Bone-Specific Reactions to Injury
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I. Disruption of endochondral ossification interferes with metaphyseal bone formation.

A. Normal endochondral ossification: is a type of growth pattern in bone that allows for interstitial and appositional cartilage growth with ultimate replacement of cartilage by bone. Cartilage matrix mineralizes (mediated by matrix vesicles) ->chondrocytes die (apoptosis – but does not appear that way microscopically!) ->the lacunae of the chondrocytes are opened by osteoclast-like (or pericyte-like) cells from near-by vessels->thin mineralized cartilage spicules remain (mineralized longitudinal septae: MLS)-> vascular in-growth from metaphysis brings along osteoblasts -> bone is deposited on cartilage matrix -> these initial spicules of cartilage cores with overlying bone matrix are called primary trabeculae -> primary trabeculae undergo modeling to form secondary and tertiary trabeculae (reduction in number but thicker in structure)

B. Examples of abnormal endochondral ossification.

1. Failure to form endochondral bone

a. Traumatic physitis – infractions of primary trabeculae that can physically block metaphyseal vessels from penetrating the growth plate resulting in retention of growth plate cartilage.

b. Osteomyelitis at physis or AE complex – inflammation can disrupt vascular in-growth into the growth plate resulting in retention of growth cartilage.

c. Osteochondrosis – either intrinsic metabolic error in growth cartilage preventing its mineralization and or vascular invasion or non-viable necrotic cartilage which can not initiate mineralization or produce growth factors that encourage vascular in-growth.

2. Altered trabecular bone formation/modeling during endochondral ossification

a. Growth retardation lattice - acquired and usually

temporary defect in osteoclasis resulting in band-like areas of primary trabeculae that do not model into secondary and tertiary trabecule (eg. BVD virus; CD virus).

b. Osteopetrosis – congenital defect in osteoclasis resulting in failure to model primary trabeculae into secondary trabeculae.

c. Growth arrest line – transverse trabeculation (formation of plates of bone in the metaphysis parallel to the growth plate without cartilage cores) due to cessation or slowing of longitudinal growth rate.

d. Osteochondromatosis – displaced/anomalous growth plate with subsequent mass effect due to normal endochondral ossification at an abnormal site.

II. Bone will change its shape to adapt to altered mechanical use (modeling).

A. Modeling involves changing the shape or size of bone. Normal growth involves modeling. Modeling bone surfaces can undergo osteoclastic resporption or directly undergo osteoblastic bone formation without previous resorption (as is required in remodeling). Generally in modeling, formation occurs at sites of compression and resorption at sites of tension. Normal adaptive modeling is seen in patterns of trabecular bone which are aligned to adapt to the stress on the bone.

1. Ways in which bone might detect altered mechanical use.
changes in electric currents in bone

a. Piezoelectric forces – currents due to distortion of crystal (collagen lattice)
b. Streaming potentials – currents due to fluid flow through narrow channels (canaliculi)

2. Osteoblasts have stretch receptors that alter calcium entry into the cell

B. Abnormal modeling – angular limb deformity. From the principles of modeling and adaptation to altered use, the thickness and the type of bone cellular activity on the concave and convex of each cortex can be predicted.

III. Bone can change its mass by altering the rates of remodeling in response to systemic disease and altered mechanical use.

A. Normal primary remodeling is the resorption of the bone deposited during growth and replacing it with adult bone. The bone completed at the end of growth usually is not osteonal in the cortex and might be a mixture of woven and lamellar bone both in the cortex and in trabecular bone. Remodeling of bone follows a set sequence of events: activation, resorption, reversal, formation.

1. ACTIVATION of the bone for involves stimulation of inactive osteoblasts (also called lining cells) by substances like (but not limited to) PTH (parathyroid hormone). The inactive osteoblasts contract via activation of cytoskeleton and remove unmineralized collagen (lamina limitans) from the bone surface by release of collagenases. The activated osteoblasts secrete osteoclast differentiation factor [ODF] which binds to the receptor [RANK] on osteoclasts and stimulates osteoclasts to RESORB bone. Osteoblasts can inhibit the effect of ODF by secretion of the soluble blocking protein osteoprotegerin.

