Pediatric Osteoporosis

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Pediatric bone health is determined by genetics, diet, mobility, and exercise, but it can also be affected by medications and chronic disease. Although a diagnosis of osteoporosis may inspire thoughts of the geriatric population, some children are also vulnerable. Physicians providing care to both pediatric and adult populations should particularly note the major differences in the diagnosis and management of osteoporosis in children.

Pediatric osteoporosis is defined by the International Society for Clinical Densitometry based on 2 criteria. First is "low bone mineral content or bone mineral density." Children with bone mineral density of 2 or more standard deviations below average measured using dual-energy x-ray absorptiometry (DXA) have "low bone mineral content." DXA, which exposes patients to small doses of ionizing radiation, is the only current reference standard for assessing pediatric bone mineral density. A patient's measurement is compared with standards for age, sex, and body size, and the result is reported as a *Z* score, with a value of less than –2.0 being abnormal. Unfortunately, variability in radiologic technique, the multidimensional growth of bone in childhood, and normative data that inadequately account for bone changes caused by puberty or chronic disease all present challenges to reproducible and accurate interpretation of DXA in pediatric patients.

The second criterion required for diagnosis of pediatric osteoporosis is "the presence of a clinically significant fracture history," defined as at least 1 long bone fracture in the lower extremity, at least 2 long bone fractures in the upper extremity, or a vertebral compression fracture. Some physician discretion in applying this criterion is warranted, specifically in cases of concern for fragility or low trauma fractures. For example, an adolescent with a long bone fracture of the leg after, for example, a fall down a flight of concrete stairs would be significantly less concerning than a similar fracture after minimal trauma.

The incidence of pediatric osteoporosis is not known, likely due to a combination of historical differences in diagnostic criteria, previous lack of well-established DXA reference data, and the wide variety of factors that may contribute to the development of osteoporosis. Increased risk of low bone mineral density and fractures is found with a wide range of genetic disorders, chronic illnesses, and use of specific medications. Modifiable factors such as calcium and vitamin D intake, soda consumption, and weightbearing exercise also affect the potential for pediatric osteoporosis, and pediatricians should incorporate screening questions into health maintenance visits to help assess risk.

Bone fragility is an obvious concern in children with bone disorders such as osteogenesis imperfecta, but studies have also demonstrated increased fracture risk in patients with connective tissue disorders such as Marfan syndrome and Ehlers-Danlos syndrome. One factor contributing to osteoporosis in these patients may be decreased exercise or mobility. Other patients with a limited

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Optimizing Bone Health in Children and Adolescents. Golden NH, Abrams SA; Committee on Nutrition. *Pediatrics.* 2014; 134(4):e1229–e1243

Osteoporosis in Pediatrics. Steelman J, Zeitler P. *Pediatr Rev.* 2001;22(2):56–65

Pediatric DXA: A Review of Proper Technique and Correct Interpretation. Wildman SS, Henwood-Finley MJ. *J Am Osteopath Coll Radiol.* 2012;1(3):17–26

Pediatric Osteoporosis: Diagnosis and Treatment Considerations. Marrani E, Giani T, Simonini G, Cimaz R. *Drugs.* 2017; 77(6):679–695

ability to participate in weightbearing exercise, including those with cerebral palsy, muscular dystrophy, or spinal cord injuries, have lower bone density and increased risk of fractures. Weightbearing exercise confers a variety of health benefits, and 2 studies have suggested that introducing school-based daily exercise in healthy prepubertal children has the additional advantage of increasing bone accrual. Those with restricted mobility can similarly experience improved bone health through thoughtful physical therapy.

Vitamin D deficiency with resultant impairment in calcium absorption may lead to rickets and eventual osteoporosis. Although decreased availability due to minimal sun exposure, poor nutrition, eating disorders, and prematurity are possible causes, it is also important to consider chronic disorders associated with malabsorption of vitamin D as predisposing to osteoporosis. Patients with short gut syndrome, celiac disease, and cystic fibrosis generally are at risk for deficiencies in all fat-soluble vitamins, and patients with chronic kidney disease may develop secondary hypoparathyroidism with subsequent vitamin D deficiency. Medications for seizures affect vitamin D metabolism and calcium absorption, and higher doses and use of multiple antiepileptic drugs further increase the risk of osteoporosis. Empirical vitamin D supplementation is reasonable in children with these conditions and in those receiving medical therapy for seizures.

Chronic, systemic glucocorticoids also have a host of deleterious effects on bone, including interference with vitamin D metabolism, increased bone resorption, decreased bone formation, decreased calcium absorption, increased calcium loss, and decreased sex hormone production. Patients receiving long-term immunosuppression medications, such as those with cancer, autoimmune disease, and organ transplants, are at risk for osteoporosis. Unfortunately, the underuse of these medications and inadequate control of chronic inflammation also places children at increased risk for fractures. Inflammatory cytokines associated with chronic conditions such as rheumatologic disorders or inflammatory bowel disease can decrease bone production and increase resorption. Cytotoxic chemotherapy, corticosteroids, and radiotherapy used for the treatment of childhood cancers also have a harmful effect on bone mineral density and can be of particular concern in children who may already have increased fracture risk due to bone-infiltrating malignancies. Although use of these treatment modalities is deleterious to bone health, it remains preferable to the systemic and bone risks associated with inadequate treatment of these underlying conditions.

