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Orthopaedic Knowledge Update

Pediatrics

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PEDIATRIC ORTHOPAEDIC SOCIETY
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Published 2011 by the
American Academy of Orthopaedic Surgeons
6300 North River Road
Rosemont, IL 60018

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ISBN 978-0-89203-643-1
Printed in the USA



Chapter 9

The Modulation of Skeletal Growth

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Introduction

The anatomic, biomechanical, and biochemical mechanisms regulating the growth of the skeleton include growth plate anatomy, blood supply, function, and endocrine regulation. Experimental studies are improving the understanding of the mechanical modulation of growth of the spine and extremities, and this understanding is being extended to clinical applications. Methods including permanent and reversible epiphysiodesis and hemiepiphysiodesis have been developed for modulating growth and treating angular deformities and growth arrest.

Skeletal Growth

The skeleton is composed of four organs: bone, cartilage, ligaments, and tendons. The skeleton thus is an example of an organ system in which two or more organs work together to provide a common function. Growth (the process by which organs enlarge) is better understood in bones than in other organs such as the heart.¹ The term bone growth is used to indicate an increase in the external dimensions of a bone before skeletal maturity; modeling describes the establishment of a refined architecture of bone tissue after its initial formation; and remodeling describes a change in the architecture of a bone in response to a functional, pathologic, or iatrogenic environmental stimulus, whether internal (systemic) or external. Although longitudinal bone growth ends at skeletal maturity, anabolic and catabolic processes continue constantly throughout life.

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Adaptive remodeling occurs as osteoclasts gradually remove bone tissue and osteoblasts gradually make bone tissue. The remodeling process is of tremendous interest. Recent research has focused on osteoporosis, in which osteoclastic resorption outpaces osteoblastic formation and leads to a net loss of the bone tissue critical for movement and calcium storage.

The two essential processes in new bone formation are endochondral (cartilaginous) and intramembranous ossification. Some bones are formed by intramembranous ossification in the embryonic stage, and others are formed by endochondral ossification of the cartilage anlage or the cartilage model. The cartilage anlage grows in all three dimensions (length, width, and height). Cartilage growth occurs in the epiphyseal plates, apophyseal plates, and articular cartilage. Endochondral ossification also occurs in fracture healing, when vascular invasion brings oxygen essential for the complex, coordinated process of calcifying the cartilage cells and producing bone tissue or callus.

In intramembranous ossification, the cartilage intermediate is absent, and mesenchymal stem cells differentiate directly into osteoblasts that form bone tissue. Intramembranous ossification is primarily responsible for producing the clavicles and flat bones of the skull. The periosteum of long bones appears at 8 weeks' gestation with the primary bone collar. The periosteum contains an outer fibrous layer and an inner cambium layer. The cambium layer contains progenitor cells that develop into osteoblasts responsible for increasing the width of long bones. These progenitor cells also participate in fracture healing, where they develop into both callus-forming chondroblasts and osteoblasts. Fracture callus forms from both endochondral and intramembranous ossification.

Growth Plate Anatomy

The growth plate (physis) develops as the remnant of the cartilage that remains between the primary and secondary ossification centers. During embryogenesis, condensation and chondrification of mesenchymal cells form a three-dimensional cartilaginous anlage. Subsequent vascular invasion into the center of the cartilaginous anlage results in calcification of the cartilage to

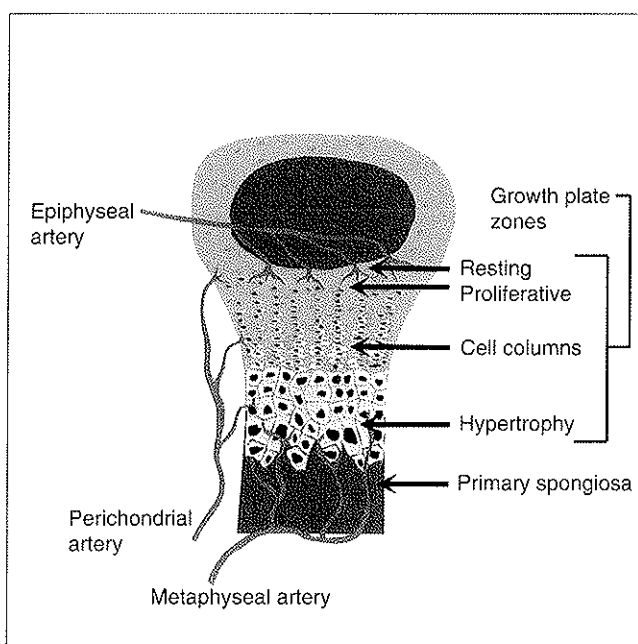


Figure 1 Schematic drawing of the zones of the growth plate and their blood supply. (Adapted with permission from Hefti F: Basic principles: Growth, in Hefti F, ed: *Pediatric Orthopaedics in Practice*. Berlin and Heidelberg, Germany, Springer Medizin Verlag, 2007, p 42.)

create the primary center of ossification. The primary center of ossification gradually replaces the surrounding cartilage, converting it first into bone and then into the medullary cavity. Cartilaginous growth cannot occur in width because of the primary bone collar. The bone grows longitudinally at the ends through endochondral growth; it grows in width by appositional growth, in which new layers of bone tissue are added onto those previously formed. Vascular invasion of the cartilage at the ends of long bones calcifies the cartilage to form secondary centers of ossification.

