HHS Public Access

Author manuscript

Curr Opin Endocrinol Diabetes Obes. Author manuscript; available in PMC 2016 February 01.

Published in final edited form as:

Curr Opin Endocrinol Diabetes Obes. 2015 February ; 22(1): 35–40. doi:10.1097/MED.0000000000000124.

An update on childhood bone health: mineral accrual, assessment and treatment

Aviva B. Sopher, MD, MS, **Ilene Fennoy, MD, MPH**, and **Sharon E. Oberfield, MD**

Division of Endocrinology, Diabetes and Metabolism, Department of Pediatrics, Columbia University Medical Center, New York, NY

Abstract

Purpose of Review—To update the reader's knowledge about the factors that influence bone mineral accrual and to review the advances in the assessment of bone health and treatment of bone disorders.

Recent Findings—Maternal vitamin D status influences neonatal calcium levels, bone mineral density and bone size. In turn, bone mineral density z-score tends to track in childhood. These factors highlight the importance of bone health as early as fetal life. Dual-energy x-ray absorptiometry is the mainstay of clinical bone health assessment in this population due to the availability of appropriate reference data. Recently, more information has become available about assessment and treatment of bone disease in chronically ill pediatric patients.

Summary—Bone health must become a health focus starting prenatally in order to maximize peak bone mass and to prevent osteoporosis-related bone disease in adulthood. Vitamin D, calcium and weight-bearing activity are factors of key importance throughout childhood in achieving optimal bone health as bone mineral density z-score tracks through childhood and into adulthood. Recent updates of the International Society for Clinical Densitometry focus on the appropriate use of dual-energy x-ray absorptiometry in children of all ages, including children with chronic disease, and on the treatment of pediatric bone disease.

Keywords

Vitamin D; calcium; bone mineral accrual; dual-energy x-ray absorptiometry; bisphosphonates

Introduction

Bone is a metabolically active connective tissue that adapts its activity to specific developmental stages throughout the lifespan. It is a repository of calcium, magnesium and phosphorous in the form of hydroxyapatite within a collagen matrix and is intricately involved in the homeostasis of these minerals and in maintaining skeletal structure. Factors that affect bone mineral accrual during growth include genetics, sex, race, diet, mobility, weight-bearing activity and hormonal factors. Supporting the roles of genetic and

Author of correspondence: Aviva B. Sopher, 622 West 168 Street, PH 522 5E, New York, NY 10032, Phone: 212-305-6559, Fax: 212-305-4778, ahs32@cumc.columbia.edu.

Conflict of Interest: There are no conflicts of interest

environmental factors in bone development, daughters of women who experienced fracture of the distal end of the radius had lower areal bone mineral density (aBMD) of the lumbar spine and femoral neck compared to controls [1**]. Sexual differences in bone mass are illustrated in a study that shows that boys have higher forearm aBMD than females as early as four years of age [2**]. These intrinsic and environmental bone-related factors set the stage for lifelong bone health.

An overview of the factors that influence bone mineral accrual from fetal life through adolescence

Bone mineral accrual in childhood and adolescence influences long term bone health. Forty percent of bone mass is attained during adolescence, 90% of bone mass is accumulated by 18 years and peak bone mass is reached by one's late twenties [3]. Individuals with higher peak bone mass have a greater protective advantage for fractures. Bone mass attained throughout childhood is potentially the most important determinant of life-long skeletal health and risk of osteoporosis [4].

Bone development relies on the processes of modeling and remodeling. Modeling occurs only in growing children and is characterized by regulated uncoupling of osteoblast-driven bone formation and osteoclast-driven bone resorption, resulting in bone mass increase and bone shape modification [5*]. Remodeling orchestrates bone mineral turnover, repair of microdamage, and fracture healing in both children and adults. In contrast, remodeling is a tightly coupled process of bone resorption and formation. An imbalance between resorption and formation may result in abnormal bone mineral accretion. In early infancy, peripheral bones grow by increasing the outer diameter rather than the mineral content [6]. Newly formed primary bone is relatively dense and during rapid periosteal bone formation cortical bone mineral density (BMD) is high; however, during the postnatal period there is a redistribution of bone tissue from the endocortical to the periosteal surface leading to an increase in bone diameter and a decline in BMD [7].

