BONE PATHOLOGY
The Origin and Location of Bone Cells
Bone Remodeling

Four Phases of Remodeling

1. Activation of Osteoclasts
2. Resorption of Bone
3. Reversal Phase
4. Formation of Bone
   Activation of Osteoblasts
   Mineralization
Bone Lesions

• Hereditary Disorders
• Metabolic Conditions
• Benign Fibro-Osseous Lesions
• Neoplasms
• Miscellaneous conditions
Focal Osteoporotic Marrow Defect

- An area of hematopoietic marrow large enough to produce radiolucency
- 3 theories: a) aberrant bone regeneration
  b) persistence of fetal marrow
  c) marrow hyperplasia

- Asymptomatic and found incidentally
- Radiolucent lesion (few mm to cm)
- Ill-defined borders and fine trabeculations
  - 75% in women and 70% in post mandible

**Histology:** Cellular hematopoietic marrow

- Incisional biopsy often performed to establish diagnosis
Idiopathic Osteosclerosis (Bone scar)

• Focal area of increased radiodensity of unknown cause that cannot be attributed to any pathology

• Prevalence: 5% with increased frequency in African Americans and Asians

• No sex predilection with peak at 3-4 decade
• Asymptomatic with no associated expansion
• 90% of cases seen in mandible (associated with root apex)

• Well-defined opacity with no radiolucent rim surrounding

• Root resorption and movement of teeth reported (10% of cases)

• DD: Condensing osteitis, Osteoma
Paget’s Disease (Osteitis Deformens)

Uncoordinated increase in bone turnover (osteoblastic and osteoclastic activity) producing large but weak bone, increased serum alkaline phosphatase and urinary hydroxyproline

• Patients older than 40 yrs of age
• More common in Western countries
• Men > Women
• Monostotic or polyostotic (majority)
• Bone pain, fractures and bowing deformity – “simian stance”
• Progressive increase in head circumference
• Jaw involvement (17% of patients)
• Maxilla more commonly than mandible – “lionlike facies”
• Gradual enlargement of the jaw and generalized spaces between teeth
Paget’s Disease (Osteitis Deformens)

• Compression of the cranial nerves and spinal cord leading to paralysis and loss of hearing and sight

Radiographic features
• Initially it is predominantly radiolucent but later on it shows a classic “cotton wool” appearance
• Maxilla and mandible are enlarged
• Hypercementosis and loss of lamina dura
• DD: Cemento-osseous dysplasia
Paget’s Disease (Osteitis Deformens)

**Histopathology**
- Replacement of normal lamellar bone with less dense bone having a mosaic pattern and increased reversal lines
- Increased and enlarged osteoclasts

**Diagnosis:** ↑ Serum alkaline phosphatase; normal Ca and P
↑ Urinary hydroxyproline

**Treatment:** PTH antagonists (Calcitonin and Bisphosphonates)
Aspirin for pain

Major complication: Heart failure and Osteosarcoma (1% of cases)
OS in Paget’s are more aggressive and have poor prognosis
Paget’s Disease
Paget’s Disease of Bone
Central Giant Cell Granuloma (CGCG)

- Intraosseous destructive lesions of the jaws
- Far less common than peripheral giant cell granuloma
- 10-30 yrs of age; Female > Male
- Mandible > Maxilla; Ant. > Post.
- Mandibular lesions frequently cross the midline
- Asymptomatic or painless expansion
- Nonaggressive and aggressive lesions
- Perforation of the cortical plates and resorption of roots

Radiographic features
- Non-specific unilocular or multilocular radiolucency
- Well-demarcated
- DD of unilocular: periapical lesions
- DD of multilocular: ameloblastomas/other odontogenic lesions/ABC
Central Giant Cell Granuloma

Radiographic Features
• Aggressive lesions show cortical perforation and root resorption

