REVIEW ARTICLE

# The Development of Rickets in Children and Nursing Contributions to Treatment

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## ABSTRACT

Rickets is one of the most prevalent non-communicable diseases in children in the developing world. It is often found in cultures in which children follow strict vegetarian diets and are not exposed to vitamin D-enhanced foods. While a rare occurrence, X-linked hypophosphatemic rickets may be the most frequent type of the disease seen outside the Third World today. However, there is not much credible information on the extent of the development of rickets. Therefore, pediatric nurses must be able to recognize children at risk and provide best practice care for the prevention and treatment of rickets. When caring for children in hospitals, communities or classrooms, nurses play a vital role in identifying children at risk for hypovitaminosis D and advising families to, if possible, follow safe diets and take supplements in order to avoid health complications associated with low levels of vitamin D.

This study examines the prevalence and variables contributing to rickets, including hypovitaminosis vitamin D, the consequent orthopedic problems and the role of nurses in preventing and managing the pathogenesis of rickets and ultimately avoiding extreme deficits that result in bone deformities and the need for corrective surgery. (*Altern Ther Health Med.* 2022;28(1):86-91).


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## INTRODUCTION

In the late 17th century, the number of cases of rickets in crowded polluted cities such as London and New York increased because of overcrowding, poverty and coal- and wood-burning fires (which created smoke that blocked exposure to sunlight). Now rickets, widespread worldwide,[1] has a significant effect on children and adolescent fitness, growth and development. More than 25 percent of children in the UK have rickets.[2]

Rickets is currently one of the most prevalent diseases and is reported in the developing world to be a non-communicable disease in children, even though there is not much credible information on the extent of its development.[3] Rickets is an abnormality of the cartilage plates that affects mostly longer bones, causing poor bone development, deficient mineralization and osseous deformities such as bow legs and knock knees. A deficiency of calcium ions ($Ca^{2+}$) or phosphate ($PO4^{3-}$) is usually a secondary finding as it is essential for normal bone regeneration and mineralization.[4]

Wheeler, et al drew a parallel between past eras and the present, and found that several factors have been replicated in our current society that led to an increase in rickets in the past: decreased exposure to sunlight due to increased time spent indoors, seeking protection from the sun because of legitimate concerns about the risk of skin cancer.[5]

Vitamin D is a fat-soluble, calcium- and bone-health vitamin that plays an essential part in good nutrition. Few foods contain vitamin D naturally, but in the United States there are many vitamin D-fortified foods (such as milk, baby formula and cereals). The skin absorbs much of the vitamin D used by the human body from exposure to sunlight;[6] and it is then processed by the liver and kidneys to support the bones.

Vitamin D deficiency results when an individual does nor absorb sufficient vitamin D via the skin or food or if

hepatitis and/or kidney failure has caused difficulties handling a vitamin D deficiency. Everyone needs vitamin D to a different degree, so it is impossible to establish what level exactly constitutes a deficiency. 1,25(OH) 2D binds a ligand-receptor complex to the vitamin D-receptor (D-R) and heterodimerizes to the retinoic acid receptor, which is targeted to particular genome response elements. Ligand-binding vitamin D-R mutations resulting in rickets can in some instances be overcome by using high-dose calcitriol; however, DNA-binding domain mutations normally do not react to this treatment.[7] Numerous studies have shown that vitamin D deficiency is associated with various problems, including brain disorders, fractures, renal disease, liver disease, diabetes, cardiovascular complications, cancer and infection.[8-10]

As expounded in a paper by Hochberg, et al,[11] we as healthcare professionals can hopefully motivate public health campaigns to counteract modern lifestyle changes by increasing the availability of vitamin D-enriched food and make sure that high-risk groups receive the necessary supplementation to meet the demand for vitamin D, especially when demand is higher (such as in breast-fed infants). Furthermore, deficient vitamin D can cause both pediatric (rickets, osteomalacia) and adult (osteomalacia, osteoporosis) bone problems.[11-13] Therefore, we examined and analyzed the various types of rickets and nursing contributions for managing them.

## LITERATURE REVIEW

This article is based on a comprehensive search of electronic medical databases, including Google Scholar, Scientific Information Database, PubMed, Scopus, Web of Science, and Elsevier up to the end of May 2021. The search words used included: rickets, biochemical symptoms of rickets, complications of rickets, consequences of rickets. vitamin D and the nursing approach to rickets; those that appeared on reference lists of retrieved publications and personal references were also included.

