

### Bone Formation

Ossification(osteogenesis)is the process of forming new bone.

Bone formation occurs in four situations:

- Formation of bone in a late stage embryo
- Growth of bones until adulthood
- Remodeling of bone
- Repair of fractures

### Bone Formation

Osteogenesis occurs by two different methods, beginning about the 8th week of embryonic development.

- Intra-membranous ossification
- Produces spongy bone.
- This bone may subsequently be remodeled to form compact bone.
- Endochondral ossification
- Process whereby cartilage is replaced by bone.
- Forms both compact and spongy bone.

### Bone Formation

Intra-membranous ossification is the simpler of the two methods.

- It is used in formation of the flat bones of the skull, mandible, and clavicle.
- Bone forms from mesenchymal cells that develop into osteoblasts within a fibrous membrane
- Recall that mesenchyme is the tissue from which almost all other C.T. develop.
- Many ossification centers.
- Centers of bone formation
- The bone that is produced does not go through a cartilaginous stage
- Woven bone and periosteum form
- Lamellar bone replaces woven bone & red marrow appears

### Bone Formation

- Endochondral ossification is the method used in the formation of most bones, especially long bones.
- Involves replacement of a hyaline cartilage model by bone.

### Bone Formation (cont)

- Begins at the primary ossification center in center of shaft
- Blood vessel infiltration of perichondrium converts it to periosteum
- Underlying cells change to osteoblast
- Bone collar forms around diaphysis of cartilage model
- Central cartilage in diaphysis calcifies, then develops cavities
- Periosteal bud invades cavities
- Leads to the formation of spongy bone
- Diaphysis elongates & medullary cavity forms
- 2ndary ossification centers form in the epiphyses
- Epiphyses ossify

### Control of Bone Growth

- Normal bone growth depends on several factors:
- Minerals are an essential component
  - Large amounts of calcium and phosphorus and smaller amounts of magnesium, fluoride, and manganese are required for bone growth and remodeling.

### Control of Bone Growth

- Hormones are key contributors to normal bone growth.
- During childhood, the hormones most important to bone growth are human growth hormone (hGH) and growth factors called IGFs (produced by the liver).
- Both stimulate osteoblasts, promote cell division at the epiphyseal plate, and enhance protein synthesis.
- Thyroid hormone's contribution to bone growth involves the modulation of the activity of growth hormone
- Ensures proper bone proportions

### Control of Bone Remodeling

- Negative feedback hormonal loop for  $Ca^{2+}$  homeostasis
- Maintaining a normal serum  $Ca^{2+}$  level takes precedence over mineralizing bone
- Parathyroid hormone (PTH)
- Produced by parathyroid glands
- Removes calcium from bone regardless of bone integrity
- Calcitonin may be involved-Produced by parafollicular cells of thyroid gland
- In humans, high doses lowers blood calcium levels temporarily
- »Normal human physiological serum levels not high enough to cause the above effect

### Control of Bone Remodeling

- Response to mechanical and gravitational forces
- Bones stressed when bearing weight or pulled on by muscle
- Usually stress is off center, so tends to bend bones
- Bending compresses on one side; stretches on other
- Bones reflect stresses they encounter
- Long bones thickest midway along diaphysis where bending stresses greatest

### Fractures

- Fractures
- Breaks in the bone tissue•Fractures in youth
- Most result from trauma»Hold my beer!
- Fractures in old age
- Most result of bone weakness due to thinning
- »Hold my walker!

### Fracture Treatment

- Treatment
- Reduction
- Realignment of broken bone ends
- Closed reduction – physician manipulates to correct position



### Fracture Treatment (cont)

- Open reduction – surgical pins, plates, or wires secure ends
- Immobilization by cast or traction for healing
- Depends on break severity, bone broken, and age of patient

### Fracture and Repair

- Within one week new trabeculae appear in fibrocartilaginous callus
- Callus converted to bony (hard) callus of spongy bone
- ~2 months later firm union forms

### Aging and Bone Tissue

- There are two principal effects of aging on bone tissue:
  - Loss of bone mass
- The loss of calcium from bones is one of the symptoms in osteoporosis.
  - Brittleness
- Collagen fibers give bone its tensile strength, and protein synthesis decreases with age.
- The loss of tensile strength causes the bones to become very brittle and susceptible to fracture.