Histopathology
• Lesion composed of giant cells containing 5-20 nuclei in a background of fibrous connective tissue
• DD: Aneurysmal bone cyst
  Brown tumors in hyperparathyroidism
  Multifocal: Cherubism

Treatment
• Surgical curettage
• 15 – 20% recurrence rate
• Long-term prognosis is good
• No metastasis
Central Giant Cell Lesion

• 75% before the age of 30; female > male
• Anterior mandible to first molar; can cross the midline
• Non-aggressive vs aggressive:
  – Aggressive lesions: larger on presentation, painful, rapid growth, root resorption, cortical perforation, younger patients
  – Recurrence: 75% in aggressive lesions (11% in non-aggressive)
  – Questionable minor histological differences
Central Giant Cell Lesion
Central Giant Cell Lesion

- Other lesions with giant cells:
  - Brown tumor (hyperPTHism)- polyuria/ nocturia (Ca interferes with ADH), HTN, lethargy, weakness, nausea, constipation, anorexia
  - Primary hyperPTHism (gland): Increased ionized Ca, decreased phosphates in serum (75-80% adenoma; 20% hyperplasia; < 1-2% carcinoma)—Tx- surgical removal of 1 or more PTH gland; medical (CPC-JOMS 61: 1318-23, 2003)
  - Secondary hyperPTHism (kidney): Decreased 1,25 dihydroxycholecalciferol, hypocalcemia, increased phosphates in serum
    - Cherubism (autosomal dominant, bilateral, maxillary involvement)
    - Rarely in neurofibromatosis
    - Aneurysmal bone cyst: rare, posterior mandible, large blood filled spaces with areas resembling central giant cell granuloma
Cherubism

- **Autosomal dominant**
- Facial appearance similar to “cherub”-like
- 2 – 5 yrs of age
- The clinical alterations typically progress until puberty, stabilize and slowly regress
- Bilateral involvement of the posterior mandible – most common appearance – “cherub”-like (all 4 quadrants)
- “Eyes upturned to heaven” appearance – due to involvement of the infraorbital rim and orbital floor
- Painless bilateral expansion of the post. mand.
- Marked widening and distortion of alveolar ridges
- Tooth displacement and eruption failure
Cherubism

Radiographic features
- Multilocular radiolucency with massive expansion
- Both erupted and unerupted teeth are randomly distributed
- After stabilization, lesions exhibit a “ground glass” appearance

Histopathology
- Similar to giant cell granuloma
- But clinical and radiographic correlation necessary
- Vascular fibrous tissue and giant cells (smaller and more focal)
- Eosinophilic cuffing around blood vessels

Treatment
- Prognosis is unpredictable
- Delayed till after puberty (curettage)
Traumatic Bone Cyst (Simple Bone Cyst)

- Benign cavity within bone devoid of epithelial lining
- Trauma-hemorrhage theory
- Reported in almost every bone
- Common in jaws, 10-20 yrs
- Mandible (most of cases); premolar-molar area
- 60% of cases in males
- Asymptomatic; discovered on routine x-rays
- 20% have a painless swelling

**Radiographic Features**
- Well-delineated radiolucency
- **When multiple teeth involved, domelike projections scallop upward between roots** – Highly suggestive
- Rarely presents as multilocular radiolucency
Traumatic Bone Cyst (Simple Bone Cyst)

**Histopathology**
- Defect wall lined by fibrovascular connective tissue intermixed with trabecular bone
- No evidence of cyst wall
- Tissue not usually found in surgery
- 1/3rd of cases an empty cavity
- Diagnosis primarily based on clinical, radiographic and surgical findings

**Treatment**
- Simple surgical exploration
- Submit any tissue available for histopathology
- Excellent prognosis
Aneurysmal Bone Cyst (ABC)

Intraosseous accumulation of variable-sized blood-filled spaces surrounded by cellular fibrous connective tissue admixed with reactive bone

- Trauma; vascular malformation; neoplasm
- One theory: CGCG and ABC are related
- Most commonly in long bones; < 30 yrs
- Jaw lesions – only 2% of cases; 20 yrs
- No sex predilection with ↑ posterior mandible
- Rapid swelling with pain; crepitus rarely seen

Radiographic Features
- Unilocular or multilocular radiolucency with cortical expansion
- Rarely small radiopaque foci seen
At surgery, tissue similar to “blood-soaked sponge is seen.

