GROWTH PLATE AND BONE DEVELOPMENT

Essay

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Chapter 1

Introduction

Introduction

All skeletal structural elements initially form as mesenchymal cellular condensations during the embryonic period. Some of these cellular groupings modulate to fibrocellular tissue and ossify directly, forming membrane-derived, or intramembranous, bone. This is characteristic of all cranial and most facial bones, as well as the initial formation of the clavicle.

In contrast, the appendicular and axial skeletal elements are derived from the initial transformation of the mesenchymal model to a cartilaginous model, and its subsequent transformation to an ossified structure by two discrete processes: the formation of an osseous collar around the mid shaft of the cartilaginous anlage, with associated vascular invasion to form the primary ossification centre, and a later, usually postnatal, vascular-mediated, osseous transformation of the chondroepiphysis to form the secondary epiphyseal ossification centre at each end. This progressive, integrated replacement of the preexistent and continuously dynamic cartilage model by osseous tissue is termed endochondral ossification (Ogden, 1982).

The growth plate or the physis - the cartilaginous plate which is present between the metaphysis and the epiphysis - is the essential mechanism of endochondral ossification prenatally and postnatally. The primary function of the physis is rapid, integrated longitudinal and latitudinal growth (Rockwood, 1991).

The factors that control rate of growth include: genetic, vascular, mechanical and hormonal factors.

There are two basic types of growth plates, discoid and spherical, most primary growth plates of long bones are discoid.

Microscopically the growth plate has a characteristic architectural pattern, this include the following zones: the zone of growth, the zone of cartilage maturation, and the zone of transformation.

The growth plate can be affected by many factors, the most important is traumatic. However, drugs, ionizing radiation, thermal injuries, infections and tumours can all affect the growth plate to varying degrees.

Injury of the growth plate is a very important orthopaedic problem. There are multiple patterns of injury, each carrying a different prognosis. Whenever encountering such an injury the main concern is the possibility of subsequent growth slow down or arrest which may be diffuse - total - or localized (Rockwood, 1991).

Many classifications are known for traumatic physeal injury. The most important is the Salter and Harris classificaiton. They classify physeal injury into 5 types (Rockwood - 1991).

Management of physeal injury is variable, it may be so simple and may be in need for surgical interference.

Chapter 2

Development of long bones
(Endochondral ossification)

Endochondral ossification

All bones begin as mesenchymal condensations during the embryonic period (the term mesenchyme refers to the primitive connective tissue cells and their intercellular matrix that arise from mesoderm; the term condensation refers to an increase in the number of cells or intercellular fibres, or both) (33).

At each site where a limb will later emerge, a small structure known as a limb bud grows out from the embryo nearly at the beginning of the 5th week of gestation. This limb rudiment is basically a mesodermal outgrowth covered by ectoderm (23).

The development of a cartilaginous model :

The mesenchymal cells then differentiate into chondroblasts that produce cartilage matrix (Fig. 2-1 A). This intercellular matrix appears first in the centre of the mesenchymal condensation. The cells become separated, and the region presents a lighter staining appearance. This process represents the beginning of chondrification and constitutes a stage often called precartilage. The deposition of cartilage matrix spreads peripherally to the margin of the original condensation. Here the mesenchymal cells become so oriented as to form a perichondrium (33) (Fig. 2-1 B). The perichondrium is made up of an inner chondrogenic layer and an outer fibrous layer. At this stage, no osteoblasts are produced by the cells in the chondrogenic layer because differentiation is taking place in an avascular environment. Fibroblasts differentiate in the fibrous layer and begin producing collagen, with the result that this layer becomes a dense fibrous covering (23).