After an introduction and explanation of the epidemiology of rickets, we summarize major dietary vitamin D recommendations and include an overview of global vitamin D status and intake, with particular emphasis on the discrepancy between the existing estimates of vitamin D requirements and actual vitamin D intake in populations with rickets. Following a segment on general nursing approaches to preventing and treating rickets, we discuss vitamin D safety concerns and the global status of vitamin D-fortified food. Finally, we provide recommendations on how to implement vitamin D nutrient fortification.

### Mechanism of Rickets Development

Phosphorus is a vital structural element for bone mineralization and is abundant in all body tissue. Bone is maintained in stable working condition by both $Ca^{2+}$ and PO4.[3-14] A deficiency normally results in the enhanced kidney excretion seen in phosphophenic/hypophosphatemic rickets.[4] Urinary phosphate deficiency can be either part of a systemic renal tubule defect in physiology, as seen in Fanconi syndrome or secondary to an increase in FGF-23 synthesis/ decreased catabolism or gene mutation encoding in the proximal renal tubule for phosphate-dependent transmitters.[15] Fanconi syndrome, which results in glycosuria, hypokalemia, proximal acidosis, hyperuricosuria and generalized aminoaciduria, may also lead to severe loss of urinary phosphate, resulting in hypophosphatemic rickets. Fanconian syndrome conditions such as cystinosis, Lowe syndrome, Fanconi-Bickel syndrome or medication can be primary or secondary. Control requires particular treatment for the underlying condition once diagnosed, along with acidosis and phosphate supplementation.[16]

### Calcipenic Rickets

As the name implies, calcipenic rickets occurs primarily due to a calcium deficiency, most often secondary to poor levels and/or malfunctions of the body's vitamin D supply. Calcipenic rickets may occur due to a serious vitamin D deficiency of (nutritional), inability to form or resistance to 1,25-dihydroxy vitamin D (as in chronic kidney disease [CKD]), or because there is 25-hydroxy-vitamin D (as in drug poisoning/liver failure; for example, accumulation of antiepileptic phenytoin treatment, as in CKD). The effect is reduced calcium absorption in the intestines, which increases the secretion of parathyroid hormones (PTH). The purpose of PTH is to maintain plasma $Ca^{2+}$ levels by (1) triggering resorption by osteoblast RANKL, (2) reducing $Ca^{2+}$ ion depletion in the renal cord, and (3) increasing the loss of renal phosphate due to internalization and then degrading co-transporter proteins NaPi-2a and NaPi-2c, which reduces the reabsorption of tubular phosphate.[15,17,18] The common mechanism for the development of calcipenic and phosphopenic rickets is a reduction in phosphate concentration.[19]

### Phosphopenic Rickets

Synthesis of 1,25-dihyDroxy-vitamin D is stimulated by hypocalcemia, hypophosphatemia and PTH. The osteocyte hormone FGF-23 is essential in bone metabolism. It helps prevent 1,25 dihydroxy vitamin D synthesis and binds FGF receptors via klotho, a membrane-borne protein. It increases the preservation of the retention of renal phosphate by decreasing the apical distribution of the proximal renal tubular cells and the number of main phosphate transporters, NaPi-2a, and NaPi-2c (sodium-dependent phosphate transport proteins).[20]

In addition, the absence of either klotho or FGF23 in humans leads to ectopic calcification/ hyperphosphatemia, and secretion of FGF-23 was induced in some studies by an elevated intake of phosphate, 1,25(OH)2D and parathyroid hormone.[20] Renal CYP27B1, in turn, is downregulated by FGF-23 to produce 1,25(OH)2D and 24-hydroxylase to destroy 1,25(OH)2D.20 While phosphate is needed to heal the growth plate in children with hypophosphatemic rickets,

1,25(OH)2D is necessary in osteomalacia and the bowing deformity of long bones.[21] Absence of phosphate results in the loss of mineralization of the fibrous component, the osteoid, at the periosteal bone where new bones replace existing bone in remodeling sites. Dentine matrix protein 1 (SIBLING member) mutations result in recessive autosomal type 1 hypophosphatemic rickets.[22]

The correlation in X-linked hypophosphataemic rickets between clinical and biochemical phenotypes with autosomal hypophosphataemic type 1 rickets suggests that PHEX and dentine matrix protein 1 operate in a similar way to control FGF-23 expression.[22-24] Dentinic matrix protein 1 and FGF-23 are mostly expressed in osteocytes deep in the bone and PHEX on bone surfaces in osteoblasts. The osteoid mineralization mechanism has an impact on the production of osteoblasts, which become osteocytes.[25] Therefore, spatially and temporally the mechanisms underlying these relationships are diverse and affect other features of bone structure. Of note, bone radiographs from patients with hereditary pituitary gastrointestinal rickets frequently manifest the usual vitamin D pathway disease manifestations of sclerosis rather than osteopenia.