**Histopathology**
- Spaces of varying size filled with blood surrounded by fibrovascular connective tissue with giant cells and bony trabeculae.
- Vascular spaces are not lined by endothelial cells.
- 20% of cases ABC associated with CGCG or fibro-osseous lesion.

**Treatment**
- Curettage and enucleation (sometimes with cryosurgery).
- Recurrence rate – 8% - 60%.
- The higher rate due to incomplete removal of the lesion.
- However, good long-term prognosis.
Benign Fibro-Osseous Lesions of the Jaws

Group of processes characterized by replacement of normal bone by fibrous tissue containing mineralized product

They include developmental, reactive and neoplastic lesions

Histology might be similar in all cases and therefore clinical, radiographic and histological correlation is very important

1. Fibrous dysplasia
2. Cemento-osseous dysplasia
   a. Focal cemento-osseous dysplasia
   b. Periapical cemento-osseous dysplasia
   c. Florid cemento-osseous dysplasia
3. Ossifying fibroma
4. Diffuse Sclerosing Osteomyelitis
Fibrous Dysplasia (FD)

Asymptomatic, self-limiting developmental regional alteration of bone in which the normal architecture is replaced by fibrous tissue and nonfunctional trabeculae-like osseous tissue. It is self-limiting (thus it is not a true neoplasm)

- Represents a group of disorders with variety of clinical patterns
- Mutation in GNAS 1 gene

Clinical forms of fibrous dysplasia of the jaws
- Monostotic: localized to a single bone
  - Juvenile and aggressive juvenile
  - Adult
- Polystotic: involves several bones
  - Craniofacial
  - McCune-Albright syndrome
  - Jaffe syndrome
Monostotic Fibrous Dysplasia

- 80 – 85% of cases; Jaws most commonly affected
- Painless enlargement of the affected bone
- Diagnosed during 2\textsuperscript{nd} decade
- Maxilla > Mandible; male = females
- Growth stops in late teen or early twenties
- Maxillary lesions usually involve other adjoining bones – craniofacial FD
Monostotic Fibrous Dysplasia

**Radiographic features**
- Ground glass radiographic appearance
- Margins are ill-defined
- Expansion of the cortical plates and displacement of roots
- Periapical radiographs show narrowing of PDL and obscured lamina dura
- Maxillary lesions obliterates the sinus
Polystotic Fibrous Dysplasia

McCune Albright Syndrome: Associated with skin pigmentation and endocrine dysfunction
  - Multiple bone (particularly the craniofacial bones)
  - Skin lesions - *Café-au-lait* spots
  - Endocrine dysfunction – precocious sexual development in the pituitary, thyroid, parathyroid glands

Jaffe Syndrome: Absence of endocrine disturbances

Bone defects dominated by long bone involvement
McCune-Albright syndrome
Fibrous Dysplasia (FD)

**Histopathology**
- Irregular islands of metaplastic bone in a background of cellular connective tissue that has replaced normal bone
- Trabeculae often have “Chinese script characters”
- Lesional bone blends directly with normal bone
- Progressive maturation can be seen

**Treatment**
- Biopsy performed to exclude other more serious conditions
- Treatment delayed till adult life
- 25% - 50% show recurrence after shave-down
- Malignant transformation rarely reported
- RADIATION THERAPY CONTRAINDICATED
Fibrous Dysplasia (FD)
Cemento-Osseous Dysplasia

- Most common fibro-osseous lesion of the jaws
- Occurs in tooth bearing areas
- 3 types: focal; periapical; florid

