Bone and Joint Pathology
For Second Year Dental Students

Types of Bone
- Cortical bone: defines shape
- Cancellous bone: marrow bone
  - Mandible, maxilla
  - End of long bones in the medullary canal
- Epiphysis
  - from subarticular plate to epiphyseal cartilage
- Metaphysis
  - Area between epiphyseal plate to the area where bone develops its funnel or flute shape
- Diaphysis
  - Body of bone, between metaphyses

Types of Bone
- Lamellar
  - Forms the adult skeleton
  - // arrangement of collagen fibers
  - Few osteocytes
  - Uniform osteocytes in lacunae // to long axis of collagen fibers
- Woven
  - Irregular
  - Many osteocytes of various size and shape
  - In adults signifies always a pathologic condition

Cells
- Osteoblasts
  - Produce the protein
  - Osteoid
- Osteocyte
  - Osteoblast within bone in a lacuna
- Osteoclast
  - Multinucleated
  - Resorbs bone
  - Howship’ s lacunae
Bone Lesions

- **Congenital**
  - Dysostoses, Aplasia, Supernumerary, Dysplasias
- **Hereditary**
  - Osteogenesis Imperfecta, Achondroplasia, Osteopetrosis
- **Inflammatory**
  - Osteomyelitis, Fracture
- **Metabolic**
  - Osteoporosis, Rickets & Osteomalacia, Hyperparathyroidism
- **Neoplasms**
  - Osteoma, osteochondroma, osteosarcoma, chondrosarcoma, Ewing’s sarcoma etc.
- **Miscellaneous**
  - Osteonecrosis, benign fibro-osseous lesions

Hereditary and Congenital Diseases

- **Osteogenesis imperfecta** ("brittle bone disease")
  - Many types
  - Mutations of collagen type I; α1 & α2 chains
    - Dominant negative mutation; disastrous phenotype
    - Type I have normal life-span
    - Type II is fatal
  - Multiple fractures (starting in utero)
  - Blue sclera
    - Decreased collagen; underlying choroid (vascular layer) visible
  - Dental findings: Dentinogenesis imperfecta
  - Hearing loss (conductive)
Hereditary and Congenital Diseases

- **Achondroplasia** (Major cause of dwarfism)
  - FGFR3 mutation
    - Constitutive activation; inhibition of chondrocyte proliferation
    - Thanatophoric dwarfism (missense)
    - Absence or attenuation of zone of proliferative cartilage
  - Epiphyseal disorder (plate closes prematurely preventing bone growth; affects endochondral ossification)
  - AD, 80% new mutations
  - Normal mentation and average life span
  - Head and torso are normal
  - Kypho(anterior-posterior)scoliosis(lateral curvature)
  - Cor pulmonale
    - (Right ventricular hypertrophy=respiratory cause)
  - Hip problems

- **Osteopetrosis**
  - Reduced osteoclast–mediated bone resorption
    - Defective bone remodeling, specifically reduced bone demineralization
  - AR, AD
  - Abnormal dense bone (marble or stone bone)
    - Unsound, brittle bone
  - AR: Severe form, anemia, nerve entrapment, hydrocephalus, infections, fractures
  - AD: Milder
  - Extramedullary hematopoiesis
  - Wider metaphyseal and diaphyseal areas (Erlenmeyer flask)
  - Extremely irregular bone with cartilage core

- **Hereditary multiple osteochondromatosis**
  - AD, men predominance, women can transmit
  - Multiple osteochondromas
    - Abnormality of epiphyseal plate (cartilage grows laterally to the soft tissue), metaphyseal lesions
  - Metacarpals, wrists, knees, unequal length of extremities
  - Long term increased risk for chondrosarcoma
Hereditary and Congenital Diseases

- Ollier’s disease
  - Start at the metaphysis and become diaphyseal
  - Multiple enchondromas
    - Mature hyaline cartilage within bone
  - Small bones of hands
  - Chondrosarcoma in 30-50% of cases

Inflammatory and Non-Inflammatory (Non-neoplastic) Disorders

- Fracture: discontinuity of bone
  - Complete or incomplete
  - Closed or Compound (skin)
  - Comminuted (splintered bone); displaced
  - Pathologic (tumor); stress fracture (result of chronic injury; repeated trauma)
- Three phases
  - Inflammatory
  - Reparative
  - Remodeling