### Renal Rickets

The word "rickets" is typically limited to patients with CKD. CKD leads to enzyme 1 alpha-hydroxylase deficiency, which reduces 1,25 hydroxyvitamin D (calcitriol) intake.[26] A history of renal dysfunction, excluding other bone conditions, is a clear indicator. Laboratory results typically indicate low levels of calcitriol, but low 25-hydroxyvitamin D may also be common. The most conventional result is the high phosphate level in CKD secondary to poor renal function.[3] It is instead recommended that one-alfacalcidol or calcitriol, dietary phosphate binders, oral administration and the standard 25-hydroxyvitamin D dose be maintained.[27]

## NURSING C ONTRIBUTIONS TO RICKETS MANAGEMENT

### Non-Pharmacologic

The growing number of children with rickets shows that there is much that needs to be done with regard to prevention and this requires further analysis and discussion. Sun exposure advice remains the same. Nurses understand the need for obtaining a detailed history that includes all the facts concerning the child's diet and lifestyle. A child with vitamin D deficiency has decreased absorption of calcium and phosphorus in the intestines; both are needed for healthy bone growth and development. The probability of fracture increases with a decrease in bone density. Nurses will advise parents on how to improve natural vitamin D synthesis and nutritional intake by changing the child's lifestyle and diet.

Excessive consumption of carbonated beverages has been shown to contribute to low bone density, fracture potential and poor fracture healing.[28] The acidity that impairs calcium absorption is increased by the phosphoric acid found in carbonated beverages.[29] Children today often tend to drink cola and related drinks rather than milk.

The prevalent low vitamin D levels in children are also concerning because they may continue into adult life. Parental education in the early years is important as a prevention mechanism for teenage and adult musculoskeletal disorders. Nursing staff is in a position to explain the evolving recommendations to families. Nurses will help parents by explaining the condition of low level of vitamin D and contributing factors and reminding them that the prognosis is good if the metabolic bone condition is treated with immediate pharmacologic intervention. Parents must, however, understant that it can take 12 to 18 months to remodel osteo deformities and that, finally, surgical intervention may be necessary.

Parents of kids undergoing corrective osteopathic surgery need guidance and affirmation from nurses who can help them during this period of stress and anxiety. Post-surgery management and possible problems with surgical correction should be discussed with parents. For instance, a child who undergoes frame correction is at risk for infection at the pin site,[30] which requires weekly cleansing. In addition, the child's nurse must provide regular intensive physiotherapy to maximize joint strength and range of motion above and below the fixator.

There are some key points that a nurse will discuss with a patient with rickets and their family:

- Educate patients and their parents on a calcium- and phosphate-rich diet
- Explain protective actions in kitchens, hallways, on floors (to make them non-slip) and bathrooms, including showers, tubs and toilet seats
- Teach them how to reduce patient stress and discomfort: handle the patient carefully, adjust the patient's position as needed for comfort, use pillows for support
- Encourage the patient to use helpers' handles, cane or crutches when in an ambulance
- Instruct the patient to be aware of and report symptoms of vitamin D toxicity, including anorexia, nausea/vomiting, excessive urination and muscle fatigue, as these are concerning
- Tell the patient to look around them carefully when walking and recommend workouts that help avoid muscle atrophy and joint contractures
- Assess the level of immobility caused by injuries or treatment and note the patient's sense of immobility, which helps a patient who is out of balance with their actual physical disabilities, self-awareness and self-perception and recommend treatment to facilitate improvement in well-being
- Provide physical therapy assistance when needed on how to use ambulatory devices that protect the patient's muscle tone and help avoid immobility complications
- Inform the patient and family members about the high risk for fractures, even with minor bone trauma