The growth plates are formed at the junction between the limits of the primary and secondary centers of ossification. The growth plates are responsible for endochondral cartilage growth, which accounts for most longitudinal growth of the upper and lower extremities. The four zones of the growth plate are the resting zone, the proliferative zone, the zone of cell columns, and the zone of hypertrophy. The zone of cell columns and zone of hypertrophy account for approximately one half of the total height of the growth plate. The metaphysis begins subjacent to the zone of hypertrophy, where the chondrocytes undergo apoptosis and subsequently are invaded by blood vessels from the metaphysis. The vascular invasion of the terminal hypertrophic chondrocytes in the zone of hypertrophy calcifies the cartilaginous matrix in the region, creating the primary spongiosa. Modeling of the primary spongiosa with further ossification gradually creates the secondary spongiosa and the metaphyseal bone (Figure 1).

These zones are clinically important because the proliferative zone has potential for cell proliferation, which is almost absent in the zone of hypertrophy.² On the epiphyseal side of the physis, matrix predominates over the cellular elements, whereas on the metaphyseal side the cellular elements predominate over the matrix.³ As a result, a fracture or infection that involves the proliferative zone may affect growth, whereas a fracture or infection that involves the zone of hypertrophy is unlikely to affect growth. Because the growth plate is weakest at the level of the zone of hypertrophy, most fractures propagate through this zone, with a low frequency of growth disturbance. A pediatric bone infection (osteomyelitis) most often develops in the metaphysis because it is an area of relative vascular stasis. The zone of hypertrophy is a relative barrier to blood flow, so there is a low frequency of growth disturbance in association with osteomyelitis.

The growth plate is circumferentially supported by the perichondrial fibrocartilaginous complex.⁴ The perichondrial fibrocartilaginous complex includes the ossification groove of Ranvier, which provides appositional growth expanding the bone circumference; and the perichondrial ring of LaCroix, which provides circumferential support for the growth plate. These structures are clinically important because a traumatic injury involving the ossification groove of Ranvier can affect growth on one side of the bone, thus creating an angulation deformity such as a varus deformity of the ankle (a Salter type VI fracture). At puberty the perichondrial ring of LaCroix provides less support to the growth plate, making it susceptible to a shear stress. Repetitive shear stresses during puberty can create a slipped capital femoral epiphysis.⁴ Similarly, a large shear stress involving the spine can cause a slipped vertebral apophysis having signs and symptoms similar to those of an acute herniated disk.

Blood Supply to the Growth Plate

Blood is supplied to the growth plate by the epiphyseal, metaphyseal, and perichondrial arteries. The central part of the growth plate is supplied by the epiphyseal arteries on the epiphyseal side and the metaphyseal arteries on the metaphyseal side. The periphery of the growth plate is supplied by the perichondrial arteries (Figure 1). The metaphyseal and epiphyseal vascular systems communicate with each other through a rich network of vessels from the perichondrial system. In infants, there is also a vascular communication between the epiphysis and metaphysis through vessels that directly cross the growth plate. This communication decreases with growth, and the zone of hypertrophy is relatively avascular in older children.

The vascular supply is responsible for transporting the nutrients and molecules that regulate the activity of the growth plate through systemic endocrine mechanisms. In a classic study, the epiphyseal and metaphyseal arterial supply to the growth plate of the proximal tibia was disrupted in rabbits.⁵ Disruption of the epi-

physeal arteries caused the death of bony trabeculae as early as the second day and was followed by chondrocyte death, a decrease in matrix staining, and the formation of osseous bridges between the epiphysis and metaphysis. Disruption of the metaphyseal arteries caused an increase in the height of the zone of hypertrophy that was apparent on the first day and was followed by a lack of calcification of the matrix in the primary spongiosa. There was no evidence of death of any of the osteocytes in the metaphysis. The authors concluded that the epiphyseal arteries supplied the essential nutritive and metabolic requirements of the growth plate.⁵ More recent investigators have noted that the proximal femoral growth plate does not always develop a complete growth arrest in patients with Legg-Calvé-Perthes disease. The hypothesis that disruption of the epiphyseal vasculature does not inevitably lead to a complete growth arrest was tested in piglets, with the finding that complete disruption of the epiphyseal vasculature did not lead to diffuse growth plate damage in most femoral heads.⁶ Most of the animals did not develop a growth arrest, but they had decreased growth in comparison with the normal side. The authors concluded that the epiphyseal vasculature is not the sole source of nutrition for the proximal femoral growth plate, as was traditionally believed.⁶ Laboratory studies of the delivery of fluoresceinated dextrans to the murine growth plate confirmed these findings. A study of the epiphyseal, metaphyseal, and perichondrial vascular supply to the murine growth plate found that small molecules (as large as 10 kDa) pass freely to the growth plate from the metaphyseal and epiphyseal sides.⁷ In contrast, larger dextrans (40 kDa or larger) did not enter the growth plate at all. These findings suggest that molecules of low molecular weight, such as basic nutrients and systemic hormones no larger than 10 kDa, have access to the growth plate from the epiphyseal and metaphyseal sides. Larger dextrans can enter the growth plate by diffusion through large physiologic pores for the transport of proteins or through the metaphyseal capillaries, which lack a basement membrane and are permeable even to high molecular weight molecules.

