Ever the past decade there have been an increasing number of published manuscripts dealing with pediatric bone mineral density (BMD). The reason for this interest is 2-fold. First, there is a belief that bone gained early in life is an important factor in determining the risk of osteoporosis later in life. Second, there is a desire to identify children who may benefit from drugs that are becoming available for use in treating osteopenia and osteoporosis. Despite the interest, there are several important issues with assessing BMD or the amount of bone (bone mineral content [BMC] or bone mass) that are unique to children that need to be recognized and are discussed in this review. Dual energy x-ray absorptiometry (DXA) is the most common method for assessing BMD and BMC, but other methods, including peripheral quantitative computed tomography (pQCT) and quantitative ultrasonography (QUS), may provide important additional information on bone size, geometry, and quality, and these methods also are discussed.

Approximately 90% of adult bone mass is gained in the first 2 decades of life. Optimizing peak bone mass and bone strength early in life and stabilizing it during young adulthood is believed to play a significant role in preventing osteoporosis and fracture later in life. Environmental factors important in determining whether children reach their genetic potential in achieving peak bone mass include adequate nutrition and activity levels. Pediatric diseases, or the therapeutic interventions used in their treatment, also may prevent children from reaching their genetic potential. Diseases or conditions known to affect bone density adversely include osteogenesis imperfecta, gastrointestinal illnesses (ie, inflammatory bowel disease, Crohn's disease), cystic fibrosis, juvenile rheumatoid arthritis, growth hormone deficiency, chronic steroid use, and history of previous fracture. Obese and less-active children also have been shown to have decreased BMD or bone mass compared with nonobese children of similar weight. Whether this decreased BMD among obese children is a direct effect of fat on bone or due to decreased muscle mass or reduced activity levels, or a combination of both of these factors, is not clear. However, the epidemic of childhood obesity may in part directly or indirectly explain the increase in childhood fracture incidence that has recently been reported. Identifying children with low bone mass early in life could be an important strategy for preventative or therapeutic efforts to optimize bone accrual and, consequently, bone strength.

**METHODS FOR ASSESSING BONE HEALTH AND ASSOCIATED PITFALLS DXA**

DXA is the most widely used densitometric method for diagnosing osteoporosis in adults. DXA was developed in the late 1980s for use primarily in postmenopausal women. Pediatric software became available in the early 1990s after improvements in algorithms for detecting bone edges in children with low bone density. The advantages of DXA are its wide availability, short scanning times, and relatively low radiation exposure.

DXA measures bone in 2 dimensions and provides estimates of the amount of BMC and bone area. BMD is then calculated as BMC/bone area (g/cm²). Because this is a 2-dimensional measurement and not a true volumetric density, measurements using DXA are often referred to as areal BMD (aBMD). Measurements of aBMD are influenced by bone size, with larger bones having artificially inflated aBMD measurements (Figure 1). This is an important problem in pediatric bone assessment because of the large differences in body size and bone size within and across different ages. Studies show that aBMD by DXA increases with age, but studies using computed tomography indicate that true volumetric BMD (vBMD) is relatively constant during childhood until puberty, at which time there is

**TABLE**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>BMAD</td>
<td>Bone mineral apparent density</td>
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<tr>
<td>BMC</td>
<td>Bone mineral content</td>
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<tr>
<td>BMD</td>
<td>Bone mineral density</td>
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<tr>
<td>DXA</td>
<td>Dual energy x-ray absorptiometry</td>
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<tr>
<td>QCT</td>
<td>Quantitative computed tomography</td>
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<tr>
<td>QUS</td>
<td>Quantitative ultrasonography</td>
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a large increase in vBMD.\textsuperscript{4} BMC increases with age, and the increase in aBMD that is observed is likely the result of greater bone size.