**Focal Cemento-osseous dysplasia**

- Single site involvement
- 90% of cases occur in females
- 3-6th decade
- More common in whites
- Posterior mandible
- Asymptomatic and routine X-rays

**Radiographic features**

- Varies from radiolucent to radiopaque with a thin radiolucent peripheral rim
- More often: mixed radiolucent-radiopaque
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 cemento-osseous dysplasia

- Multifocal involvement
- Both anterior and posterior mandible
- Middle-aged African-American women
- Rarely all 4 quadrants involved
- Both dentulous and edentulous areas
Florid Osseous Dysplasia


**Cemento-Osseous Dysplasia**

**Histopathology**
- All 3 patterns have similar histology
- Fragments of cellular fibrous connective tissue with fragments of bone and cementum-like material

- DD: Ossifying fibroma
- Key at surgery: ossifying fibroma separates cleanly from bone while cemento-osseous dysplasia will be gritty and fragment easily

- Regular recall with prophylaxis
- Prognosis is good
- If sclerotic – hypovascular so do not biopsy or extract teeth- osteomyelitis
Ossifying Fibroma

- True neoplasm with fibrous connective tissue that contains
  variable amount of bony trabeculae, cementum-like material or both

- Wide age range with greatest 3rd-4th decades
- Female > Male; Mandible > Maxilla
- Mandibular premolar-molar area
- Small lesions – asymptomatic
- Large lesions – painless swelling
- “Juvenile Aggressive Ossifying Fibroma”

Radiographic Features
- Well-defined unilocular radiolucency
- Large lesions: classic downward bowing of the inferior cortex of mandible
Ossifying Fibroma
Ossifying Fibroma

**Histopathology**
- Tissue submitted as one mass
- Fibrous connective tissue with varying degree of mineralized material

**Treatment**
- Enucleation; good prognosis
Osteoma and Gardner Syndrome

• Osteomas are benign tumors composed of mature compact or cancellous bone
• Restricted to the craniofacial skeleton

Gardner Syndrome

• Autosomal dominant
• Spectrum of diseases comprised of
  * familial colorectal polyps (will transform to adenocarcinomas)
  * Osteomas (90% of cases) common in the skull, paranasal sinuses and mandible
  * Epidermoid cysts
  * Desmoid tumors (locally aggressive fibrous neoplasms)
  * Increased incidence of thyroid carcinoma

Treatment and Prognosis

• By age 30, 50% of patients will develop colorectal carcinoma; Prophylactic colectomy
Cementoblastoma (True Cementoma)

- Odontogenic neoplasm of cementoblasts
- Mandible > Maxilla with 90% occur in molar/premolar area
- 50% INVOLVE THE 1ST PERMANENT MOLAR
- Children and young adults
- Pain at night relieved by aspirin
- Swelling

Radiographic Features
- Appears as radiopaque mass fused to one or more roots and is surrounded by a thin radiolucent rim
- Outline of root blurred due to fusion with tooth

Histopathology
- Sheets of thick trabeculae of mineralized material intermixed with cellular fibrovascular tissue with multinucleated giant cells

Treatment
- Surgical extraction of lesion with teeth
Osteosarcoma

- Malignancy of mesenchymal cells that produce osteoid or immature bone
- Can arise following radiation - * Intramedullary
  * Juxtacortical
  * Extraskeletal
- Osteosarcomas of jaws: 6% to 8% of all osteosarcomas
- 3rd to 4th decade (roughly 10-15 yrs older than for long bones)
- Mandible=Maxilla
- Swelling, pain, loosening of teeth, paresthesia and nasal obstruction

Radiographic features
- Vary from radiopaque; mixed radiopaque-radiolucent; radiolucent
- Periphery is ill-defined; Resorption of teeth “sunburst or sun ray” appearance
- Symmetric widening of the periodontal ligament
Osteosarcoma

