Bone Accrual in Children: Adding Substance to Surfaces

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ABSTRACT

The mass of growing bones increases through changes in outer dimensions and through the net addition of tissue on inner bone surfaces. In this overview I examine bone accrual as it occurs on trabecular (inner) and periosteal (outer) surfaces. In the axial skeleton, the amount of trabecular bone increases during development, because trabeculae grow thicker as a result of bone remodeling with a positive balance. Remodeling is a process in which osteoblasts and osteoclasts are tightly linked (“coupled”) in time and space. In contrast to trabecular thickness, trabecular number and material density change little throughout development. Bone accrual on periosteal surfaces leads to an increase in bone size, which is a crucial determinant of bone strength throughout life. Periosteal osteoblasts deposit new bone on an extended surface area and over an extended period of time without being interrupted by osteoclasts. This type of bone metabolic activity is called modeling, which is much more efficient than remodeling for increasing bone mass. In the past, research has focused on bone remodeling on trabecular surfaces. However, the key to an improved understanding of bone mass and strength development in children will lie with studies on bone modeling on periosteal surfaces.
For a long time, studies on human bone development have focused on changes in bone mineral mass (expressed as bone mineral content) and bone mineral density (BMD). Nevertheless, describing bone development just in terms of changes in mass or density means looking at bones as if they were amorphous heaps of calcium and phosphorus. In reality, of course, bones are complex three-dimensional structures. Taking structural aspects into account should allow for a more realistic understanding of bone development.\(^1\)\(^2\)

What are the structures on which bone tissue accrues? Schematically, new bone can be added on the outside, which makes bones bigger, or on the inside, which makes bones denser. Bones get bigger by 2 different processes: growth in length and growth in width. Bone growth in length is driven by the growth plate, whereas bone growth in width is the task of the periosteum. The inner bone surface is called the endosteal surface, which can be subdivided into the trabecular, endocortical, and intracortical surfaces.\(^3\) In this contribution, I focus on 2 sites of bone accrual: the periosteal and trabecular surfaces.

**Bone accrual on trabecular surfaces**

At the lumbar spine, volumetric BMD, as measured by quantitative computed tomography, increases by \(\sim 25\%\) during puberty.\(^4\) What structural changes underlie this increase? Schematically, there are 3 ways to increase trabecular BMD. First, material density might increase. Second, there might be a rise in trabecular number (ie, the trabeculae could be packed more closely together). Third, it is possible that trabeculae become thicker. Which of these 3 possibilities contributes most to the increase in lumbar spine BMD? Material bone density cannot be measured with currently available noninvasive techniques but can be determined in histologic bone sections by using methods such as back-scattered electron-imaging analysis. With this technique, Roschger et al\(^5\) found that material trabecular bone density in the L4 vertebral body increased by only 3\% from 1 to 80 years of age. Thus, material density does not seem to be a major contributor to changes in trabecular BMD during bone development.

Trabecular number, in histomorphometric terminology, reflects the number of trabeculae that a line through the bone would hit per millimeter of its length.\(^1\) Kneissel et al\(^6\) did not find any increase in trabecular number in the L4 vertebral body between 10 and 20 years of age. Thus, both trabecular number and material density cannot account for the increase in trabecular BMD during puberty. By default, then, trabecular thickening must the explanation.

I am not aware of any studies that have examined trabecular thickness in the vertebral bodies of children and adolescents. However, our own studies\(^7\) of a different part of the axial skeleton, the ilium, indeed revealed an increase in trabecular thickness during bone development. Similar to vertebral bodies, no change in trabecular number was found throughout the growing period. Dynamic histomorphometric measurements suggested that the increase in trabecular thickness was attributable to remodeling with a positive balance,\(^7\) which means that during each remodeling cycle osteoblasts add more bone than was previously resorbed by osteoclasts. The difference is small, however, and only leads to a gain of a few micrometers of trabecular thickness per remodeling cycle. As in growing children each location on the iliac trabecular surface undergoes a remodeling cycle every 9 to 10 months, on average, remodeling with a positive balance results in a very slow and gradual increase in trabecular BMD.

**Bone accrual on periosteal surfaces**

Bone growth in width is much less well characterized than growth in length, although it is of paramount importance for bone stability. If bones just grew in length without increasing in size, they would become unstable and break at some point.\(^8\) The bending strength of an elongated structure such as a long-bone diaphysis is related to its diameter raised to the third power (Fig 1). In contrast, bending strength is inversely related to length raised to the third power.\(^8\) Thus, bone growth in length and growth in cross-sectional size have opposite effects on a bone’s ability to withstand mechanical loads. Growth in size, therefore, must be closely linked to growth in length. How this works is unknown. After the growth period, bone size changes only slowly. Consequently, bone growth in size is one of the most important determinants of bone strength throughout life.\(^9\)

A bone’s cross-sectional size increases through the action of osteoblasts that add mineralized tissue on the outer (periosteal) bone surface, a process called periosteal apposition.\(^10\) The periosteum surrounds the bone