### Risk Factors for Osteoporosis

- Risk factors
  - Most often aged, postmenopausal women
  - 30% 60 – 70 years of age; 70% by age 80
  - 30% of caucasian women will fracture bone because of it
  - Men to lesser degree

### Postnatal Bone Growth

- After initial bone formation, bones grow by via two methods
- Interstitial (longitudinal) growth•Increase in length of long bones
  - Appositional growth
  - Increase in bone thickness

### Interstitial Growth

- Requires presence of epiphyseal cartilage
- Epiphyseal growth plate maintains constant thickness
- Rate of cartilage growth on one side balanced by bone replacement on other
  - Concurrent remodeling of epiphyseal ends to maintain proportion
  - Result of five zones within cartilage
    - Resting (quiescent) zone
    - Proliferation (growth) zone
    - Hypertrophic zone
    - Calcification zone
    - Ossification (osteogenic) zone

### Interstitial Growth

- Resting (quiescent) zone
  - Cartilage on epiphyseal side of epiphyseal plate
  - Relatively inactive
- Proliferation (growth) zone
  - Cartilage on diaphysis side of epiphyseal plate
  - Rapidly divide pushing epiphysis away from diaphysis
  - lengthening
- Hypertrophic zone–Older chondrocytes closer to diaphysis and their lacunae enlarge and erode interconnecting spaces
- Calcification zone
  - Surrounding cartilage matrix calcifies, chondrocytes die and deteriorate
- Ossification zone
  - Chondrocyte deterioration leaves long spicules of calcified cartilage at epiphysis-diaphysis junction
  - Spicules eroded by osteoclasts
  - Covered with new bone by osteoblasts
  - Ultimately replaced with spongy bone

### Control Of Bone Growth

- Vitamins are necessary for normal bone growth:
- Vitamin A is important for the activity of osteoblasts
  - Vitamin C is needed for synthesis of collagen.
  - Vitamin D is essential to healthy bones because it promotes the absorption of calcium from foods in the gastrointestinal tract into the blood.
  - Vitamins K and B12 are needed for synthesis of bone proteins.

### Control of Bone Growth

- Hormones continued...
- The sex hormones (estrogen and testosterone) cause a dramatic effect on bone growth, such as the sudden “growth spurt” that occurs during adolescence.
  - The female sex hormones also promote widening of the pelvis in the female skeleton.
  - Sex hormones are responsible for closing the epiphyseal plates at the end of puberty.
  - Also important in bone density maintenance during adulthood

### Control of Bone Remodeling

- The process of regulating serum  $Ca^{2+}$  levels by mineralizing bone is under hormonal control, and is carefully balanced
- Day to day control of calcium regulation mainly involves:
  - PTH stimulates osteoclastic activity and raises blood serum calcium level. Stimulates reabsorption of calcium ions in the kidneys
  - To a small extent, calcitonin – maybe –, hGH, and the sex hormones (estrogen and testosterone) stimulate osteoblastic activity and lower serum calcium level.
  - Vitamin D is produced for absorption of the  $Ca^{2+}$  and  $PO_4^-$  ions from the small intestine.

### Results of Mechanical Stressors: Wolff's Law

- Bone grows or remodels in response to demands placed on it
- Explains
  - Handedness (right or left handed) results in thicker and stronger bone of that upper limb
  - Curved bones thickest where most likely to buckle
  - Trabeculae of spongy bone form trusses along lines of stress
  - Large, bony projections occur where heavy, active muscles attach
- Even more pronounced on professional weight lifters
- Bones of fetus and bedridden featureless

### Fracture Classification

- Three "either/or" fracture classifications
  - Position of bone ends after fracture
- Nondisplaced—ends retain normal position
- Displaced—ends out of normal alignment
  - Completeness of break
- Complete—broken all the way through
- Incomplete—not broken all the way through
  - Whether skin is penetrated
- Open (compound) - skin is penetrated
- Closed (simple) – skin is not penetrated

### Fracture and Repair

- Once a bone is fractured, repair proceeds in a predictable pattern:
- The first step is the formation of a fracture hematoma (clot) as a result of blood vessels breaking in the periosteum and in osteons.
- Site swollen, painful, and inflamed

### Fracture and Repair

- The final step takes several months and is called remodeling :
  - Spongy bone is replaced by compact bone.
  - The fracture line disappears and little to no evidence of the break remains once complete

### Fracture and Repair (cont)

- Final structure resembles original because bone subject to same mechanical stressors

### Aging and Bone Tissue

- As we age, a decrease in bone mass occurs as the level of sex hormones diminish (especially in women after menopause)
  - Human females undergo a drop in estrogen levels typically many years before testosterone decreases in men
- Women can lose as much as 15-35% of their bone mass in the first five years after menopause
  - Since human female bones are generally smaller and less dense than males to begin with, old age has a greater adverse effect in females.
  - Bone resorption by osteoclasts outpaces bone deposition by osteoblasts with low levels of sex steroids.