**Table 1**. Orthopedic Conditions and Dysfunction Due to Low Levels of Vitamin D

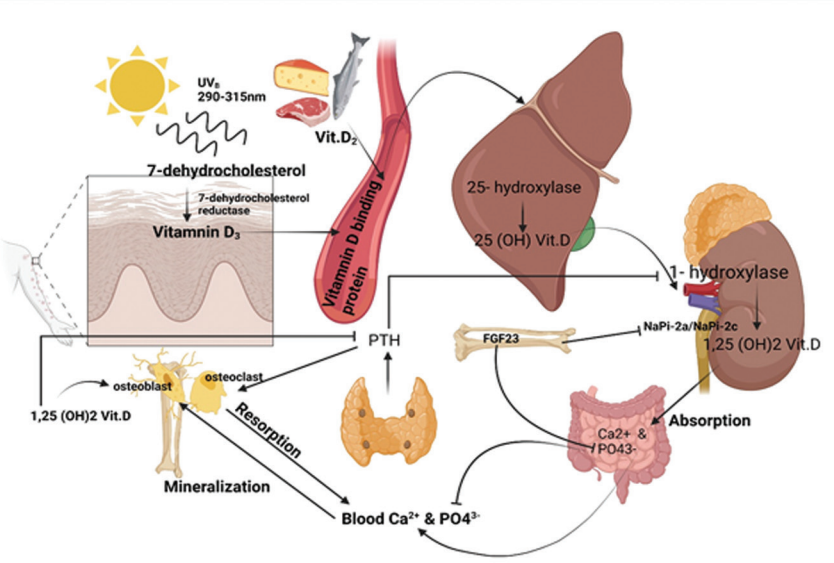
| Orthopedic Complications of Vitamin D Deficiency | Percentage of Patients |
|---|---|
| Leg pain, eg, growing pains | 60% |
| Genu varum (bow legs) and Genu valgum (knock knees) | 16% |
| Knee pain, eg, anterior knee pain | 32% |
| Hip pain, eg, slipped capital femoral epiphysis | 12% |
| Other | 36% |

**Note**: Some patients have more than 1 symptom/dysfunction.

**Table 2**. Range of Vitamin D Insufficiency and Severity

| Vitamin D Status | ng/ml |
|---|---|
| Deficiency | <30 |
| Insufficiency | 30 to 50 |
| Adequate | >50 |
| Toxicity | >250 |

**Figure 1.** Role of vitamin D in absorption and mineralization of calcium and phosphate during rickets treatment in children




**Pharmacologic**

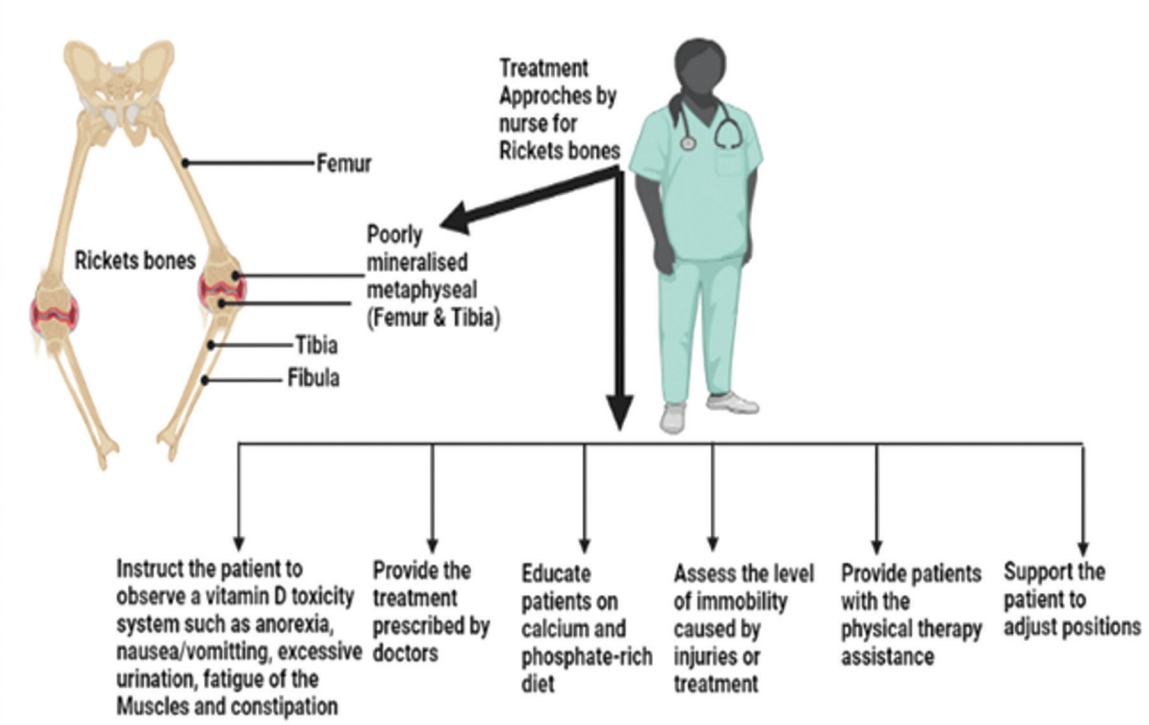
A revival in pediatric vitamin D deficiency rickets worldwide was reported in the 1990s. These cases occurred in various demographic populations but were more common in individuals with less sunlight exposure (people living in high latitudes, especially during winter months), with dark skin pigmentation, full female body covering, and were associated with breastfeeding. This type of illness was seen in several different populations. Affected newborns generally present with alopecia with hypocalcemia and extreme rickets. These babies require high-dose intravenous calcium infusions every day up to the age of 2 years and then high levels of oral calcium are required. Intact vitamin D receptors but irregular proteins blocking or reducing transcription are rare.[31] The primary effect of vitamin D is to improve intestinal $Ca^{2+}$ ion absorption by increased the channel of calcium TRPV6, calbindin D and PMCA1b intracellular transport systems to transfer calcium from the enterocyte to the serum gradients.[32-34]