Histopathology
• Direct production of osteoid by malignant cells
• Sometimes, chondroid and fibrous tissue also be produced

Treatment and Prognosis
• INITIAL COMPLETE SURGICAL EXCISION
• Combination therapy
• 30-50% survival rate; metastasis to lung and brain
Osteosarcoma
Chondrosarcoma

- Half as common as osteosarcomas
- 1% to 3% arise in head and neck area
- Extragnathic lesions: older patients
- Jaw lesions: Younger (<20yrs; mean=41.6 yrs)
- Maxilla > mandible
- Painless mass
- Ill-defined radiolucency with scattered radiopaque areas
- “Sunburst” pattern

Histopathology
- Composed of cartilage showing varying degrees of maturity and cellularity

Treatment
- INITIAL COMPLETE SURGICAL EXCISION
- Radical surgical excision
- Metastasis is rare
- 15 year survival rate: 44%
Metastatic Tumors of the Jaws

• Most common form of cancer involving bone
• Breast and prostate carcinomas are most common
• Lung and kidney carcinomas also occurs
• Most patients are older
• >80% of jaw metastasis occurs in mandible
• Variety of symptoms: pain, swelling, loose teeth, paresthesia
• Rarely patients are asymptomatic
• Metastasis found in nonhealing extraction
• Site from which tooth was removed for local pain or mobility

• Irregular radiolucency (moth eaten appearance)

• More often is undifferentiated and does not resemble primary lesion and difficult to tell primary
• Immunohistochemistry is important
• Prognosis is poor; most patients die within a year
• 44y/o man
• H/O renal cell ca with lung and bone mets (humerus)
• Presents with painful, non-healing exposed bone in the mandible following dental extraction of teeth #30 and 31, one year after the dental treatment
Bisphosphonate Related Osteonecrosis of the Jaws (ONJ)

- Current or recent treatment with a bisphosphonate
- Exposed bone in the maxillofacial region that has persisted for more than 8 weeks
- No history of radiation therapy to the jaws
What is a bisphosphonate?

- **Used to treat cancer related conditions**
  - Multiple myeloma
  - Solid tumors
    - Breast, prostate, lung
- **Osteoporosis/Osteopenia**
- **More than 190 million oral bisphosphonate prescriptions dispensed worldwide**
Zoledronic acid and pamidronate

Patients present with painful exposed bone in the jaw which simulate dental abscess, denture sore spots, “tooth aches” or osteomyelitis.

Exposed bone occurs most commonly after a tooth extraction but can also occur spontaneously (most patients had dental trauma).

Multiple cases of spontaneous ONJ also reported.

True incidence is not known, but as high as 10% reported.
It is not known how long after bisphosphonate treatment osteonecrosis will develop

Difficult to treat as the lesion is unresponsive to antibiotics

Currently managed by local irrigation, periodic debridement, surgical trimming and sometimes bone resection

Current theories are attributed to effects on blood vessels and the exposure to external environment
Two key points:

1. A thorough oral exam by a dentist and/or oral surgeon before patients are treated with bisphosphonates, so that teeth that require extraction can be removed prior to initiation of therapy.

2. Patients who are currently on, or have used, bisphosphonates in the past, and are considering extensive elective procedures like implants, should be appropriately informed and counseled.
ONJ-Risk Factors

Drug Related
- Potency (Zometa>Aredia>oral)
- IV route
- Duration of therapy

Local-DA surgery
- Extractions
- Dental implant placement
- Periapical surgery
- Periodontal surgery (osseous)

Local- Anatomic
- Exostoses and prominent mylohyoid ridge

Concomitant Oral Disease
- Periodontal and dental abscess

Demographic/Systemic
- Age
- Cancer type
- Dose of BP
- Duration of BP

Other Risk Factor
- Corticosteroid Tx
- Chemotherapy Tx
- Smoking
- Diabetes
- Alcohol use
- Poor oral hygiene