### Additional Risk Factors for Osteoporosis

- Petite body form
- Insufficient exercise to stress bones
- Diet poor in calcium and protein
- Smoking
- Other hormone-related conditions
  - Hyperthyroidism
  - Low blood levels of thyroid-stimulating hormone
  - Diabetes mellitus
  - Low hGH and IGF production
- Immobility
- Males with prostate cancer taking androgen-suppressing drugs

### Interstitial Growth

- Ossification contributing to bone length (Interstitial growth) occurs throughout childhood and adolescence
  - Near end of adolescence chondroblasts divide less often
  - Epiphyseal plate thins then is replaced by bone
- Epiphyseal plate closure

### Interstitial Growth (cont)

- Bone lengthening ceases
- Bone of epiphysis and diaphysis fuses
- Usually complete by 18-21 years of age.
  - 18 in females
  - 21 in males
- Fractures (breaks) to the epiphyseal growth plate can accelerate its closure. –The fractured bone may be shorter than normal when adulthood is reached
  - Inhibits length-wise growth of bone

### Appositional Growth

- Allows lengthening bone to widen
- Occurs throughout life • Majority of osteoblast contribution to appositional growth occurs in the periosteum
  - secretes bone matrix on external bone
- Majority of osteoclasts contribution to appositional growth occurs in the endosteum
  - removes bone on endosteal surface
- Usually more building up than breaking down (Thicker, stronger bone but not too heavy)

### Bone Growth and Remodeling

- A balance must exist between the actions of osteoclasts and osteoblasts.
- If too much new osseous tissue is formed, the bones become abnormally thick and heavy, as seen with acromegaly.
  - Excessive loss of calcium weakens the bones, as occurs in osteoporosis.
  - Bones may also become too "soft", as seen in the bone diseases rickets (children) and osteomalacia (adults).

### Vitamin D and Calcium Deficiency

- Can happen in places with low sun exposure or low calcium content in diet
- Rickets • Weakening of bone hardness due to insufficient absorption of dietary calcium from lack of vitamin D or prolonged diets deficient in calcium
  - More common in children than adults

### Vitamin D and Calcium Deficiency (cont)

- Called osteomalacia in adults
- Increase in dietary Vitamin D or Ca intake can be used to treat

### Control of Bone Remodeling

- Occurs continuously but regulated by genetic factors and two control loops
- Negative feedback hormonal loop for  $\text{Ca}^{2+}$  homeostasis
- Controls blood  $\text{Ca}^{2+}$  levels, not bone integrity
- Serum  $\text{Ca}^{2+}$  concentrations are very important for proper nervous and muscle function
- Even minute changes in blood calcium are dangerous
- Responds to mechanical and gravitational forces

### Negative Feedback Hormonal Loop for blood $\text{Ca}^{2+}$

- Calcium is controlled by the parathyroid hormone (PTH)
- Decreases Calcium $^{2+}$  blood levels
- Increase PTH release
- PTH stimulates osteoclasts to degrade bone matrix, releasing  $\text{Ca}^{2+}$
- Blood Calcium $^{2+}$  levels increase
- PTH release amount is decreased

### Results of Hormonal and Mechanical Influences

- Hormonal controls determine whether and when remodeling occurs in response to changing blood calcium levels
- Mechanical/gravitational stress determines where remodeling occurs

### Classification of Bone Fractures

- Also described by location of fracture
- External appearance
- Nature of break
- Eponym (someone's name)

### Fracture and Repair

- The second step involves the formation of a callus
- Capillaries grow into hematoma-Phagocytic cells clear debris
- Fibroblasts secrete collagen fibers to span break and connect broken ends
- Fibroblasts, chondroblasts, and osteogenic cells begin reconstruction of bone
- Create cartilage matrix of repair tissue
- Osteoblasts form spongy bone within matrix•Mass of repair tissue called fibrocartilaginous callus

### Exercise and Bone Tissue

- Under mechanical stress, bone tissue becomes stronger through production of collagen fibers by osteoblasts and subsequent deposition of mineral salts. •Unstressed bones, on the other hand, become weaker.
- Astronauts in orbit suffer rapid loss of bone density.
- As much as 1% a week

### Aging and Bone Tissue

- Osteoporosis refers to a group of diseases where bone resorption outpaces bone deposition.
- Depletion of calcium from the body or inadequate intake in young adults
- Sex hormones maintain normal bone health and density
- As secretion wanes with age, osteoporosis can develop
- Spongy bone of spinal column and neck of femur most susceptible
- Heavy weight-bearing responsibilities
- Vertebral and hip fractures common

### Preventing Osteoporosis

- Plenty of calcium in diet in early adulthood
- Can help to increase bone deposition
- Reduce carbonated cola consumption
- May lower serum Ca levels causing an increase in the release of minerals from bone thus decreasing bone density
- Reduce alcohol consumption
- Heavy drinking during adolescence and young adulthood may have permanent effects on bone density
- Plenty of weight-bearing exercise
- Increases bone mass above normal for buffer against age-related bone loss

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