Both maternal-fetal mineral metabolism and adaptations immediately following birth maintain positive calcium balance in newborns. Maternal 25-hydroxyvitamin D (25(OH)D) status during pregnancy may program skeletal development and body composition in offspring by influencing interactions between osteoblasts and adipocytes [8]. In fact, low maternal 25(OH)D is associated with shorter gestation and reduced growth of newborn long bones [8]. Infants born to vitamin D supplemented mothers had a lower incidence of hypocalcemia than placebo without an increased frequency of hypercalcemia, supporting the hypothesis that maternal 25(OH)D influences transplacental calcium transfer [9**].

Bone mineralization and growth in childhood is associated with bone health and fracture risk in adulthood. Vitamin D plays an essential role in bone programming by stimulation of osteoblastogenesis in human mesenchymal stem cells and production of IGF-1 in osteoblasts [6,10]. Indeed, 25(OH)D status late in pregnancy is associated with whole body and lumbar spine bone mineral content (BMC) and aBMD at nine years [11]. Additionally, newborns of women with 25(OH)D above 17 ng/mL had higher tibia BMC and bone cross-sectional area by peripheral quantitative computed tomography (pQCT) than those below that level [8].

However, at 14 months the only difference that persisted between the groups was in bone cross-sectional area [6]. Thus, despite catchup in BMC, fetal bone growth tracks during the first year, emphasizing the key role of maternal nutrition in determining bone trajectory early in life. It is likely that maternal 25(OH)D during gestation programs skeletal development, body composition and tracking of bone mass throughout life [8]. The clinical implication is that maternal 25(OH)D may influence long-term fracture risk since bone size is a major determinant of bone strength [8].

Vitamin D and bone mineral

Vitamin D is essential to bone mineralization due to its effects on intestinal calcium absorption and on bone mineral accretion. Deficiency of vitamin D in childhood may lead to suboptimal bone mineralization and rickets. In turn, insufficient bone mineral accrual during childhood may ultimately lead to osteoporosis [12]. Vitamin D sufficiency is generally measured by serum 25(OH)D levels, rather than its active form, 1,25- dihydroxyvitamin D [13].

There continues to be debate regarding vitamin D supplementation and optimal 25(OH)D in children and adults. The Institute of Medicine, American Academy of Pediatrics and the 14th vitamin D workshop recommend that 25(OH)D be maintained above a value of 20 ng/mL in children [12,14]. Sixty-one to 70% of children in the United States have 25(OH)D greater than 20 ng/mL [15], which would be achievable with the current United States Recommended Daily Allowance of vitamin D of 600 IU. In contrast, the Endocrine Society supports maintaining vitamin D levels greater than or equal to 30 ng/mL [13].

Widespread vitamin D deficiency in childhood described by epidemiological studies is confirmed in a study that showed only 29% of Finnish children and adolescents with an average daily vitamin D intake of 416 IU had 25(OH)D greater than 20 ng/mL [16]. In a recent study of school age children, 25(OH)D greater than 30 ng/dL was associated with higher forearm and whole body but not lumbar spine aBMD^2, whereas insufficient 25(OH)D was associated with lower aBMD [16]. The effect of 25(OH)D was greater than that of physical activity on lumbar spine and whole body aBMD. Overall, 25(OH)D explained about 9.9% of the variation in aBMD z-score and physical activity determined 5.7 – 7.1% of the variability in total hip and whole body aBMD z-score [16].

Assessment: Bone Markers in Infancy, Childhood and Adolescence

Bone markers are necessary to interpret bone turnover status; however, there is a lack of information regarding the interpretation of bone markers in pediatrics. Markers of bone formation and resorption increase during pregnancy with the highest levels in the cord blood [8]. Newborns whose mothers had low 25(OH)D, did not have coupling of bone turnover markers in cord blood, suggesting altered fetal bone turnover [8]. There was no correlation between 25(OH)D and bone markers, although maternal total intake of vitamin D correlated negatively with cord blood tartrate resistant acid phosphatase, a marker of bone resorption [8]. Bone specific alkaline phosphatase, a marker of bone formation, increased from baseline to 14 months whereas tartrate resistant acid phosphatase remained the same [8]. Change in tartrate resistant acid phosphatase correlated positively and change in bone specific alkaline

phosphatase correlated inversely with 25(OH)D, suggesting that vitamin D affects bone turnover [6].