2. RESORPTION of bone initially is by osteoclasts by release of hydrogen ions (acid) produced in the cell as carbonic acid which dissolves the mineral and proteolytic lysosomal enzymes which dissolve the matrix. It has been suggested that completion of the resportion is by mononuclear cells that might be even be of osteoblastic lineage!!!

3. The inhibition of resorption and initiation of formation at the resorption site is called REVERSAL. This is likely under the stimulation of non-collagenous bone matrix proteins such as the cytokine TGF beta. The front on at which the reversal takes place is called a cement line. The new bone that is deposited at the resorption site once the reversal begins is NOT in direct contact with the adjacent preexisting bone but is separated by a very narrow gap called a cement line. Cement lines are collagen poor, proteoglycan rich, and mineral rich sleeves that allow for slippage between remodeled units and possibly act as sumps to dissipate microcracks.

4. FORMATION is done by osteoblasts that fill in the excavated space with lamellar bone.

B. Normal secondary Remodeling is the replacement of old bone by new bone (replace old BSUs and Osteons with new ones by the ARRF process as above. Secondary remodeling likely it is to repair microdamage (remove microcracks before they become full fractures) in the bone.

C. Examples of diseases of imbalanced remodeling.

1. Osteoporosis - hormonal/nutritional. In protein calorie malnutrition, the osteoporosis might be due mostly to NORMAL R and DECREASED F. In postmenopausal osteoporosis the initiating factor might be decreased NORMAL suppression of R (loss of estrogen allows "normal" R signals to go unhibited). This allows for INCREASED AF with resultant more R sites at any one time. Unexplained DECREASED in F to completely fill the resorbed cavities likely also is important.

2. Osteoporosis – disuse. Analogous to pathogenesis of osteopenia due to estrogen loss. NORMAL mechanical inhibits R (mechanisms???). DECREASED mechanical releases the inhibition of R (mechanisms???) and there is INCREASED AF. The vigor of osteoblasts is reduced by unknown mechanisms. Modeling (or periosteal remodeling?) might play a larger role in osteopenia of multiple types.

3. Osteosclerosis - nutritional/hormonal. Presumably DECREASED AF but some agents (fluoride/vitamin D) might have anabolic effects at certain exposure levels.

4. Osteosclerosis - increased mechanical use. DECREASED AF. Modeling of periosteum?

IV. Repair bone/rapidly deposited bone is woven rather than lamellar

A. Woven bone is recognized by the disorderly arrangement of collagen fibers and the increased size and irregular shape of the osteocytes.

1. Trauma
2. Neoplasia
3. Inflammation.

V. Periosteum responds to "injury" usually by formation of woven bone
(Covered in normal review of cortical bone development in IV)

A. Normally, bones grow in width by depositing new bone tissue on top of the outer surface of the existing cortex. This is done by the periosteum. The periosteum has a fibrous outer layer and an osteogenic inner layer. The inner osteogenic layer is capable of depositing new bone directly on top of the preexisting bone. This is done by metaplasia of the ostegenic layer from a fibrous tissue to an osteoblastic tissue – no cartilage intermediary is present. Although ultimately cortical bone in the domestic animals is osteonal periosteal bone formed during rapid early growth usually does NOT take the form of osteonal bone. In larger animals that need to walk or run at birth, the periosteum deposits multiple thin laminae (laminar bone) oriented parallel to the cortex. The spaces between these thin laminae will fill in (compact) with a combination of woven and lamellar bone to form the cortex of the young animal (compacted laminae of bone which consists of a mixture of woven and lamellar bone but none of it arranged in true osteons). This compacted bone has yet to undergo primary remodeling so that it becomes osteonal bone. In smaller animals, the developing cortex is also derived from the osteogenic layer of the periosteum. It deposits bone in the form of thick anastamosing trabeculae of woven bone. The spaces between these trabeculae fill in (compact) with a combination of woven and lamellar bone. As in larger animals, true osteons are not formed.

B. Abnormal periosteal bone formation.

Trauma; Infammation; Neoplasia
Vascular
Inherited
Viral
Sterile Inflammatory
Nutritional/Metabolic