Inflammatory Phase

- First week
- Rupture of blood vessels in the periosteum and soft tissues
- Bone necrosis at the site
- Neovascularization peripheral to blood clot
- PMNs, macrophages and other mononuclear cells
- Clot organization and early fibrosis
- Callus formation
  - Woven bone, some cartilage (eventually resorbed)

Reparative Phase

- Months
- Proliferating fibroblasts and osteoblasts
- Blood clot resorption
- Callus bridge
Remodeling Phase

- Several weeks - years
- Callus has sealed the bone ends
- Remodeling

Disruptions of remodelling

- Deformity ↔ displacement
- Fibrous remodeling
- Pseudoarthrosis
- Infection
- Impairment because of lack in Ca, P, vit.D, systemic infection, medications, diabetes, etc.

Osteonecrosis

- Avascular, aseptic
- Ischemic death of bone and marrow in absence of infection
  - Trauma
  - Emboli: bone infarction
  - Systemic diseases
    - sickle cell disease, lupus, gout, metabolic diseases
  - Radiation
  - Corticosteroids
  - Site specific: head of femur, navicular bone
  - Alcoholism
  - Osteochondritis dissecans: dead piece of cartilage

Myositis Ossificans

- Formation of reactive bone in muscle as a result of injury
- Mimics neoplasm radiographically and histologically
- Lower limbs
Osteomyelitis

- Inflammation of bone caused by an infectious organism
- Staphylococcus, streptococcus, escherichia coli, neisseria gonorrhrea, haemophilus influenza, salmonella (sickle cell disease)
- Direct penetration
  - Wounds, fractures, surgery
- Hematogenous
  - Bloodstream, teeth; metaphyses
  - Knee, ankle, hip

Vocabulary

- Cloaca: hole in bone during formation of the draining sinus
- Sequestrum: fragment of necrotic bone in the pus
- Brodie abscess: reactive bone from periosteum and endosteum which surrounds and contains infection
- Involucrum: Periosteal new bone covering the sequestrum

Complications of Osteomyelitis

- Septicemia
- Acute bacterial arthritis
- Pathologic fractures
- Squamous cell carcinoma
- Amyloidosis
- Chronic osteomyelitis
- Tuberculous osteomyelitis: long bones, vertebrae (Pott’s disease)
Osteoporosis

- Reduction of bone mass per unit of bone volume
- Metabolic bone disease
- Bone displays normal ratio of mineral to matrix
- Primary and secondary

Primary Osteoporosis

- Most common
  - Reduced bone mass
- Uncertain etiology
- Postmenopausal women
- Elderly persons (senile)
  - Genetic: peak bone mass
  - Estrogens: decline
  - Aging
  - Calcium intake (800mg/day)
  - Exercise
  - Environmental factors: smoking leads to estrogen ↓

Some terms

- **RANK**: receptor activator for nuclear factor κB
  - Macrophages, stromal cells
- **RANKL**: ligand for RANK
  - under the influence of factors such as PTH and 1,25-dihydroxyvitamin D
- RANKL and Macrophage-Colony Stimulating Factor convert macrophages to osteoclasts
- RANK-RANKL is regulated by Osteoprotegerin (OPG)
- OPG-RANKL curtails osteoclast formation and bone-resorption activity

Primary Osteoporosis

- Osteopenia
- Decrease thickness of cortex
- Reduction in the number and size of trabeculae
- Fractures can be the first sign
- Compression fractures of vertebrae
Menopause

- Decreased serum estrogen
- Increased IL-1, IL-6 and TNF-levels
- Increased expression of RANK and RANKL
- Increased osteoclastic activity

Aging

- Decreased replicative activity of osteoprogenitor cells
- Decreased synthetic activity of osteoblasts
- Decreased biologic activity of matrix-bound growth factors
- Reduced physical activity

Secondary Osteoporosis

- Corticosteroids
  - Inhibition of osteoblastic activity
  - Impairment of vit. D dependant intestinal calcium absorption (secondary hyperparathyroidism)
- Hematologic malignancies
- Malabsorption: GI and liver diseases
- Alcoholism
  - Inhibition of osteoblasts,
  - ↓ absorption of calcium