Parathyroid hormone (PTH) plays an essential role in calcium homeostasis and may become statically elevated in the presence of vitamin D deficiency. Elevated PTH leads to mobilization of calcium from bone resulting in reduced bone mass and increased fracture risk [12]. In children, a 25(OH)D level of 50 ng/mL was associated with a plateau in PTH [2**]. PTH was highest when 25(OH)D was 15 ng/mL or lower and lowest when 25(OH)D was greater than 40 ng/mL [16]. Additionally, PTH was lowest in those with daily calcium intake of more than 1200 mg and there was an inverse correlation between 25(OH)D and PTH regardless of calcium intake [16]. In newborns there was no correlation between PTH and 25(OH)D. PTH was undetectable in 80% of newborns and increased over time. By three months there was no difference among the groups of infants who had been supplemented with different doses of vitamin D [7].

Assessment: Dual-energy x-ray absorptiometry (DXA) as a measure of long-term bone health

Although it is accepted that DXA values in childhood have long-term implications, there is still a paucity of supporting data. The Bone Mineral Density in Childhood Study (BMDCS) demonstrated that when categorized by baseline aBMD z-scores, children generally continued to track in their initial group [17*]. Tracking was stronger for aBMD compared to BMC, when height-adjusted z-scores were used, and was better for girls than for boys [17*] . Tracking was weakest in mid-puberty but improved with use of height adjusted z-score. Fewer than 4% of subjects moved from intermediate to low aBMD and there were no identifying characteristics that distinguished the few children who crossed z-score categories [17*]. In fact, DXA measures of BMC and aBMD at baseline accounted for 50 to 70% of the variation observed at skeletal maturity. These data indicate that DXA measures of aBMD and BMC track through childhood until skeletal maturity in both the axial and the appendicular skeleton in males and females[17*].

The BMDCS also sought to confirm whether bone mineralization and bone strength differ among races. Despite having smaller bones, premenopausal Chinese American women have thicker and denser bone cortices and thicker trabeculae at the radius and tibia measured by pQCT and fewer fractures than their white counterparts [18]. Compared to children of African descent, those of European descent have lower cancellous BMD in the axial skeleton and smaller bone size in the appendicular skeleton [19]. Adolescence is an opportune time to assess differences among races due to a characteristic temporary imbalance between bone resorption and formation when increases in muscle mass, strength and activity result in unprecedented bone loading [20]. The overall fracture incidence in BMDCS was 0.034 fractures per person-year. Fractures were mostly due to sports-related injuries and the prevalence of fractures was highest in boys and in whites [21]. Of note, there was an inverse relationship between DXA bone measures and fracture risk in all groups except for white boys. Fracture risk was greatest between the ages of 10 and 14 years and during puberty likely due to the increased physical demands associated with physical activity, which could not be offset readily due to the lag in increased BMD [21]. The authors

noted that skeletal characteristics related to bone structure not captured by DXA may also contribute to the variance in bone strength in this population [21]. DXA reference curves for BMC and aBMD for total body less head (TBLH), lumbar spine, hip, femoral neck and distal one-third of the radius for black and non-black children were recently published [22]. These curves confirmed a pattern of greater BMC and aBMD for Blacks compared to non-blacks. The authors also provided equations for calculating height z-score adjusted aBMD z-scores [22].