In an infant, the vessels crossing the growth plate may allow an osteomyelitis developing in the metaphysis to rapidly decompress into the epiphysis and adjacent joint, leading to osteonecrosis and septic arthritis. These vessels persist into childhood, although they become less patent; as a result, the growth plate, unlike the articular cartilage, does not form an absolute barrier to the spread of tumors. Vascular communication between the metaphysis and epiphysis gradually diminishes during childhood, and the perichondrial vascular system gradually begins to break down. Any injury to the perichondrial vascular system during this time can have disastrous consequences for the epiphysis, including osteonecrosis (as in patients with Legg-Calvé-Perthes disease), an unstable slipped capital femoral epiphysis, or femoral neck fracture.

Growth Plate Function

The endochondral growth of an epiphyseal growth plate is monopolar, with longitudinal growth directed away from the resting zone. In contrast, the endochondral growth of the apophyseal growth plate is bipolar, with the resting zone in the middle and growth in both directions. The approximate rate of epiphyseal endochondral growth can be calculated as the final chondrocyte height, in microns, multiplied by the chondrocyte proliferation rate over a given period of time.⁸ Higher growth rates are associated with an increase in chondrocyte height, matrix synthesis, height of the zone of hypertrophy, and chondrocyte proliferation rate.²

Endocrine Regulation of Growth

The process of longitudinal bone growth is governed by a complex network of endocrine signals produced by growth hormone, insulin-like growth factor-I (IGF-I), glucocorticoid, thyroid hormone, estrogen, androgen, vitamin D, and leptin.⁹ Some of the local hormonal effects are mediated by paracrine factors that control chondrocyte proliferation and differentiation. Nutritional factors, mechanical loading, and soft-tissue constraints also modulate longitudinal growth, but their effects are ultimately mediated by complex endocrine controls; for example, IGF-I levels decline in malnourished patients. Maturation of the growth plate and the eventual cessation of growth are associated with changing levels of systemic hormones, especially estrogen; it also appears that the growth plate chondrocytes can undergo only a finite number of cell divisions.⁹

Clinical studies of diseases characterized by deficient growth hormone and IGF-I, as well as animal studies, have established the importance of these hormones in regulating longitudinal bone growth.^{9,10} Recombinant forms of growth hormone and IGF-I are available for clinical use in augmenting longitudinal bone growth, and they have a positive effect in reversing the deleterious effects of hormone deficiency. Both hormones act directly on the growth plate, although the exact biochemical pathways by which they affect bone growth remain to be elucidated. Growth hormone appears to act both directly, by causing an increase in the chondrocyte proliferation rate; and indirectly, by stimulating local production of IGF-I, which primarily stimulates chondrocyte differentiation and hypertrophy. The stimulatory effects of IGF-I on longitudinal bone growth also may be related to its antiapoptotic effects in the growth plate.¹⁰ Increasing the height of the zone of hypertrophy may decrease the ability of the physis to resist shear forces, and these anatomic changes may contribute to the increased risk of scoliosis progression and slipped capital femoral epiphysis in patients taking growth hormone.¹¹

The proliferation of chondrocytes in the growth plate is under the control of a local feedback loop that determines the rate at which cells leave the proliferative zone and enter the zone of cell columns.¹² This feed-

back loop primarily involves three signaling molecules synthesized by growth plate chondrocytes: parathyroid hormone-related peptide, Indian hedgehog, and transforming growth factor- β .

During puberty, increases in growth hormone and testosterone can negatively affect the strength of the growth plate. Growth hormone not only stimulates growth by increasing the activity of the growth plate but also lowers the loading capacity of the growth plate. Testosterone promotes growth and reduces the mechanical strength of the growth plate. Although estrogen promotes maturation, indirectly increasing the mechanical strength of the growth plate, the negative effects of growth hormone and testosterone may overpower the positive effects of estrogen.¹ The decrease in mechanical strength during puberty creates a predisposition to epiphyseal separation, particularly in growth plates that are subjected to high shear loads. Slipped capital femoral epiphysis occurs with relative frequency in overweight individuals.⁴

The Mechanical Modulation of Skeletal Growth

Growth alteration by mechanical forces was first identified in the early 19th century by Jacques Delpech, at the University of Montpellier, France. Delpech stated that the release of abnormal pressure from a physis causes growth stimulation. The concept was expanded into the Hueter-Volkmann law, which states that growth is inhibited by compression and stimulated by distraction;¹³ and Wolff's law, which states that bone tissue remodels over time in response to prevailing mechanical demands.¹⁴ Decreased physical activity rapidly leads to osteopenia; conversely, bone density increases in physically active individuals. The internal architecture of bones includes both cortical thickness and trabecular parameters such as density, connectivity, and trajectories. The strength of a bone is determined by a complex interplay of these architectural variables so that a simple measurement of bone mineral density is not an accurate predictor of bone strength. Although it appears that the remodeled bone architecture is optimal for providing maximal strength in relation to tissue mass, neither experimental studies nor analytical simulations have discovered any objective rules governing the adaptation of bone to mechanical demands.^{14,15} Repetitive loading, rather than static loading, is necessary to maintain homeostasis and induce remodeling.¹³

Quantification of the Hueter-Volkmann Effect

Several studies have confirmed that sustained loading in distraction causes an increase in the growth rate, whereas loading in compression causes a decrease. Growth rates were compared using two different compression and distraction loads in two anatomic locations (tibia and vertebra) in rats, rabbits, and calves at two different ages.¹⁶ The modulation of growth was found not to differ between species or by age. The

growth rate sensitivity to stress averaged 17% per 0.1 MPa, and the range was 9% to 24% per 0.1 MPa for different growth plates. The fast-growing proximal tibia appeared to be slightly more sensitive to stress than the slow-growing vertebra.