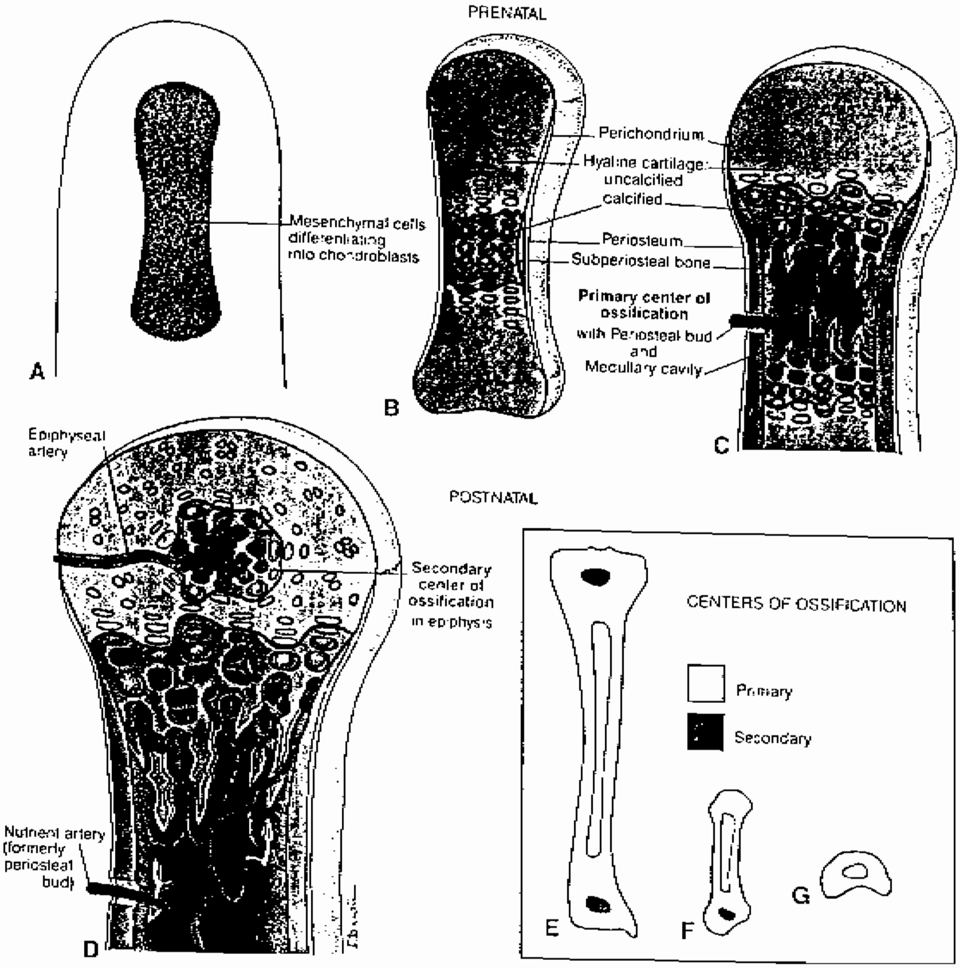

*Fig. 2-1: Diagrammatic representation of endochondral ossification. (A) Mesenchymal cells condense and differentiate into chondroblasts. (B) Cartilage in midregion of model calcifies, and a collar of bone forms under the periosteum. (C) Calcified cartilage begins to break down, and periosteal bud (periosteal capillaries with osteogenic cells) grows in and establishes primary (diaphyseal) centre of ossification. Medullary cavity begins to form. (D) Secondary (epiphyseal) centres of ossification develop postnatally by the same process. (Inset) The arrangement of primary and secondary centres of ossification in long and short bones. (E) Typical long bone with primary centre and a secondary centre at both ends (tibia). (F) A long bone with primary centre and only a proximal secondary centre (phalanx). (G) Typical short bone with primary centre but no secondary centres (lunate bone of wrist). (From: **Cormack D. H.** : Ham's Histology. 9th. ed., chapter 12, p. 273- 323. Philadelphia, J. B. Lippincott company, 1992).*

Growth of the cartilage model :

Ensuing growth of the cartilage model is a combined result of interstitial and appositional growth. Its increase in length is mostly due to repeated division of its chondrocytes, accompanied by the production of additional matrix by the daughter cells, whereas widening of the model is primarily due to the further addition of matrix to its periphery by new chondroblasts that are derived from the chondrogenic layer of its perichondrium.

Most of the cellular proliferation responsible for the increase in the length of the model occurs near its ends rather than in its midsection. As the model continues to grow, the chondrocytes in its midsection undergo hypertrophy (enlarge) and mature. However, this stage is associated with the deposition of insoluble calcium salts in the thin partitions of matrix that separate their lacunae (Fig. 2-1 B). This heavy mineralization of cartilage matrix eventually impedes the free diffusion of nutrients and oxygen through it which is essential for the viability of chondrocytes. So that after the midsection of the cartilage model has become heavily calcified, it begins to become replaced by bone. In the meantime, capillaries grow into the part of the perichondrium that ensheaths the midsection of the model (23).

The cells produced by the inner layer of the perichondrium then begin to differentiate in a vascular environment, with the result that they become osteoblasts that start to lay down a thin collar of bone matrix around the midregion of the model (Fig. 2-1 B). Now that differentiation of the cells arising from the inner layer of the perichondrium leads to bone production, this membrane is referred to as a periosteum. The bony collar that forms below the periosteum and that strengthens the midregion of the model where it has become weakened through loss of calcified cartilage is described as subperiosteal bone, but it is the same kind of bone that is formed at other sites (Fig. 2-1 B-C). With increasing vascularity of the periosteum (a change that is necessary for continuing bone formation), the osteogenic and fibrous layers of this membrane become more distinct.