Assessment: DXA in the pediatric population

DXA is the most commonly used technique for BMD assessment in children worldwide due to its speed, precision, safety, low cost and availability [23*]. Its primary limitation is that it measures aBMD rather than volumetric BMD (vBMD) [24], which is an issue in children because growth results in changes in bone size, shape and density. Additionally, there are still many unknowns regarding use of DXA in pediatrics including appropriate reference populations, the relationship of DXA measurements to fracture risk, and the application of DXA to children and adolescents with chronic illnesses [25*]. The 2013 International Society for Clinical Densitometry (ISCD) Position Statement includes the following updates regarding performing DXA in the pediatric population: 1. The preferred sites for BMC and aBMD in most pediatric subjects are the lumbar spine and TBLH; 2. The hip is not a preferred site due to variability in its development in growing children; 3. The minimum interval between DXA scans should be between six and 12 months [23*]. The Committee also suggested that DXA soft tissue studies, such as body fat and lean body mass, may be useful in evaluating patients with nutritional issues related to chronic conditions [23*]. Several new recommendations were made for the interpretation if DXA including use of height z-score rather than actual age in children with short stature or growth delay and use of an appropriate reference data set that includes a sample of healthy children from the general population [23*].

The ISCD recommended several updates for DXA reporting: 1. Tanner Stage or bone age, height z-scores, and adjustments made for growth should be reported; 2. Serial DXA reports should include the same sites as baseline testing and study results should be compared; 3. Whereas osteoporosis is diagnosed by t-score less than or equal to −2 SD in adults, in the pediatric population the diagnosis of osteoporosis requires the presence of both a clinically significant fracture history and low BMC or aBMD [23*]. A clinically significant fracture history is at least one of the following: 1. long bone fracture of the lower extremities; 2. vertebral compression fracture; 3. two or more long bone fractures of the upper extremities. Low BMC or aBMD is defined as a z-score less than or equal to −2.0 adjusted for age, sex and body size (height z-score) [26*]. “Low bone mineral mass or bone mineral density” is the phrase that is recommended for low BMC or aBMD rather than osteopenia or osteoporosis [26*].

The Committee addressed the use of DXA in children with chronic disease characterized by increased fracture risk, specifically in those with primary or secondary bone disease [25*]. Primary bone disease includes osteogenesis imperfecta (OI) and juvenile idiopathic osteoporosis. Secondary bone disease included endocrine diseases; disorders resulting in

impaired mobility; hematologic disorders; inflammatory disorders; chronic kidney disease; and solid organ and bone marrow transplantation. The Committee recommended that these patients should have DXA performed if interventions are available to decrease their risk of a clinically significant fracture; however, DXA should not be performed if safe and appropriate positioning of the child cannot be assured [25*].

Recent studies have recommended use of the lateral distal femur as the preferred site for DXA studies in children who cannot undergo the standard DXA scans due to contractures, positioning issues or metal implants [27]. Another benefit of lateral distal femur DXA is that it more directly assesses a site that commonly fractures. The lateral distal femur has been used in several pediatric populations including those with cerebral palsy, muscular dystrophy, spina bifida as well as in healthy children [28**].

Research on bone assessment in children below five years has lagged behind that of older children; however, similar to older children, this population experiences many chronic medical conditions and undergoes treatments that may affect bone accretion and fragility [29*]. Although fractures are uncommon in infancy, fracture rates increase starting at age two and peak in adolescence [29*]. The 2013 Positions determined that DXA is an appropriate method in infants and young children and recommended that lumbar spine measurements be used for children between 0 and 5 years and that TBLH be used starting at three years [29*]. Whereas forearm and lateral distal femur measurements may be technically easier in this population, there is insufficient information regarding methodology, reproducibility and reference data for these measurements [29*].

There are several new technologies for assessment of bone health with potential applicability to the pediatric population including quantitative ultrasound and pQCT [30*]. In particular, pQCT has the advantage of providing vBMD for specific bone compartments; however, these methodologies are currently primarily used as research tools because of the lack of pediatric reference data [29*].