The mechanical modulation of growth by sustained compression or distraction is associated with alterations in the growth plate. The reduction or increase in growth rate with compression or distraction, respectively, is associated with a corresponding change in the number of proliferative chondrocytes, the mean chondrocytic height, and the height of the zone of hypertrophy.^{17,18} Compression loading causes a decrease in the chondrocyte proliferation rate, chondrocyte cell height, and height of the zone of hypertrophy; distraction loading causes an increase in these parameters.¹⁹

Dynamic Loading and Growth Modulation

The effect of dynamic loading on growth is unclear. One study reported decreased growth, but another found no change in growth in animals subjected to three different levels of physical activity.^{20,21} In a lamb model, 90% of proximal tibia growth occurred during periods of recumbency, when the growth plate was not subjected to dynamic loading.³ Further study is needed to determine the overall effects of dynamic loading relative to the effects of continuous or sustained loading.

The Effect of Periosteal Resection on Growth

Longitudinal growth can be influenced by the integrity of the periosteum, possibly through a vascular effect or, in part, the growth-inhibiting effect of tension in the periosteum.^{13,22} Periosteal stripping alone has a limited clinical effect. In a lamb model, the proximal tibial periosteum was resected, and subsequent growth velocity was measured using implanted microtransducers or fluorochrome labeling.²³ The average growth velocity was 273 microns per day after periosteal resection, compared with 201 microns per day in the contralateral limb of the same animals. This growth rate difference had only a small effect on overall bone length, however. The increased growth was secondary to increased chondrocyte height rather than to an increase in chondrocyte proliferation or matrix production.

Growth Modulation and Scoliosis

The Cobb angle measurement of scoliosis represents the sum of the angular wedging of each vertebra and disk between the end vertebrae.²⁴ The progression of the vertebral-wedging component of scoliosis during growth is often attributed to the operation of the Hueter-Volkmann law of mechanically modulated endochondral growth. As a result, the rapid progression of scoliosis during the adolescent growth spurt may occur because a scoliotic spine has greater loading on the concave side. This asymmetric loading causes asymmetric growth, which causes vertebral wedging and leads to a vicious cycle of scoliosis progression.²⁵ To test the

vicious cycle hypothesis, an Ilizarov-type external fixator with an imposed 30° scoliosis and axial compression was applied to the tail vertebrae of 10 immature rats for 6 weeks.²⁶ The tail vertebrae gradually developed a vertebral wedge deformity averaging 15°, which was reported to be secondary to asymmetric growth. The reversibility of the growth disturbance was studied by reversing the loading in one group of rats and removing the loading in a second group.²⁷ The mean vertebral wedging was 0° when the loading was reversed, and the mean wedging was 7° when the loading was removed.

Part-Time Versus Full-Time Loading

A study of the effect of compression loading on the longitudinal growth of rat tibiae and vertebrae found that full-time loading (24 hours a day) had twice the effect of part-time loading (12 hours a day).²⁸ Part-time loading had the same effect regardless of whether it was applied during daytime or nighttime hours. The findings of this laboratory study cast doubt on the clinical value of part-time (night) bracing, compared with full-time bracing. If the appropriate loading can be applied, full-time bracing should lead to the most rapid possible correction of skeletal deformity.

Procedures to Modulate Skeletal Growth

Physal Bar Resection

Physal bar resection is recommended for children if a bony bridge across a growth plate is tethering growth and causing deformity. The procedure involves surgical resection of the bony bar that is tethering the growth plate, with placement of a spacer such as fat to allow normal growth to resume. If the bony bridge involves less than 50% of the growth plate and the child has considerable remaining growth, physical bar resection is reported to be 70% successful in restoring some longitudinal growth.²⁹ In a young child with a bony bar that has caused a severe deformity, physal bar resection can be combined with an osteotomy to simultaneously correct the deformity and allow growth resumption.

Epiphysiodesis

In the traditional Phemister epiphysiodesis, a block of bone was removed from the medial and lateral sides of the bone, including a portion of the metaphysis, growth plate, and epiphysis. The entire growth plate was then ablated using curets, and the bone blocks were rotated 90° and reinserted into the bone. An epiphysiodesis treated a limb-length discrepancy by creating a growth arrest in one growth plate to allow a gradual correction as normal growth occurred on the opposite side. The Phemister technique was modified as a percutaneous technique that had similar results and caused less scarring.³⁰

The results of a growth arrest procedure depend on an accurate assessment of the amount of remaining growth. Chronologic age is unreliable for estimating remaining growth; skeletal age, as depicted in the Greulich and Pyle atlas, is more accurate.³¹ An evaluation of the growth centers of the elbow and hand, in association with skeletal age determined using the Greulich and Pyle atlas, was found to increase the accuracy of estimates of remaining growth.^{32,33}

Reversible Epiphysiodesis

Epiphyseal stapling has been used to arrest growth, with resumption of growth allowed by removing the staples.³⁴ The initial tendency of the staples to break was remedied by reinforcing the corners where most breaks occurred. The currently used Blount staples (Zimmer; Warsaw, IN) are constructed of cobalt-chromium and are more durable than earlier staples.

