## 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 8thweek 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 ofthe 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 growthdepends 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 Ca2+homeostasis
–Maintaining a normal serum Ca2+ 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 theactivity 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 apredictable pattern:
•The first stepis 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 andlittle to no evidence of the breakremainsonce 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 produuction
•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 it's 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.
–Bonesmay 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 Ca2+homeostasis
•Controls blood Ca2+ levels, not bone integrity
•Serum Ca2+ concentrations are very important for proper nervous and muscle function
•Even minute changes in blood calcium are dangerous
–Responses to mechanical and gravitational forces

### Negative Feedback Hormonal Loop for blood Ca2+

Calcium is controlled by the parathyroid hormone (PTH)
Decreases Calcium2+ blood levels
Increase PTH release
PTH stimulates osteoclasts to degrade bone matrix, releasing Ca2+
Blood Calcium2+ 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 involvesthe 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 a 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

### 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

### 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