Treatment

The mainstay of treatment for low BMD in pediatric patients is the bisphosphonates. Bisphosphonates are potent inhibitors of bone resorption that reduce the recruitment and activity of osteoclasts and osteoblasts and decrease bone turnover [31]. This class of medications has traditionally been used in adults with osteoporosis; however, bisphosphonates have been used with increasing frequency to treat both primary and secondary bone disease in pediatrics. The bulk of evidence for bisphosphonate use in pediatrics has been in children with OI; however, it is now used for various pediatric disorders. Pamidronate, which is administered intravenously (IV), has been the most studied bisphosphonate in pediatric OI and its main effect is to improve bone strength by increasing bone cortical width [32]. Children with OI randomized to alendronate, an oral agent, had a 38.8% greater increase in lumbar spine aBMD than placebo [31]. Secondary outcomes were significant for decreased urinary n-telopeptides in the alendronate group, but no difference in long-bone fracture rate, fracture healing rate, vertebral height, cortical thickness, mobility or pain [31]. In contrast to prior studies of IV pamidronate, there was no difference between

the groups in compliance rate, adverse events, serious adverse events or withdrawal from the study [31]. Of note, the beneficial effect of alendronate on lumbar spine vBMD was not as pronounced as that seen in observational studies using IV pamidronate therapy. Thus, despite the ease in administration of alendronate, there is insufficient evidence for its use compared to that of IV pamidronate [31].

Bisphosphonates are being increasingly used in the treatment of low BMD in children with impaired mobility [5*]. A two-year placebo-controlled trial of risedronate, an oral agent, in non-ambulatory children with cerebral palsy and spina bifida showed improved lumbar spine aBMD in the intervention group with no increase in adverse events; however, the effects were not as pronounced as in prior studies of treatment with IV pamidronate [33*]. A small cohort of boys with Dunchenne muscular dystrophy treated with IV pamidronate or zoledronic acid for symptomatic vertebral fractures experienced improvement in back pain and stabilization to improvement in height ratios of previously fractured vertebral bodies [34].

Conclusion

Although there have been many recent advances in the understanding of pediatric bone mineral accrual from fetal life through adolescence and in the assessment and treatment of bone disease in children, there are still many unknowns. Recent advances include the widespread use of DXA throughout the pediatric population and the availability of pediatric references values. There has been progress made in treating children with bone disease, but there is still little information about bone development in children with chronic disease. Future areas of research are certain to include further elucidation of bone health in children with chronic disease focusing on prevention, assessment and treatment.

Acknowledgments

This publication was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number KL2 TR000081, formerly the National Center for Research Resources, Grant Number KL2 RR024157. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Abbreviations

aBMD	Areal bone mineral density
BMD	Bone mineral density
25(OH)D	25-hydroxyvitamin D
BMC	Bone mineral content
pQCT	Peripheral quantitative computed tomography
PTH	Parathyroid hormone
BMDCS	Bone Mineral Density in Childhood Study
vBMD	Volumetric bone mineral density

TBLH	Total body less head
ISCD	International Society for Clinical Densitometry

References

Papers of particular interest, published within the annual period of review (18 months/ 2013-2014) have been highlighted as:

*Of special interest

**Of outstanding interest

1**. Fernandez-Ojeda R, Moruno RM, Miranda MJ, et al. Study of bone mass in young daughters of women with fracture of the distal end of the radius. J Clin Densitom. 2013; 16:87–91. [PubMed: 22980490] [A case-control study that demonstrated that 96 young and healthy daughters of women with fractures of the distal end of the radius had lower bone mass at the spine and femoral neck than 91 controls.]

2**. Hazell TJ, Pham TT, Jean-Philippe S, et al. Vitamin D status is associated with bone mineral density and bone mineral content in preschool-aged children. J Clin Densitom. May 28.2014 :S1094-6950(14)00168-1. doi: 10.1016/j.jocd.2014.04.121. [Epub ahead of print]. [PubMed: 24880497] [A cross-sectional study of 488 randomly selected Canadian children enrolled in daycare showed that 25-hydroxyvitamin D greater than 30 ng/mL was positively associated with BMC and aBMD.]

3. Bailey DA, McKay HA, Mirwald RL, et al. A six-year longitudinal study of the relationship of physical activity to bone mineral accrual in growing children: the University of Saskatchewan bone mineral accrual study. J Bone Miner Res. 1999; 14:1672–1679. [PubMed: 10491214]

4. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001; 285(6):785–795. [PubMed: 11176917]

5*. Boyce AM, Tosi LL, Paul SM. Bisphosphonate treatment for children with disabling conditions. Physical Med Rehab. 2014; 5:427–436. [A current review of the use of bisophosphonates for the treatment of children with disabling conditions.]