Need and colleagues[35] examined data from 319 adults and concluded that $Ca^{2+}$ ion uptake only declines by 25 OHD with robust bioavailability and bone profile results; however, similar research in pediatric populations has not been performed and the calcium requirement for adults is lower than that for children, which extrapolates to growing infants (Table 1; Figure 1).

Despite the modest yet important decrease in prevalence, the United States National Academy of Medicine reduced its recommendation for vitamin D supplementation from 10 to 5 g/day in 1997, citing research showing that this dosage offered sufficient vitamin D to reach a 25-hydroxyvitamin D (25[OH]D) status of 27.5 nmol/L (11 ng/mL), which was assumed to prevent rickets in "most" populations.[36] Infants receiving a 8.5 to 10 µg (340 to 400 units) daily injection of vitamin D were an average of 2 cm longer than infants who received a intake of 60 to 135 units yearly. Children on the lower dose who were exposed to sunlight grew more than children without sun exposure on the higher dose.[37,38] Moreover, research in children receiving these higher doses did not demonstrate slower growth (Table 2).[39]

Replacement of phosphate with either calcitriol or 1α-calcidiol is needed for the types of hypophosphataemic rickets associated with elevated serum FGF-23. Regular examination of and treatment for development, osseous deformities, and the complications associated with these disorders such as root abscess, craniosynostosis, nephrocalcerosis and parathyroid gland hyperplasia a specialist pediatric metabolic bone clinic is required to monitor patients. Balancing phosphate intake with 1α-calcidiol, particularly in periods of fast development, can be difficult.[40,41] Bone bending deformation, leading to genu varum intercondylar of more than 12 cm, is likely to require surgery; such a procedure can only be performed once the bone condition is under control. In 2010, strong guidance was released on clinical management of this condition.[42] In the X-linked hypophosphataemic ricket model (HYP mouse), anti-FGF 23 antibody therapy was tested and both hypophosphataemia and conversion to 1,25(OH)2D from 25OHD were corrected and longitudinal growth and improved osteomalacia were seen (Figure 2).[43]

**Figure 2.** Role of nursing officer in rickets management.




## CONCLUSION

Rickets is a disorder that can be prevented, and prevention can begin in pregnancy. Suitable sunlight exposure is the easiest preventive measure; however, vitamin D supplementation should be developed in communities where this is not viable or not plausible. There is no global consensus on the required supplementation level of vitamin D. The UK Health Ministry guidance is fragmentary and confusing. Vitamin D 400 IU a day is sufficient to preserve vitamin D status and is highly unlikely to have detrimental skeletal effects. It is concluded by us that a daily supplement would make it possible to cover the growing skeleton irrespective of skin color, geographic latitude, sensitivity to sunshine, contamination and social or cultural strain. Thus, the education of parents is the most critical element in ensuring children have sound bones, and it is a critical issue for healthcare professionals, including nurses.

### CONFLICT OF INTEREST

There are no conflicts of interest associated with this article.

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