Minimally invasive procedures for reversibly arresting bone growth include reinforced Blount stapling and percutaneous epiphysiodesis using transphyseal screws (PETS).³⁵ Growth is arrested while the implant is in place but is allowed to resume when the implant is removed. This innovation allows for a limb-length discrepancy to be corrected before a major deformity develops. It is no longer necessary to perform the surgery at the precise skeletal age at which there is just enough remaining growth in the contralateral extremity to correct the limb-length discrepancy. In the newer procedures, accurate placement of the staples is crucial (if staples are used). In 50% of patients, a mechanical axis deviation of 1 cm or more was found after staple epiphysiodesis, compared with preoperative measurements;³⁶ 89% of these mechanical axis deviations were varus in nature. Most of the axis deviations occurred in the proximal tibia, and particular caution therefore is required when placing staples in this location.

Hemiepiphysiodesis

Angular deformities of the lower extremity or spine can be treated using hemiepiphysiodesis. The lower extremity procedure is similar to epiphysiodesis, and it requires an accurate assessment of remaining growth to avoid undercorrection or overcorrection. Blount staples and PETS have been successfully used to induce a reversible hemiepiphysiodesis. The recently developed 8-plate (eight-Plate; Orthofix, McKinney, TX) can be used to create guided growth.³⁷ This implant is similar to a staple except that the screws toggle in the holes in the plate, using a tension band concept to move the fulcrum of asymmetric growth to the bone surface (Figure 2). The technique slows growth on one side of the bone while allowing normal growth on the opposite side to correct a deformity such as genu varum. A slight overcorrection is recommended because some rebound growth stimulation has been reported after the removal of a guided-growth implant.³⁷ If too much dissection is used to place the implant, growth arrest is a possible complication. Therefore, a careful approach is

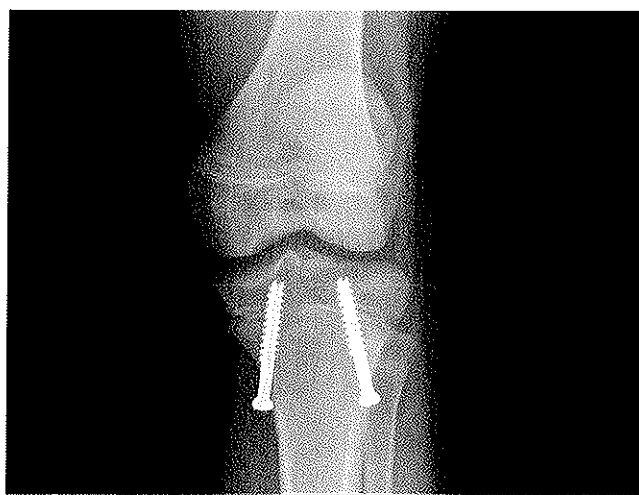


Figure 2 AP radiograph showing 7.3-mm transphyseal screws crossing the proximal tibial growth plate of a 13-year-old boy to create a percutaneous epiphysiodesis (the PETS technique).

recommended, with limited dissection during implant insertion.

The PETS Technique

The PETS technique involves placing 7.3-mm cannulated, threaded screws across the growth plate to tether growth. A screw may be placed on one side to function as a hemiepiphysiodesis for correcting an angular deformity, or screws may be placed on both sides to function as an epiphysiodesis for correcting a limb-length discrepancy (Figure 3).³⁵ The advantages of the minimally invasive PETS technique include percutaneous screw placement through small incisions; a minimal risk of screw dislodgement; reversible growth arrest; and the use of reverse-cutting threads, which permit easy screw removal, if necessary. Percutaneous hemiepiphysiodesis using the PETS technique was found to be simple, fast, and reproducible, with a low morbidity rate and rapid rehabilitation.³⁸ The screws can cause pain if they are left protruding, particularly in the proximal medial tibia, where the screw can irritate the pes anserinus tendons. The PETS technique is designed to arrest growth, and it will fail if there is insufficient remaining growth to achieve the desired effect. In one study, complete angular correction occurred early in 13 growth plates of 6 patients who had significant remaining growth; growth resumed in all growth plates when the screws were removed.³⁹

The 8-Plate Technique

The 8-plate is a tension band plate construct designed to allow guided growth in deformity correction.³⁷ The cannulated screw-plate device was designed to decrease the frequency of staples backing out of the bone, particularly in young children. The 8-plate is positioned on the cortex of the bone, moving the fulcrum of correc-



Figure 3 AP radiograph showing 8-plates in the distal medial femur and proximal medial tibia, as used to create a hemiepiphysiodesis for correcting genu valgum by guided growth in a 12-year-old girl. Although the screws are diverging with growth (arrow), no growth is allowed at the medial cortices.

tion to the side of the bone, to allow more rapid correction of angular deformities (Figure 2). The toggling of the screws allows most of the growth plate to grow normally while preventing growth directly under the 8-plate.