Several mathematical methods have been proposed to adjust aBMD to either control for bone size differences or more closely reflect vBMD. These methods include the calculation of bone mineral apparent density (BMAD) that divides BMC by a calculated bone volume rather than by bone area.\textsuperscript{5} This method has been used for the spine and hip and assumes that the bone has a cuboidal or cylindrical shape, respectively. Other investigators have proposed including bone area and body size parameters in a multiple regression approach to calculate a size-adjusted BMC.\textsuperscript{6} Molgaard et al\textsuperscript{7} have proposed a logical approach to assessing bone accrual in children that includes a 3-step examination of growth and bone data: height-for-age, bone area-for-height, and BMC-for-bone area. This type of examination would help distinguish whether a child has "short" bones, "narrow" bones, or "light" bones. Unfortunately, normative pediatric curves for these relationships are not available as part of the DXA software. Some DXA machines have normative data for aBMD-for-age at some bone sites, but use of these curves for diagnosing low aBMD or BMC may not be appropriate, especially if the child has decreased stature.\textsuperscript{8,9}

Although adult aBMD has been shown to be predictive of future fracture risk in longitudinal epidemiologic studies,\textsuperscript{10,11} there is no evidence in children indicating this is so, and even among adults the sensitivity of DXA for assessing vertebral fracture risk is relatively low (65% using World Health Organization criteria).\textsuperscript{12} The aBMD results are often presented as T and Z scores. The World Health Organization criteria for diagnosing osteoporosis in adults are based on BMD T scores (defined as the standard deviation [SD] score of the observed aBMD compared with that of a normal young adult). A T score of less than $-1$ SD indicates osteopenia, and a T score of less than $-2.5$ SD indicates osteoporosis.\textsuperscript{13}

There are significant differences in the relationships observed between total body BMC measurements and body weight depending on the DXA model and software that is used. There also are significant differences among published pediatric norms. Leonard et al\textsuperscript{14} have shown that there are inconsistencies in the diagnosis of osteopenia among children with chronic diseases depending on the reference database used.

Because T scores compare the observed aBMD with that of young adults, they are not appropriate for growing children and should never be used. Z scores, defined as the SD score based on age and gender-specific norms, are often used to determine how a child’s aBMD compares with other children’s. This is a more appropriate method of comparison of aBMD in pediatrics. As previously described, however, aBMD is highly correlated to body and bone size, and in children with chronic diseases there often is stunting of growth, and comparison of aBMD measurements to age-matched norms may not be appropriate.

In situations where a child’s growth is stunted, it may be more appropriate to determine whether the aBMD or BMC is appropriate for his or her body size by comparing their measurements with those of children of similar height or weight. However, if these reference databases are not available on the DXA software, they must be obtained from the pediatric literature on published normative values. When this is done it is important to realize that there are different DXA manufacturers, different models by the same manufacturer, and different software analyses that are available. As shown in Figure 2, there are significant differences in the relationships observed between total body BMC measurements and body weight depending on the DXA model and software that is used.
predominantly trabecular bone, will be affected by different factors than the total body or forearm, which are predominantly cortical bone. Dietary calcium intake has been shown to affect primarily appendicular bone sites that are predominantly cortical bone,15 whereas hypogonadism and steroid use affect primarily axial bone sites or the ends of long bones, which are predominantly trabecular bone.16,17

Although regional DXA scans can measure BMD and BMC at sites that are predominantly trabecular or cortical bone, it is not possible to obtain separate cortical and trabecular BMD results using DXA. The aBMD assessed by DXA is a function of both the amount of bone within the peristomal envelope and the size of the bone.

Quantitative Computed Tomography

Quantitative computed tomography (QCT) assesses bone in 3 dimensions and allows for separation of cortical and trabecular bone. QCT also provides assessment of bone size and geometry, both of which are known to significantly influence bone strength.18 Volumetric BMD (vBMD) at both peripheral and axial bone sites can be measured with QCT scanners. However, the primary disadvantage is the high radiation doses, making it unsuitable for use in determining factors that influence bone in healthy children. Without normative pediatric databases for QCT, it is difficult to use this method clinically.