6. Viljakainen HT, Korhonen T, Hytinantti T, et al. Maternal vitamin D status affects bone growth in early childhood – a prospective cohort study. Osteoporos Int. 2011; 22:883–891. [PubMed: 21153404]

7. Homlund-Suila E, Viljakainen H, Hytinantti T, et al. High-dose vitamin D intervention in infants-effects on vitamin D status, calcium homeostasis, and bone strength. J Clin Endocrinol Metab. 2012; 97:4139–4147. [PubMed: 22933541]

8. Viljakainen HT, Saarnio E, Hytinantti T, et al. Maternal vitamin D status determines bone variables in the newborn. J Clin Endocrinol Metab. 2010; 95:1749–1757. [PubMed: 20139235]

9**. Harrington J, Perumal N, Al Mahmud A, et al. Vitamin D and fetal-neonatal calcium homeostasis: findings from a randomized controlled trial of high-dose antenatal vitamin D supplementation. Pediatr Research. Jun 17.2014 doi: 10.1038/pr.2014.83. [Epub ahead of print]. [A double-blind placebo-controlled trial showed that infants of 160 Bangladeshi pregnant women randomized to 35,000 IU per week of vitamin D had higher serum calcium on day of life three than infants of mothers who received placebo.]

10. Zhou S, LeBoff MS, Glowacki J. Vitamin D metabolism and actin in human bone marrow stromal cells. Endocrinology. 2010; 151:14–22. [PubMed: 19966181]

11. Javaid MK, Crozier SR, Harvey NC, et al. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. Lancet. 2006; 367:36–43. [PubMed: 16399151]

12. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008; 122:1142–1152. [PubMed: 18977996]

13. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment and prevention of vitamin D deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011; 96:1911–1930. [PubMed: 21646368]

14. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on Dietary Reference Intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011; 96:53–58. [PubMed: 21118827]

15. Looker AC, Johnson CL, Lacher DA, et al. Vitamin D status: United States, 2001-2006. NCHS Data Brief. Mar.2011 :1–8. [PubMed: 21592422]

16. Pekkinen M, Viljakainen H, Saarnio E, et al. Vitamin D is a major determinant of bone mineral density at school age. PLoS One. 2012; 7:e40090. [PubMed: 22768331]

17*. Wren TAL, Kalkwarf HJ, Zemel BS, et al. Longitudinal tracking of dual-energy x-ray absorptiometry bone measures over 6 years in children and adolescents: Persistence of low bone mass to maturity. J Pediatr. 2014; 164:1280–85. [PubMed: 24485819] [A longitudinal study of 513 children between the ages of 6 and 17 showed that DXA aBMD z-scores tracked during the time period studied.]

18. Walker MD, Liu XS, Stein E, et al. Differences in bone microarchitecture between postmenopausal Chinese-American and white women. J Bone Miner Res. 2011; 26:1392–1398. [PubMed: 21305606]

19. Gilsanz V, Skaggs DL, Kovonalikaya A, et al. Differential effect of race on the axial and appendicular skeletons of children. J Clin Endocrinol Metab. 1998; 83:1420–1427. [PubMed: 9589632]

20. Wang Q, Wang XF, Iuliano-Burns S, et al. Rapid growth produces transient cortical weakness: a risk factor for metaphyseal fractues during puberty. J Bone Miner Res. 2010; 25:1521–1526. [PubMed: 20200962]

21. Wren TAL, Shepherd JA, Kalkwarf HJ, et al. Racial disparity in fracture risk between white and nonwhite children in the United States. J Pediatr. 2012; 161:1035–1040. [PubMed: 22974572]

22. Zemel BS, Kalkwarf HJ, Gilsanz B, et al. Revised reference curves for bone mineral content and areal bone mineral density according to age and sex for black and non-black children: results of the bone mineral density in childhood study. J Clin Endocrinol Metab. 2011; 96:3160–3169. [PubMed: 21917867]

23*. Crabtree NJ, Arabi A, Bachrach LK, et al. Dual-energy x-ray absorptiometry interpretation and reporting in children and adolescents: The revised 2013 ISCD Pediatric Official Positions. J Clin Densitom. 2014; 17:225–242. [PubMed: 24690232]

24. Fewtrell MS. Bone densitometry in children assessed by dual x-ray absorptiometry: uses and pitfalls. Arch Dis Child. 2003; 88:795–798. [PubMed: 12937102]

25*. Bianchi ML, Leonard MB, Bechtold S, et al. Bone health in children and adolescents with chronic diseases that may affect the skeleton: The 2013 ISCD Pediatric Official Positions. J Clin Denitom. 17:281–294. [A summary of the ISCD Pediatric Official Positions regarding bone health in children with chronic disease.]

