescription	
Vitamin D_2 (ergocalciferol)	50,000 IU/capsule
Drisdol (vitamin D_2) liquid	8000 IU/ml supplements
Over the counter	
Multivitamin	400 IU vitamin D, D_2, or D_3‡
Vitamin D_3	400, 800, 1000, and 2000 IU

Definition and Prevalence of Vitamin D Deficiency: vitamin D deficiency is defined by most experts as a 25-hydroxyvitamin D level of less than 20 ng per milliliter (50 nmol per liter).[8-10] 25-Hydroxyvitamin D levels are inversely associated with parathyroid hormone levels until the former reach 30 to 40 mg per milliliter (75 to 100 nmol per liter), at which point parathyroid hormone levels begin to level off (at their nadir).[10-12] Furthermore, intestinal calcium transport increased by 45 to 65% in women when 25-hydroxyvitamin D levels were increased from an average of 20 to 32 nag per milliliter (50 to 80 nmol per liter).[13] Given such data, a level of 25-hydroxyvitamin D of 21 to 29 ng per milliliter (52 to 72 nmol per liter) can be considered to indicate a relative insufficiency of vitamin D, to indicate sufficient vitamin D the level of 25-hydroxyvitamin D should be 30 ng per milliliter or greater .

according to this definitions, it has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency.[7-12] Children are also potentially at high risk for vitamin D deficiency In Europe, where very few foods are fortified with vitamin D, children and adults would appear to be at especially high risk.[1,7,11] In studies in Saudi Arabia, the United Arab Emirates, Australia, Turkey, India,

and Lebanon, 30 to 50% of children had 25-hydroxyvitamin D levels under 20 ng per milliliter. There is no current definitive prevalence estimates available for vitamin D– deficiency rickets because recent publications have been mainly case reports or case series obtained from hospital admissions records. The 2 largest series reported 126 cases over a period of 10 years in Australia and 104 cases over 2 years in Canada. Reported and published cases of nutritional rickets in the United States increased from 65 between 1975 and 1985 to 166 between 1986 and 2003.[14]

EFFECT OF VITAMIN D DEFICIENCY:

Calcium and Phosphorus Metabolism and Bone: In a vitamin D–sufficient state [25(OH)-D levels of 50 nmol/L (20 ng/mL)], net intestinal calcium absorption is up to 30%, although calcium absorption can reach 60% to 80% during periods of active growth. In a vitamin D– deficient state, intestinal calcium absorption is only 10% to 15% and there is a decrease in the total maximal reabsorption of phosphate. In conditions of vitamin D deficiency, low ionized calcium levels stimulate parathyroid hormone (PTH) secretion, which [1] increases calcium reabsorption in renal tubules and [2]increases 1--hydroxylase activity, which causes increased 1,25-dihydroxy vitamin D [1,25(OH)2-D] synthesis.. Decreased levels of phosphorus (and also calcium) and decreased calcium*phosphorus product result in decreased bone mineralization. Osteomalacia in immature bones is referred to as rickets. The term rickets also describes the abnormal organization of the cartilaginous growth plate and the accompanying impairment of cartilage mineralization. The clinical presentation of vitamin D– deficiency rickets includes symptoms and signs of bone deformity and/or pain and may be associated with hypocalcaemia and associated clinical features.

Extra skeletal Effects of Vitamin D: The vitamin D receptor is present in the small intestine, colon, osteoblasts, activated T and B lymphocytes, islet cells, and most organs in the body such as the brain, heart, skin, gonads, prostate, breast, and mononuclear cells. Epidemiologic studies over the last 2 decades have suggested important effects of vitamin D on the immune system and in preventing certain cancers.

Skin: Keratinocytes express the vitamin D receptor, and when these cells are exposed to vitamin D, their growth is inhibited and they are stimulated to differentiate.[16]This has led to the use of topical vitamin D analogs to treat psoriasis.

Immune Effects: Vitamin D modulates B- and T-lymphocyte function. Epidemiologic evidence exists of vitamin D deficiency being associated with autoimmune diseases such as type 1 diabetes and multiple sclerosis.

Cancer: Vitamin D concentrations of >75 nmol/L (30 ng/mL) keep cell growth in check and prevent cells from becoming autonomous and developing into unregulated cancer,40–42 and vitamin D deficiency has been related to breast, prostate, and colon cancer.

Psychiatric Conditions: Adequate vitamin D levels in pregnancy are associated with decreased risk of schizophrenia; conversely, low levels of sun exposure are associated with seasonal affective disorder and mood disturbances.

CAUSES OF VITAMIN D DEFICIENCY:

Decreased vitamin D synthesis: The reemergence of vitamin D– deficiency rickets in northern Europe and North America is primarily associated with dark-skinned children on strict vegetarian diets, cult or fad diets, dark-skinned infants exclusively breastfed beyond 3 to 6 months of age, premature infants, and infants born to vitamin D– deficient mothers. Excessive use of sunscreen may also contribute to decreased cutaneous vitamin D synthesis. Worldwide, rickets persists in infants who are breastfed for a prolonged period of time or kept out of sunlight for prolonged periods, as in India, China, and the Middle East. Fetuses of pregnant women who have severe vitamin D deficiency from wearing the traditional veil can develop rickets in utero and present with hypocalcaemia and tetany at birth (congenital rickets). All this has prompted an in-depth look at factors that affect vitamin D synthesis such as skin pigmentation, exposure to sunlight, geography, and infant-feeding patterns.