Osteomalacia and Rickets

- Inadequate mineralization of newly formed bone matrix (osteomalacia)
- Rickets: children, epiphyseal plates open; also problem with cartilage
  - Beaded appearance of costochondral junctions
  - Pectus carinatum
  - Dental abnormalities
- Vitamin D deficiency (dependent)
- Phosphate deficiency (resistant)
- Defects in mineralization process

Osteomalacia and Rickets

- Osteopenia
- Exaggeration of osteoid seams
- Poorly localized pain
- Femoral neck, pubic ramus, spine, ribs

Hyperparathyroidism

- Parathyroid adenoma, hyperplasia, rare malignancy
- Parathyroid hormone
  - Promotes excretion of phosphate in the urine and stimulates osteoclastic activity resulting in hypercalcemia
  - Stimulates tubular reabsorption of calcium and excretion of phosphate
  - Stimulates intestinal calcium absorption
Hyperparathyroidism

- Stones: Kidney
- Bones: Brown tumors
- Moans: Psychiatric depression
- Groans: GI tract irregularities

Secondary hyperparathyroidism

- Renal osteodystrophy
- Chronic renal failure
  - Decreased filtration of phosphate
    - Hyperphosphatemia
  - Effect on active vit. D
  - Decreased Ca absorption in GI
    - Hypocalcemia
  - Secondary hyperparathyroidism
Paget Disease of Bone

• Disorder of bone remodeling
• Three phases
  – Osteoclastic (hot)
  – Mixed osteoblastic/osteoclastic
  – Burnt-out stage (cold)
• Skull involvement
  – Cotton wool appearance
  – Hypercementosis of jaws
• Tests
  – Alkaline phosphatase
  – Urine hydroxyproline levels

Fibrous Dysplasia

• McCune Albright syndrome
• Jaffe syndrome
• Monostotic
• Ground glass radiographic appearance
Bone Tumors

• Bone Forming
  – Benign
    • Osteoma (face, skull; 40-50yrs; similar to normal bone)
    • Osteoid Osteoma: metaphysis femur, tibia; 10-20yrs; (woven bone)
    • Osteoblastoma: vertebral column; 10-20yrs; similar to osteoid osteoma
  – Malignant
    • Primary and secondary osteosarcoma (Paget’s disease)
      – 1º: Metaphysis of distal femur, proximal; 10-20 yrs; malignant cells produce osteoid
      – 2º: Femur, humerus, pelvis

• Cartilagenous
  – Benign
    • Osteochondroma: Metaphysis of long bones; 10-30 yrs; bone and cartilage as a cup
    • Chondroma: Small bones of hands and feet; 30-50 yrs; medullary cavity
  – Malignant
    • Chondrosarcoma: Femur, humerus, pelvis; 40-60 yrs; Within medullary cavity; malignant cells form cartilage (abnormal)
Bone Tumors

- Other
  - Giant cell tumor of bone
    Epiphysis of long bones; 20-40 yrs; cortical lesions
  - Ewing sarcoma (tumor)
    Diaphysis and metaphysis; 10-20 yrs; medullary lesions; small round cells; t(11;22); FLI-EWS gene fusion

Osteomas

Cemento-Osseous Dysplasia

Periapical cemento-osseous dysplasia
- Periapical region of anterior mandible
- Middle-aged African-American women
- 30-50yrs
- Associated teeth are vital

Radiographic Features
- Early lesions: Periapical circumscribed radiolucencies
  DD: Periapical granuloma and cyst
- Late lesions: Linear pattern of radiolucency
- Mature lesions: Mixed radiolucent-radiopaque
Periapical Cemental Dysplasia

Florid Osseous Dysplasia

Osteosarcoma

Osteosarcoma
Osteosarcoma is the most common form of cancer involving bone. Breast and prostate carcinomas are most common. More than 80% of jaw metastasis occurs in the mandible. Various symptoms include pain, swelling, loose teeth, and paresthesia. Metastasis can be found in nonhealing extraction sites from which teeth were removed for local pain or mobility. Irregular radiolucency (moth eaten appearance) is a common finding. The prognosis is poor; most patients die within a year.
Osteoarthritis
- Most common joint disease
- Slow progressive degeneration of articular cartilage
- Weight bearing joints
- Fingers
- Primary: defect in cartilage, not an inflammatory disease
- Secondary: trauma, crystal deposits, infection
- Interphalangeal joints, knees, hips, cervical and lumbar spine