Breakage of the titanium screws was reported in large patients treated with the 8-plate, and the study authors concluded that staple hemiepiphysiodesis is as effective with respect to rates of correction and complications as the 8-plate for guided correction of angular deformity.⁴⁰

Surgical planning for any type of guided growth procedure to correct skeletal deformity must simultaneously address the postoperative asymmetric growth and the amount of growth remaining. If the surgery is performed too early with respect to remaining growth, an overcorrection may develop; this can be rectified by removing the implant if the hemiepiphysiodesis or guided growth procedure is reversible. If the surgery is performed too late, an undercorrection or failure may develop; this cannot easily be reversed. Lateral hemiepiphysiodesis was reported to be unsuccessful in 66% of patients with adolescent tibia vara who were at least 10 years of age at the time of surgery; 94% of the patients had a body mass index above the 95th percentile.⁴¹ The high failure rate was associated with patient age of 14 years or older, severe tibia vara, and patient obesity, which contributed to the Hueter-Volkman effect of decreased growth on the compression side of the physis.

Summary

There is tremendous potential for developing less invasive surgical techniques to modulate growth and correct skeletal deformities, following basic science principles. In the future, an understanding of the biochemical feedback mechanisms involved in growth will allow the development of nonsurgical techniques to modulate growth and correct skeletal deformities. Novel techniques will be extremely valuable for the fusionless treatment of spine deformities, but care must be taken to responsibly develop and apply these techniques.

Acknowledgment

The authors thank Keith M. Bagnall, PhD for his constructive critique of the contents of this chapter and Paul J. Zimakas, MD for his contribution to the hormonal regulation of longitudinal growth.

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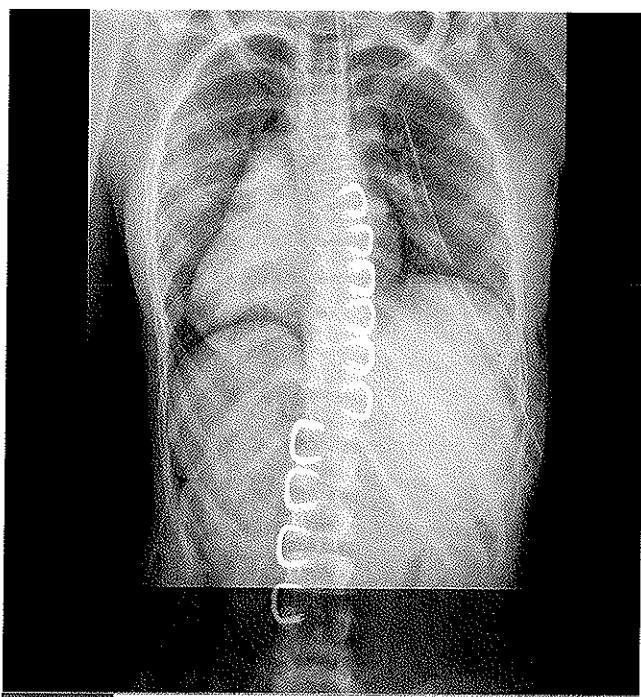


Figure 4 PA radiograph showing the use of nitinol shape-memory staples in a 12-year-old girl with adolescent idiopathic scoliosis. A convex vertebral hemiepiphysiodesis was created to correct the scoliosis by growth modulation. (Courtesy of John T. Braun, MD, Burlington, VT.)

Methods to Modulate Spine Growth

Hemiepiphysiodesis

A combined anterior and posterior hemiepiphysiodesis of the spine has been successful in treating children with congenital scoliosis caused by a hemivertebra or an unsegmented bar. This procedure allows for gradual correction of the scoliosis with growth. Fusionless instrumentation systems using a growing rod or vertical expandable prosthetic titanium rib (VEPTR) have been developed for treating congenital scoliosis.⁴²⁻⁴⁴

Vertebral Stapling

Vertebral stapling is designed to span the disk and growth plates of two adjacent vertebrae to tether growth on the convex side of a scoliosis deformity. This technique was used as a model of spine hemiepiphysiodesis in creating a thoracic scoliosis in pigs; the staple was supplemented by two screws to preclude staple dislodging.⁴⁵ The height of the zone of hypertrophy, the chondrocyte cell height, and the cell width were found to be decreased on the stapled side compared with either the contralateral side or control vertebrae.

In principle, the process of convex tethering of growth to allow gradual correction of a scoliosis secondary to growth on the concave side appears to be sound. Early experience with vertebral stapling was disappointing, however. There was limited correction be-

cause the patients had severe scoliosis and little remaining growth. Staples dislodged because they spanned the disk spaces; investigators speculated that the forces generated by the staples might be absorbed by the flexible disks, thus minimizing the forces across the growth plates, as observed in a porcine model of spine stapling.⁴⁵

A staple constructed of nitinol, which is a shape-memory alloy, was designed to prevent vertebral staple dislodgement. The prongs of the nitinol staple are a standard straight shape when cool, to allow easy insertion. At body temperature, the prongs clamp down into the bone in a C-shape to prevent staple dislodgement (Figure 4). In an uncontrolled case series, curve progression of more than 10° was reported in 18% of curves greater than 30° and 0% of curves smaller than 30° after nitinol vertebral stapling.⁴⁶ Thoracoscopic insertion is recommended for nitinol staples. The role of vertebral stapling has not been determined, and no intermediate- or long-term results are available. This procedure currently is recommended only for a low-grade scoliosis if the alternative is observation, bracing, or casting. The device has not been approved by the US Food and Drug Administration for this use.