Peripheral QCT (pQCT) provides a 3-dimensional assessment of bone size and geometry of the appendicular skeleton with much lower radiation doses. Although the pQCT method is not routinely used currently in the United States for clinical purposes, its popularity has grown in Europe among pediatricians and pediatric bone researchers.

pQCT permits analysis of cortical and trabecular vBMD and derivation of specific geometric parameters of cortical bone from cross-sectional images (periosteal and endosteal circumferences, cortical thickness, cortical area, etc) (Figure 3). These measures provide important information not available using DXA.

The importance of bone size and geometry, in addition to bone mass, is apparent from an evolutionary viewpoint. If optimizing bone mass were of primary importance, then evolutionary processes would have led to the formation of bones with solid, not hollow, diaphyses. However, this did not occur, and the anatomic structure of bone suggests that bone development is set to attain peak bone strength by using as little material as possible. For a bone with a given structure, bone mass usually correlates with strength. However, structure strength will differ depending on the size of the structure and where the material or mass is located.

Architectural parameters have been developed that allow calculation of structural strength on the basis of the amount or size of the structure and the distribution of the material. Such parameters include the polar moment of inertia and the section modulus. The polar moment of inertia is a measure of the distribution of material around the center of the structure (Figure 4). The shear stress created in a bone by torque is inversely related to the polar moment of inertia; therefore, in bones with a high polar moment of inertia, the same torque will result in a smaller shear stress than in a bone with a lower polar moment of inertia. A closely related parameter, the section modulus, indicates the resistance of a bone to stress. The influence of bone size on moment of inertia and section modulus are shown in Figure 5. This example illustrates that bone strength is not primarily a function of bone mass, but size. The polar moment of inertia and the section modulus are used in bone biomechanical studies and have been found to be good indicators of bone strength and can be easily and precisely determined using pQCT.

The material properties of the bone also play a role in determining bone strength. The elastic modulus, or stiffness,
is a material property of bone that has been found to correlate with vBMD measurement using pQCT technology. Schiessel et al. developed the strength strain index (SSI), which is calculated as the product of the section modulus and cortical vBMD normalized to the maximal physiological cortical vBMD of human bones. The SSI combines both architectural and material components of bone strength (Figure 4).

An example of how determination of bone size by pQCT can provide insight into mechanisms influencing pediatric bone development is a recent trial of physical activity and calcium intake on bone. In this study of 239 preschool children, calcium intake modified the leg size-adjusted BMC response to physical activity in young children, but the specific effects on bone parameters were not clear until the pQCT results were investigated (Figure 6). Gross motor activity, which included bone loading exercises, increased periosteal circumference, whereas calcium supplementation appeared to decrease the endosteal expansion that also occurred. Although DXA leg BMC did not appear to be influenced by physical activity among the children receiving placebo, the periosteal circumference was greater in the children participating in gross motor activities compared with fine motor activities.

In spite of the important information that can be obtained using pQCT, there are several problems with its use in pediatric populations. Pediatric reference databases have been published for the radius, and the tibia but are not provided with the software. There are also numerous scan sites and analysis options that have been used in pediatric reports, making comparison among studies difficult. Thresholds for defining cortical and trabecular bone need to be specified by the investigator, and the use of different thresholds will have a significant effect on the values that are obtained for cortical and trabecular bone area, as well as volumetric density. Problems specific to pediatrics include standardization of scan acquisition and analysis programs, including consensus on where to mark the end of the bone in young children with large growth plates. In addition, measurement of cortical BMD in bones less than 2 mm thick is problematic because of the partial volume effect, which is described in greater detail elsewhere.