Development of the primary centre of ossification :

Periosteal capillaries, accompanied by osteogenic cells, invade the calcified cartilage near the middle of the model and thereafter supply its interior (Fig. 2-1 C). Together with their associated osteogenic cells, these vessels comprise a structure called the periosteal bud (Fig. 2-1 C); however, some bones develop more than one periosteal bud. These periosteal capillaries grow into the cartilage model and initiate development of a primary centre of ossification that is so called because the bone tissue it produces eventually replaces most of the cartilage in the model. The majority of long bones develop such an ossification centre toward the end of the second month of gestation. In this newly vascularized environment, the osteogenic cells brought in by the periosteal bud give rise to osteoblasts that begin to deposit bone matrix over the residual calcified cartilage. This process results in the formation of cancellous bone that has small remnants of calcified cartilage in its trabeculae (Fig. 2-1 C-D). Eventually, the central portion of the cancellous bone in the midsection of the model undergoes resorption, and this leaves a central medullary cavity (Fig. 2-1 C-D) surrounded by cortical bone (bone cortex). After the medullary cavity has begun to form, it becomes seeded by circulating multipotential hematopoietic stem cells that give rise to myeloid tissue (23).

Formation of the epiphyses and diaphysis :

Developing bone tissue has now replaced the middle third or so of what was formerly a solid mass of cartilage, and a medullary cavity filled with myeloid tissue has developed in its central region. The two ends of the developing bone are nevertheless still composed entirely of cartilage. Hence at this stage, the forming bone tissue consists of an elongating collar of subperiosteal bone that extends along the midsection of the bone and a decreasing amount of cancellous bone that borders on an enlarging central medullary cavity. The midsection of the bone becomes its shaft or diaphysis whereas the cartilaginous ends of the bone become its epiphyses. Its primary centre of ossification is accordingly often referred to as its diaphyseal centre of ossification. Interstitial growth occurs in the cartilaginous epiphyses, causing the bone to lengthen. Yet the epiphyses themselves do not lengthen because the cartilage on either side of the diaphyseal centre of ossification undergoes progressive maturation, calcification, and replacement by bone. Because elongation of the diaphyseal centre of ossification keeps pace with interstitial growth of the cartilaginous epiphyses, the epiphyses remain approximately the same size while the bony diaphysis between them lengthens. Cartilage models of the developing short bones (e.g., carpals of the wrist and most of the tarsals of the feet) lengthen as a result of interstitial growth. After they have finished growing, their cartilaginous epiphyses become almost entirely replaced by bone from the diaphysis; only a thin rim persists as each articular cartilage. Immediately beneath the articular cartilage, bony trabeculae form a supporting plate like structure (23).

Establishment of secondary centres of ossification:

The formation of long bones is slightly more complex because these bones develop secondary (epiphyseal) centres of ossification (Fig. 2-1 D-E). The majority of secondary centres are formed postnatally, but those in the lower end of the femur and the upper end of the tibia begin to appear just prior to birth. In the simplest kind of long bone, a secondary centre of ossification develops in each cartilaginous epiphysis. In due course the cartilaginous epiphysis gives rise to a bony epiphysis that retains a covering of articular cartilage. The chondrocytes in the middle of an epiphysis hypertrophy and mature, whereupon the matrix partitions between their lacunae calcify. Capillaries with associated osteogenic cells then invade cavities in the calcified cartilage, much as the periosteal bud grew into the diaphysis, and in this newly vascularized environment, the osteogenic cells give rise to osteoblasts that deposit bone matrix on the remnants of calcified cartilage. Meanwhile, the chondrocytes that are situated at the periphery of this region also start to hypertrophy, whereupon their surrounding matrix becomes calcified and then becomes replaced by bone. The resulting wave of ossification spreads from the secondary centre in all directions. In this manner, the cartilage in the middle of the epiphysis gradually becomes replaced by a mass of cancellous bone with its associated marrow spaces. Cartilage nevertheless remains as the articular cartilage that covers the articular surface and a transverse disk of hyaline cartilage called the epiphyseal plate that borders on the diaphysis (23).

It was found that the functional significance of the epiphyseal plate is that it enables the bone to grow until full adult stature is attained, at which time it becomes entirely replaced by bone tissue. The majority of long bones develop two secondary centres in addition to a primary centre of ossification. However, a few long bones develop a secondary centre at one end only. Typical short bones ossify entirely from their primary centre.

Postnatal growth of long bones :

Until skeletal growth is completed, a long bone continues to lengthen as a result of interstitial growth of the cartilage that is retained as its epiphyseal growth plates. However, the production of new cartilage matrix does not increase the thickness of such a plate because cartilage formation within the plate is only sufficient to keep pace with its replacement by bone tissue on the diaphyseal aspect of the plate. Because the epiphyseal plates grow on one side and become replaced by bone on the other, they are gradually shifted farther apart, lengthening the bony diaphysis that lies between them. Bony replacement eventually catches up with cartilage production, at which time the bone attains its adult size and its cartilaginous growth plates disappear.