Anterolateral Vertebral Tethering

A novel fusionless treatment method for scoliosis attempts to modulate growth by tethering the anterolateral aspect of the spine.⁴⁷ An anterolateral tether was created in 12 minipigs by placing four staple-screws connected by a polyethylene tether over the anterolateral aspect of four consecutive thoracic vertebrae. After 12 months, radiographs showed an average scoliosis of 30°, with associated vertebral wedging in all four vertebrae. This fusionless procedure can be performed thoracoscopically.

A recent case report described an intriguing preliminary outcome of treatment for a boy with juvenile idiopathic scoliosis, whose right thoracic curve from T6 to T12 had progressed from 25° to 40° in 3 years.⁴⁸ He was treated with a minithoracotomy, and vertebral body screws were placed at each level. A polypropylene tether 4.5 mm in diameter was secured into the screw heads to create an anterior tether without fusion. The postoperative curve was 25°; 4 years later, the curve was 6°.

Limitations of Growth-Tethering Techniques

A potential limitation of the use of growth modulation procedures involving vertebral staples, nitinol staples, or anterolateral flexible tethering is the limited remaining spine growth in a patient with progressive adolescent idiopathic scoliosis. The ideal time for a growth-tethering procedure is 1 to 2 years before peak growth velocity, the onset of menses, and closure of the triradiate cartilage. However, most patients have a small curve at this age, and the clinician cannot be certain whether the scoliosis will continue to be mild or will progress to a large curve.

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32. Charles YP, Diméglio A, Canavese F, Daures JP: Skeletal age assessment from the olecranon for idiopathic scoliosis at Risser grade 0. *J Bone Joint Surg Am* 2007; 89(12):2737-2744.
A simplified olecranon method was developed to assess skeletal age at 6-month intervals during puberty. The method was evaluated in 100 boys and 100 girls with idiopathic scoliosis and was found to be simple, reliable, and precise, complementing the Risser sign and triradiate cartilage evaluation. Level of evidence: II.
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A simplified skeletal maturity staging system using the Tanner-Whitehouse-III descriptors was found to correlate more strongly with the curve progression behavior of patients with idiopathic scoliosis than the Risser sign or Greulich and Pyle skeletal ages. Level of evidence: I.
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The preoperative and final radiographs of 54 patients who underwent staple epiphysiodesis revealed a mechanical axis shift of 1 cm or more in 50%, most of which were into varus. Poor proximal lateral tibial staple placement accounted for some of the deformities. Level of evidence: IV.
37. Stevens PM, Klatt JB: Guided growth for pathological physes: Radiographic improvement during realignment. *J Pediatr Orthop* 2008;28(6):632-639.
The authors performed a guided growth procedure in 14 children with rickets. Of the 53 deformities treated with staple fixation (in 10 children), 45% had staple migration. Of the 15 deformities treated with 8-plate fixation (in 4 children), none had migration. Guided growth to maintain alignment is recommended to avoid later surgery. Level of evidence: IV.
38. Mesa PA, Yamhure FH: Percutaneous hemiepiphysiodesis using transphyseal cannulated screws for genu valgum in adolescents. *J Child Orthop* 2009.
The authors conducted a prospective evaluation of 52 patients (100 knees) using the PETS technique to create a distal femoral hemiepiphysiodesis. The tibiofemoral angle was satisfactorily corrected, and the authors concluded that PETS is a simple, fast, and reproducible technique with a low morbidity rate.
39. Khoury JG, Tavares JO, McConnell S, Zeiders G, Sanders JO: Results of screw epiphysiodesis for the treatment of limb length discrepancy and angular deformity. *J Pediatr Orthop* 2007;27(6):623-628.
The PETS technique was used in 30 patients to treat a limb-length discrepancy and 30 patients to treat an angular deformity. Improvement occurred in all patients. In 13 growth plates of 6 patients, screws were removed after correction and growth resumed. PETS combines a minimally invasive percutaneous technique with reversibility.
40. Wiemann JM IV, Tryon C, Szalay EA: Physeal stapling versus 8-plate hemiepiphysiodesis for guided correction of angular deformity about the knee. *J Pediatr Orthop* 2009;29(5):481-485.
The authors compared 39 limbs treated with staple hemiepiphysiodesis and 24 limbs treated with an 8-plate. There was no difference between the two groups in the rate of correction or the frequency of complications. The rate of complications was greater in patients with pathologic physes. Level of evidence: III.
41. McIntosh AL, Hanson CM, Rathjen KE: Treatment of adolescent tibia vara with hemiepiphysiodesis: Risk factors for failure. *J Bone Joint Surg Am* 2009;91(12):2873-2879.
Lateral hemiepiphysiodesis was unsuccessful in 66% of 49 patients with adolescent tibia vara who were at least 10 years of age and had an average body mass index of 40.7. Lateral hemiepiphysiodesis may be an option for thin patients with mild tibia vara, but it is likely to fail in older adolescents with a high body mass index and greater deformity. Level of evidence: II.
42. Thompson GH, Akbarnia BA, Campbell RM Jr: Growing rod techniques in early-onset scoliosis. *J Pediatr Orthop* 2007;27(3):354-361.
Early onset scoliosis can be treated using a single growing rod, dual growing rods, or a VEPTR. Dual growing rods with lengthening every 6 months had better results than single growing rods. The VEPTR was particularly beneficial for treating congenital scoliosis and fused ribs or for children with severe thoracic insufficiency syndrome.
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44. Yazici M, Emans J: Fusionless instrumentation systems for congenital scoliosis: Expandable spinal rods and vertical expandable prosthetic titanium rib in the management of congenital spine deformities in the growing child. *Spine (Phila Pa 1976)* 2009;34(17):1800-1807.
A review of research articles and presentations was used to compare growing rods and VEPTR. The authors conclude that growing rods should be used if the primary