Children with type I diabetes, abnormal corticosteroid production, and disorders causing hypogonadism are all at increased risk for osteoporosis. Whereas these patients are typically already under the care of an endocrinologist, adolescents with exercise-related amenorrhea and Turner syndrome and those receiving depot medroxyprogesterone therapy are less commonly followed by these subspecialists and therefore should be monitored by their primary care physicians for fractures and the need for further evaluation and intervention.

Inherent difficulties exist in performing and interpreting pediatric DXA, and there is a lack of clear predictive value in children without significant fracture history. The American Academy of Pediatrics recommends DXA for children with clinically significant fractures and those with medical conditions that place them at increased risk for fractures. Specifically, DXA should be performed in pediatric patients with vertebral fractures, fractures out of proportion to the inciting trauma, and multiple long bone fractures. Although screening questions and counseling to prevent modifiable causes of osteoporosis are appropriate in all children, DXA is not indicated in otherwise healthy children. In all pediatric patients, therapeutic interventions should focus on addressing underlying etiologies of bone fragility.

The treatment team caring for a child with low bone density should optimize medical management of the underlying condition while simultaneously employing general strategies for improving bone health. For example, an adolescent with anorexia nervosa will have improved bone density with weight gain and return of normal estrogen production alone, and bone remineralization can be further augmented with supplementation with vitamin D and calcium. Bisphosphonates are not indicated to be appropriate for first-line use in otherwise healthy pediatric patients with low bone density. Use of bisphosphonates should be reserved for children with symptomatic or severe osteoporosis that is refractory to supplementation and management of comorbid conditions, and for conditions such as osteogenesis imperfecta where, despite disease management, recurrent painful fractures may be ameliorated and risk of vertebral collapse minimized.

Regardless of the source, pediatricians can ensure that all patients at risk for low bone mineral density have adequate vitamin D and calcium intake. Unfortunately, there are no standardized recommended daily allowances for children with these conditions, but adequate amounts recommended for healthy children should be a minimum expectation.

Currently, adequate vitamin D intake for healthy infants younger than 1 year is 400 IU/d and for healthy children 1 year and older is 600 IU/d. Vitamin D levels do not need to be measured as a routine screening tool but are reasonable in children with a history of clinically significant fractures. Similarly, calcium intake in high-risk patients should at least match the recommended daily allowance for healthy children, which varies based on age. Consultation with a registered dietitian may be helpful for parents striving to optimize nutrition. Pediatricians should encourage and facilitate participation in weightbearing exercise; collaboration with pediatric physical therapists can help to safely maximize activity in children at higher risk for osteoporosis and fractures.

COMMENT: The field of pediatric bone health has rapidly expanded during the past decade. Pediatricians are a critical part of the health-care team in addressing preventive strategies. Studies have demonstrated that bone health in adulthood is affected by intrauterine factors such as maternal vitamin D deficiency, smoking, alcohol consumption, caffeine intake, decreased physical activity, intrauterine growth retardation, and maternal diabetes. The period of childhood, from infancy through adolescence, is critical for bone health because 90% of bone density is determined by the end of puberty. Hence, pediatricians have the important responsibility to counsel families and patients about the importance of vitamin D intake, calcium intake, and exercise. We all know some of the challenges of encouraging vitamin D and calcium intake for children. In one study it was noted that calcium intake by diet alone is approximately 50% of the recommended dietary allowance for girls. But asking specifics about what types of food and dairy products are eaten and the quantities is essential. And, when found not to be sufficient, encouraging other alternatives, such as calcium-fortified cereals, juices, other foods, and supplements. Pediatricians are also essential in coordinating the care of children with special health-care needs because bone health may not always be a primary concern through the lens of the subspecialists.

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Correction

An error appeared in the print version of the January 2019 review "Sleep-Disordered Breathing in Children" (Gipson K, Lu M, Kinane TB. *Pediatr Rev.* 2019 Jan;40(1):3–13. doi: 10.1542/pir.2018-0142). In the first paragraph of the "Physical Examination" section on page 6, the text should reference the Friedman scale instead of the Brodsky scale. The online version of the article has been corrected, and a correction notice has been posted with the online version of the article. The journal regrets the error.

ANSWER KEY FOR MAY 2019 PEDIATRICS IN REVIEW

Infant Peanut Introduction Simplified: 1. D; 2. D; 3. C; 4. D; 5. D.
Allergy Testing and Immunotherapy: 1. C; 2. B; 3. E; 4. B; 5. C.
Immunodeficiency Disorders: 1. D; 2. D; 3. D; 4. B; 5. E.