Osteoarthritis
- Narrowing of joint space (loss of disk)
- Increased thickness of subchondral bone
  - Eburnated bone
- Subchondral bone cysts
- Osteophytes (Haberden nodes)
  - Fingers, distal interphalangeal joints

Rheumatoid arthritis
- Systemic chronic inflammatory disease
- Autoimmune disease
- Diarthrodial joints bilaterally
- STARTS AS SYNOVIAL DISEASE
- 3:1 women
- Remissions and exacerbations
- Heredity; EBV(?)
- HLA-Dw4 haplotype and related B-cell alloantigen

Theory of Pathogenesis
- Genetically susceptible patient
- Infection ?
- Formation of Abs
- Abs act as new antigens
- Production of rheumatoid factor
- Deposits of immune complexes in the synovium
- Activation of complement cascade
- Inflammation
- Activation of macrophages
- Homing of T cells
- Secretion of cytokines

Histologic features
- Rice bodies
- Hyperplastic synovium
- Pannus
- Allison-Ghormley bodies
- Rheumatoid nodules

Spondyloarthropathy
- Used to be a type of RA
- NOW comprises a group of diseases
  - Ankylosing spondylitis
    - Vertebral column & sacroileac joints, young men
  - Reactive arthritis (Reiter syndrome)
    - Polyarthritis, conjunctivitis, non-gonococcal urethritis, oral lesions
  - Psoriatic arthritis
  - Arthritis and inflammatory bowel disease
    - Crohn’s, ulcerative colitis
Juvenile arthritis
- Still disease
- Children
- Females

Gout
- Increase in serum uric acid and deposition of urate crystals in the joints and kidneys
- Only 15% of patients with ↑ uric acid suffer from gout
- Gout can result from:
  - Overproduction of purines
    - Heterocyclic organic compound consisting of a pyrimide ring attached to imidazole ring; e.g. A, G
  - Augmented catabolism of nucleic acids
  - Decreased salvage of dietary purines and hypoxanthines
  - Decreased uric acid secretion
- Primary gout
- Secondary gout

Primary gout
- Hyperuricemia in the absence of other disease
  - Asymptomatic hyperuricemia can precede gout
- Impaired secretion by kidneys
**Secondary gout**

- Tumors
  - Leukemias
  - Lymphomas
  - After chemotherapy
- Alcoholism
  - Accelerated ATP catabolism

**Clinical features**

- Acute gouty arthritis
  - Painful
  - Involves one joint initially, then polyarticular
  - Podagra (painful, red metatarsophalangeal joint)
- Tophaceous gout
  - Development of tophi
  - Chalky, cheesy, yellow-white, pasty deposits of monosodium urate crystals
  - Helix and antihelix of ear
  - Achilles tendon

**Gouty Arthritis**

Hyperuricemia

- Neutrophil chemotaxis
- Phagocytosis of crystals by neutrophils
- Lysis of neutrophils
- Release of lysosomal enzymes
- Release of LTR, PG
- Reactive secretion of proteases by joints

**Gout**

- Pathology
  - Formation of granulomas with needle-shaped crystals
- Renal failure, urate stones
- Treatment
  - Colchicine
    - Prophylactic
  - Probenecid & sulfinpyrazone
    - Interfere with urate resorption
  - Allopurinol
    - Inhibitor of enzyme that converts the xanthine and hypoxanthine to uric acid

**Pseudogout**

- Chondrocalcinosis
- Calcium pyrophosphate crystals
- Older individuals
- No gender, race predilection
- 30-60% prevalence
  - There is a hereditary form
- Can cause significant joint damage
  - Knees, wrists, elbows, shoulders, ankles

**Lyme disease**

- Ring-like rash at the site of the bite
  - Erythema chronicum migrans
- Migratory joint pain and subsequent oligoarthritis
Bursitis

- Inflammation of the bursa
  - elbow, shoulder, knee
- Fibrous thickening of the bursa wall
- Tendency to double-fault in tennis and develop a bad slide in golf

Tumors and Tumor-like Conditions

- Ganglion cyst: Wrist; connective tissue cyst; near the joint capsule or the tendon sheath
- Synovial cyst: herniation of synovium through the joint capsule (Baker cyst; popliteal fossa)
- Pigmented villonodular tenosynovitis
  - Knee, hip, ankle, pain
- Giant cell tumor of tendon sheath
  - Painless mass; wrist; Most common soft tissue tumor of the hand