**QUS**

QUS assesses bone by measuring the speed of sound (SOS) of an ultrasound wave along the bone. The theory behind QUS is that the propagation of ultrasound waves through a medium and the attenuation of the signal strength are influenced by the physical properties of the medium. In the case of bone, the speed of propagation is influenced by the bone density, elasticity modulus, and the microstructure and macrostructure of bone. There is no uniform terminology of ultrasound velocity; the terms speed of sound, velocity of sound, and apparent velocity of ultrasound all refer to the same measure. When the ultrasound beam travels through material, energy is lost, in a phenomenon known as attenuation. In the range of frequencies used, total attenuation is linearly proportional to frequency. The slope of attenuation as a function of frequency in dB/MHz/cm has become known in clinical practice as broadband ultrasound attenuation. Different methods of measurement have been developed, including pulse-echo (reflection) and transmission techniques. QUS has been shown to be comparable to DXA in identifying adults with multiple vertebral fractures, and its use for pediatric populations is appealing due to the low cost, lack of radiation exposure, and portability. Fielding et al. recently reported that calcaneus ultrasound measurements detected low bone mineral in young patients with fragility fractures, as well as DXA, and concluded that QUS is a viable screening tool for detecting children with osteopenia. However, interpretation of QUS measurements at other sites, especially tubular bones, may be more problematic and influenced by bone size and cortical thickness.

In summary, the use of QUS in pediatric populations is still in its infancy, and not all ultrasound devices are appropriate for use in pediatric populations because of inappropriate transducer sizes. In addition, adequate reference databases are not currently available for a large number of existing ultrasound devices. There is wide diversity in commercially available techniques, and there are minimal studies...
It is important to recognize that these pediatric populations do not provide a solution to the problem of measuring aBMD in children. There are, however, several problems with the common method for assessing bone health in pediatric populations. The British Paediatric and Adolescent Bone Group recently published pediatric guidelines for the clinical use of DXA. They suggested that children with conditions that may increase their risk of low bone density and fracture should be considered for a DXA scan if they also present with low trauma or recurrent fractures, back pain, spinal deformity or loss of height, change in mobility status, or malnutrition. The list of conditions that place children at increased risk is given in Table I, along with some of the more rare conditions that also may be associated with decreased BMD. Because of the lack of pediatric reference databases, the variation between machines, and the different software analyses that are performed, it is important that clinicians consult with pediatric bone specialists before using DXA diagnostically or prescribing treatment on the basis of DXA results. Preferred skeletal sites for measurement are spine and total body. The value of BMD to predict fractures in children is not clearly demonstrated. Standards for adjusting BMD or bone mineral content (BMC) for factors such as bone size, pubertal stage, skeletal maturity, or body composition have not been agreed upon. Clearly state any adjustments in the report.

## WHO SHOULD HAVE BONE MEASUREMENTS MADE?

There are currently no standard recommendations by either a U.S. pediatric or bone organization on who should have bone measurements for clinical purposes. The British Paediatric and Adolescent Bone Group recently published pediatric guidelines for the clinical use of DXA. They suggested that children with conditions that may increase their risk of low bone density and fracture should be considered for a DXA scan if they also present with low trauma or recurrent fractures, back pain, spinal deformity or loss of height, change in mobility status, or malnutrition. The list of conditions that place children at increased risk is given in Table I, along with some of the more rare conditions that also may be associated with decreased BMD. Because of the lack of pediatric reference databases, the variation between machines, and the different software analyses that are performed, it is important that clinicians consult with pediatric bone specialists before using DXA diagnostically or prescribing treatment on the basis of DXA methods.

The International Society of Clinical Densitometry recently published an official position paper on recommendations for performance and clinical application of bone density testing, which included recommendations specific for diagnosis in children. These recommendations are summarized in Table II. It is important to recognize that these recommendations, although they acknowledge the problems with bone and body size in interpreting the results, do not provide a solution to the problem of measuring aBMD in pediatric populations.

## SUMMARY

Bone acquisition early in life is considered an important predictor of osteoporosis risk later in life. DXA is the most common method for assessing bone health in pediatric populations. There are, however, several problems with interpreting DXA scans in children that need to be considered by clinicians before therapeutic interventions are implemented on the basis of DXA results. PQCT is a promising method that is currently being used in pediatric bone research that may find its way into clinical use for assessing bone strength and fracture risk. Further research is needed to determine whether QUS could be used as a radiation-free alternative for assessing bone development clinically and in epidemiologic studies.

### REFERENCES