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**FIGURE 1**

Left, The 2 rods have the same length, but the larger rod has twice the diameter of the thinner rod; therefore, the thicker rod is 8 times stronger in bending. Right, A doubling of length with unchanged bone diameter decreases bending strength to one eighth of the original value. (Reproduced with permission from Rauch F. J Musculoskelet Neuronal Interact. 2005;5:197.)
like a stocking, which in children is thick and is only loosely attached to the diaphysis. Toward the bone ends, the periosteum continues directly into the perichondral ring that encircles the periphery of the growth plate. The periosteum and perichondrium are both firmly anchored to the epiphysis.\textsuperscript{11}

On the microscopic level, the periosteum consists of 2 readily distinguishable layers. The outer layer is composed mainly of fibrous tissue, and the inner layer, called the cambium layer, harbors osteogenic cells. These osteogenic cells have not been characterized in any great detail, and little is known about their differentiation pathways.\textsuperscript{12} In 2-week-old rabbits, osteoblasts remain active on the periosteal surface for only 3 days.\textsuperscript{13} They then seem to lose steam, get buried in newly deposited bone matrix, and turn into osteocytes.

Histomorphometric studies of rib and iliac bone have yielded the expected result that periosteal bone formation is much more active in children than in adults.\textsuperscript{7,14,15} However, there may be a more fundamental difference between periosteal bone metabolism in children and adults. In children, bone formation is continuous, which is the hallmark of modeling.\textsuperscript{7,16} In adults, periosteal bone may undergo cyclical resorption and formation, which is characteristic of remodeling.\textsuperscript{17,18} Because remodeling is the process responsible for bone loss in adults, it is widely studied in the field of osteoporosis research. Bone modeling, however, has received little attention until now.

Most of the available information on human periosteal bone growth is based on radiographic studies, and most were performed at the midshaft of long bones. Studies by Garn et al\textsuperscript{19,20}, which were performed using this approach, are widely cited classics. They measured the width of the second metacarpal in a large number of healthy subjects. The corresponding periosteal apposition rates showed changes with age that resemble percentile charts for height velocity (Fig 2). Growth is rapid during early life but then continuously slows down until it reaches a nadir during early school age. This is followed by a pubertal peak, after which periosteal growth (almost) comes to a standstill.

It is clear that wider bones must have higher midshaft periosteal apposition rates, because this is how they become wider. For example, during male puberty the estimated peak periosteal apposition rate of the metacarpal is \( \approx 0.5 \, \mu m/day \), but it is close to \( 2 \, \mu m/day \) at the midshaft humerus.\textsuperscript{21} What is less widely appreciated is that periosteal growth is not necessarily synchronized between bones. For example, in 3-month-old infants, the humerus grows in width one-third faster than the femur\textsuperscript{8} (Fig 3). At the age of 1 year, the 2 bones expand at approximately the same rate, whereas at 33 months of age, periosteal apposition is almost 4 times as fast at the femur as it is at the humerus. At 5 years of age, this difference in periosteal apposition rate between the 2 bones shrinks to 25% in favor of the femur. These differences in bone growth in width between the humerus and femur mirror the mechanical usage of these extremities during development between 1 and 4 years of age.\textsuperscript{22} When infants start to walk, the femur is exposed to much higher forces and gets stronger quickly. At the same time, the humerus is used less and less for locomotive purposes and, accordingly, humerus strength increase is slow.

**THE CONTROL OF PERIOSTEAL BONE GROWTH**

Research on the regulation of periosteal bone development has focused mainly on systemic hormones. A number of elegant studies have demonstrated that estrogen inhibits, and androgen and growth hormone stimulate, periosteal apposition at diaphyseal bone sites.\textsuperscript{23-25} However, this focus on systemic factors should not make us lose sight of the fact that periosteal bone
development is site specific, whereas systemic hormones and nutrition are blind to structure. Systemic factors, therefore, cannot be the main determinants of what is going on at the peristeum. Clearly, local regulation must predominate, albeit modulated by systemic agents.

One of these site-specific factors is the mechanical load that acts on a bone. For example, when the radius of young pigs is overloaded by partially removing the ulna, the radius is strengthened by rapid periosteal apposition.26 When plastic surgeons transplant a fibula to replace a tibia that has been destroyed by tumor or infection, the fibula quickly hypertrophies and comes to replace a tibia that has been destroyed by tumor or infection, the fibula quickly hypertrophies and comes to replace a tibia that has been destroyed by tumor or infection, the fibula quickly hypertrophies and comes to replace a tibia that has been destroyed by tumor or infection.27 Conversely, disorders that result in removal of mechanical stimulus during growth, such as cerebral palsy, spina bifida, or poliomyelitis, lead to thin bones in the affected segments.28–30

CONCLUSIONS

In the past, research on bone metabolism and development has focused on events that occur on trabecular surfaces. However, in children and adolescents, the changes on these surfaces are relatively small compared with the marked increase in cross-sectional bone size. Much more bone accrues through periosteal bone modeling than through trabecular remodeling. The key to an improved understanding of bone mass accrual in children, therefore, lies with studies on bone modeling on periosteal surfaces.

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