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An apparently linear relationship between stress and growth rate was found. Vertebrae and the proximal tibiae had relatively small differences in growth rate sensitivity to stress despite large differences in growth rates. The results may apply to human growth plates.
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18. Stokes IA, Clark KC, Farnum CE, Aronsson DD: Alterations in the growth plate associated with growth modulation by sustained compression or distraction. *Bone* 2007;41(2):197-205.
Growth plates that had been subjected to sustained loading were examined histologically. Reduced growth rate with compression and increased growth rate with distraction were associated with corresponding changes in the number of proliferative chondrocytes and the final (maximum) hypertrophic chondrocytic height. Chondrocytic enlargement was the most important contributor to altered growth rates.
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Tail vertebrae of immature rats were subjected to a static or dynamic (1 Hz) asymmetric load. The resulting wedge angles were greater in the dynamically loaded vertebrae. This finding suggests that growth modulation devices applied to a spine with scoliosis should use dynamic loading.
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This study of growth plates of chick embryonic tibiotarsi refuted the generally accepted hypothesis that growth augmentation after division of the periosteum results from release of compressive force created by tensioned periosteum. The measured residual stress would not have produced substantial growth rate alteration based on present understanding of stress-induced growth modulation.
23. Sansone JM, Wilsman NJ, Leiferman EM, Noonan KJ: The effect of periosteal resection on tibial growth velocity measured by microtransducer technology in lambs. *J Pediatr Orthop* 2009;29(1):61-67.
The authors circumferentially resected the proximal tibial metaphyseal periosteum in five lambs. Sustained growth acceleration developed secondary to axial elongation of the hypertrophic chondrocytes, but its limited magnitude suggests that this technique should be considered as an adjunct to other procedures.
24. Stokes IA, Aronsson DD: Disc and vertebral wedging in patients with progressive scoliosis. *J Spinal Disord* 2001;14(4):317-322.
25. Stokes IA: Analysis and simulation of progressive adolescent scoliosis by biomechanical growth modulation. *Eur Spine J* 2007;16(10):1621-1628.
Different rates of growth were simulated in the convex and concave sides of vertebrae in a scoliosis, using published data on spine load asymmetry and growth sensitivity to altered stress. The rate of scoliosis progression was similar to that observed in adolescents, suggesting that biomechanical factors are responsible for progression during the growth spurt.
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The growth plates of growing rats were compression loaded for 8 days, during 12 daytime hours, 12 nighttime hours, or all 24 hours. Growth suppression (modulation) was in proportion to the duration of loading and was approximately half as much in the growth plates that received part-time loading.
29. Marsh JS, Polzhofer GK: Arthroscopically assisted central physal bar resection. *J Pediatr Orthop* 2006;26(2):255-259.
After 37 central physal bars were resected using an arthroscopically assisted technique, growth occurred in 70% of patients, with failure in 13%. Failures occurred when the bar was caused by infection or its size approached 50% of the physal surface. This technique provides the best visualization of the bar.
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deformity is in the spine. Expansion thoracostomy and VEPTR should be used if the primary deformities include rib fusions and thoracic insufficiency syndrome.

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Staples were applied unilaterally to midthoracic vertebrae of skeletally immature pigs. After 8 weeks, the vertebral hypertrophic zone height was reduced in inverse proportion to the distance from the staples, indicating a graded growth modulation across the vertebra.

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After vertebral body stapling in 39 patients with adolescent idiopathic scoliosis, 87% had curve stability (progression of no more than 10°). A fusion was necessary in 2 patients. Stapling is recommended for immature patients with adolescent idiopathic scoliosis who have curves of 20° to 45°, with 5° of progression for curves of less than 25°. Level of evidence: IV.

47. Newton PO, Upasani VV, Farnsworth CL, et al: Spinal growth modulation with use of a tether in an immature porcine model. *J Bone Joint Surg Am* 2008;90(12): 2695-2706.

A staple-screw construct connected by a polyethylene tether was applied over four consecutive thoracic vertebrae of 7-month-old minipigs. There was a progressive increase in Cobb angle to 30° at 12 months, along with an unexpected wedging of disks opposite to that of the vertebrae, with nucleus migration to the side of the tether.

48. Crawford CH III, Lenke LG: Growth modulation by means of anterior tethering resulting in progressive correction of juvenile idiopathic scoliosis: A case report. *J Bone Joint Surg Am* 2010;92(1):202-209.

This case report describes the treatment of a boy with juvenile scoliosis using an anterior tethering procedure without fusion, which caused a gradual correction of the scoliosis from 40° preoperatively to 6° at 48-month follow-up. The authors were not aware of any similar earlier report.