26*. Bishop N, Arundel P, Clark E, et al. Fracture prediction and the definition of osteoporosis in children and adolescents: The ISCD 2013 Pediatric Official Positions. J Clin Denitom. 2014; 17:275–280. [A summary of the ISCD Pediatric Official Positions regarding fracture prediction and the definition of osteoporosis in children.]

27. Zemel BS, Stallings VA, Leonard MB, et al. Revised pediatric reference data for the lateral distal femur measured by Hologic Discovery/Delphi dual-energy x-ray absorptiometry. J Clin Densitom. 2009; 12:207–218. [PubMed: 19321369]

28**. Mueske NM, Chan LS, Wren TAL. Reliability of lateral distal femur dual-energy x-ray absorptiometry measures. J Clin Densitom. Mar 26.2013 :S1094-6950(13)00032-2. doi: 10.1016/j.jocd.2013.02.010. [Epub ahead of print]. [PubMed: 23541123] [This study assessed variability in DXA of the lateral distal femur in 10 children and determined that DXA measures of the LDF are reliable and may be useful when standard DXA measures cannot be obtained in disabled or young children.]

29*. Kalkwarf HJ, Abrams SA, DiMeglio LA, et al. Bone densitometry in infants and young children: The 2013 ISCD Pediatric Official Positions. J Clin Denitom. 2014; 17:243–257. [A summary of

the ISCD Pediatric Official Positions update regarding bone densitometry in infants and young children.]

30*. Adams JE, Engelke K, Zemel BS, Ward KA. Quantitative computer tomography in children and adolescents: The 2013 ISCD Pediatric Official Positions. J Clin Denitom. 2014; 17:258–274. [A summary of the ISCD Pediatric Official Positions regarding use of quantitative computer tomography in children and adolescents.]

31. Ward LM, Rauch F, Whyte MP, et al. Alondronate for the treatment of pediatric osteogenesis imperfecta. A randomized placebo-controlled study. J Clin Endocrinol Metab. 2011; 96:355–364. [PubMed: 21106710]

32. Munns CF, Rach F, Travers R, Glorieux FH. Effects of intravenous pamidronate treatment in infants with osteogenesis imperfecta: clinical and histomorphometric outcome. J Bone Miner Res. 2005; 20:1235–1243. [PubMed: 15940378]

33*. Cohran V, Cassedy A, Hawkins A, et al. Oral risedronate sodium improves bone mineral density in non-ambulatory patients: A randomized, double-blind, placebo-controlled trial. J Pediatr Rehab Med. 2013; 6:85–93. [A small randomized, double-blind, placebo-controlled trial showed that risedronate improved lumbar spine BMD scores in non-ambulatory children and adults compared to placebo.]

34. Sbrocchi AM, Rauch F, Jacob P, et al. The use of intravenous bisphosphonate therapy to treat vertebral fractures due to osteoporosis among boys with Duchenne muscular dystrophy. Osteoporos Int. 2012; 23:2703–2711. [PubMed: 22297733]

Key Points

- Bone mineral accrual in childhood and adolescence influences long term bone health and is associated with fracture risk in adulthood.
- Vitamin D is an essential factor in bone mineralization and its deficiency may lead to suboptimal bone mineralization and eventual osteoporosis.
- DXA is the most commonly used technique to assess pediatric bone health worldwide due to its speed, precision, safety, low cost and availability.
- Further studies are needed to better understand bone development in children with chronic disease
- Bisphosphonates are being increasingly used to treat low bone mineral content or density in children with a variety of chronic diseases.