Skin pigmentation: Skin pigmentation determines the duration of sun exposure necessary to achieve a certain concentration of vitamin D.

Physical agents blocking UVR exposure Sunscreen, clothing, shades: The amount of skin that is exposed to the sun is important. Exposure of the whole body versus only the face, hands, and arms is associated with marked differences in vitamin D synthesis.

Sunscreen absorbs UV-B and some UV-A light and prevents it from reaching and entering the skin. A sunscreen with a sun protection factor (SPF) of 8 can decrease vitamin D3 synthetic capacity by 95%, and SPF 15 can decrease it by 98% (reviewed in ref 56).

In adults who apply sunscreen properly (2 mg/cm2), the amount of vitamin D3 produced is decreased 95%.

Increased urbanization and increased time spent indoors at work may lead to decreased time spent outdoors and, therefore, decreased vitamin D synthesis, even in light-skinned populations. Shade reduces the amount of solar radiation by 60%, and windowpane glass blocks UVR.

Geography Latitude, season Air pollution, cloud cover, altitude: This is attributed to a decrease in incident UVR with increasing latitude, because the oblique angle at which sunlight reaches the atmosphere leads to a greater path being traversed through the atmosphere and ozone layer, with greater resultant scatter and absorption of UVR. Children of all ages are more susceptible to low vitamin D levels during the winter compared with the summer months

Cloud cover, increasing water vapor, and industrial pollution can reduce the amount of UV-B that reaches the earth's surface, and industrial pollution has been associated with a greater prevalence of vitamin D– deficiency rickets.

Decreased nutritional intake of vitamin D: Lower intake of vitamin D–fortified foods, particularly milk and fortified cereals, may result in vitamin D–deficiency rickets in certain populations, particularly in dark-skinned people who live in higher latitudes and in the winter months.

Decreased maternal vitamin D stores and exclusive breastfeeding: Low vitamin D levels during pregnancy have been associated with intrauterine growth retardation, premature labor, and hypertension, all of which increase the risk of low birth weight. Prematurely born infants have a shorter duration in which to accumulate vitamin D stores from trans placental transfer from the mother and also have a higher requirement for vitamin D than term infants.

9 exclusive breastfeeding without sun exposure would provide only 11 to 38 IU/day of vitamin D. It is important to note that the vitamin D content of breast milk varies on the basis of skin color, with lower vitamin D concentrations in breast milk of black compared with white women. Therefore, breastfed infants need to obtain additional vitamin D through either sun exposure or supplementation.

Malabsorption: Vitamin D absorption is chylomicron dependent; consequently, children with diseases that interfere with fat absorption are at risk of developing vitamin D deficiency.

Treatment of Vitamin D–Deficiency Rickets: Vitamin D and Calcium Supplementation and Monitoring of Therapy

Vitamin D (ergocalciferol):
Double-dose vitamin D: 20 g (800 IU)/d 3–4 mo ; or Pharmacological doses of vitamin D: 25–125 g (1000–10 000 IU) per day Depending on the age of the child for 8-12 weeks, then maintain at 10–25 g (400–1000 IU) per day; or Stoss therapy: 2.5–15.0 mg or 100 000–600 000 IU of vitamin D orally (over 1–5 d), then maintain at 10–25 g (400–1000 IU) of vitamin D per day, or 1.25 mg or 50 000 IU of vitamin D_2 weekly for 8 wk orally (teenagers and adults) Calcium 30–75 mg/kg per d of elemental calcium in 3 divided doses (start at a higher dose, and wean down to the lower end of the range over 2–4 wk) Monitoring of therapy At 1 mo: calcium, phosphorus, ALP At 3 mo: calcium, phosphorus, magnesium, ALP, PTH, 25(OH)-D, urine calcium/ creatinine ratio (frequency depends on severity of rickets and hypocalcemia); recheck radiologic findings in 3 mo At 1 y and annually: 25(OH)-D

CONCLUSION:

The increasing numbers of reports of rickets in Western industrialized nations are related to the practice of exclusive breastfeeding without concomitant vitamin D supplementation in northern latitudes, decreased UV-B exposure (particularly in dark-skinned people), and the excessive use of sunscreen. Recommendations for fortification of commonly used foods with vitamin D are necessary in keeping with various cultural norms of food intake and geography. Current recommendations of sun exposure and vitamin D supplementation are limited because of a paucity of studies in children A low threshold for assessing vitamin D sufficiency in infants, children, and adolescents is recommended given the growing knowledge about effects of vitamin D not only on bone mineral metabolism but also on the immune system and in preventing various kinds of cancer.

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