GENERAL OVERVIEW

- Bone is a living tissue, constantly remodeling.
- Diseases of bones are important in Veterinary Medicine.
- Diseases of bones result in significant economic loss.
- Diseases of bones are often overlooked.

BONE STRUCTURE AND FUNCTION

**Bone** is a specialized form of connective tissue in which the extracellular components are mineralized.

There are two main morphologic types of bone:

- **Cortical (Compact) bone** forms the dense walls of the diaphysis. The compact bone has high density and it is composed of concentric layers of bone tissue with a channel in the center where blood vessels, lymphatic vessels and nerves longitudinally traverse the bone. All these structures form the so-called **Haversian system**.

- **Trabecular (Spongy or Cancellous) bone** constitutes the spongy bone of the medullary cavity. The trabecular bone is formed by a three-dimensional lattice of interlacing spicules or trabeculae. The spaces between these spicules contain the bone marrow.
There are three cell types admixed with extracellular matrix in bone tissue.

1. Osteoblasts (The maker) derive from bone-marrow stromal cells and their main function is to produce a protein called osteoid (bone matrix). Osteoblast activity is dependent on various stimuli such as parathyroid hormones (PTH), and vitamins C and D. Osteoblasts eventually become surrounded by mineralized bone matrix and become osteocytes.

2. Osteocytes (The preserver) reside inside the bone lacunae and are actively involved in the mineral resorption (osteocytic osteolysis) under the stimuli of PTH, vitamin D, calcitonin, etc.

3. Osteoclasts (The destroyer) are multinucleated cells derived from blood monocytes (macrophages). Osteoclasts are primarily involved in the resorption (lysis) of bone (osteoclastic osteolysis). Osteoclasts are typically found along the osseous surface undergoing resorption where they produce microscopic bone concavities known as Howship's lacunae. Cellular activity of osteoclasts is also dependent on various stimuli including PTH, vitamin D, calcitonin (negative feedback), PG2, osteoblast-derived factor, etc.

The extracellular matrix is composed of collagen fibers, glycoproteins and inorganic salts (predominately crystals of calcium hydroxyapatite).
CALCIUM AND PHOSPHATE METABOLISM (read on your own).

Calcium plays a vital role in cellular reactions (muscle, nerve cells), the release of hormones, enzyme activators, coagulation, and the integrity of bones and teeth.

There are three independent but interconnected pools of calcium:

1. **Bone calcium** comprises about 99% of this mineral;
2. **Intracellular calcium**;
3. **Etracellular calcium** (smallest pool).

Movement of calcium between pools (homeostasis) is tightly controlled in the intestine, bones and kidneys through hormones produced in the parathyroid (PTH), thyroid (calcitonin) and skin-liver (vitamin D).

**Phosphate** is also an important component of bones and teeth, and an important element of the cell membrane and organelles. Inorganic phosphate is also involved in pH regulation. The physiologic mechanisms for phosphate homeostasis are the same as those for calcium.

When the levels of plasmatic Ca become low (hypocalcemia) or when the Ca:P ratio is changed, calcium is immediately transferred from the bones to the extracellular pool. This tight dependence on plasma calcium may explain why nutritional, renal, and hormonal imbalances often result in bone disease.

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**BONE GROWTH (OSSIFICATION)**

Bones grow in width and length by two distinct processes:

1. **Endochondral ossification** is responsible for the longitudinal (length) growth of long bones and bones with growth plates. Proliferating cartilage is subsequently replaced by bone.

   Good vascular supply is essential for proper endochondral ossification in the growth plate. Note the capillary loops in the top and bottom of the growth cartilage in the adjacent figure.

   Endochondral ossification occurs in ossification centers (immature bones) and in the growth plates (epiphyseal plates) of developing bones.

   Once the growth plates are closed, no further longitudinal growth (length) can occur. It is important to mention that long bones grow by both endochondral and appositional growth.


2. **Apositional (aka Intramembranous) ossification.** Growth in width takes place by intramembranous ossification. This form of ossification occurs primarily along periosteal surfaces in flat bones and long bones. It starts with proliferation of mesenchymal connective cells that form a
“membrane” which subsequently is replaced by mature bone (apposition).

Types of Bone Tissue based on maturity:

Woven and Lamellar Bone: According to the stage of maturation, bone (cortical and cancellous) could be either woven bone or lamellar bone.

- **Woven bone** is immature bone present during fetal development or in the early stages of bone repair. The collagen fibers in woven bone are randomly distributed and microscopically have a crisscross pattern (woven).

- **Lamellar bone** is mature bone present in normal adult stages. The collagen fibers in lamellar bone are perfectly arranged in a parallel pattern.

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Chondrodysplasia (chondrodystrophia fetalis or popularly knowns as Disproportionate Dwarfism.) It is characterized by a defective endochondral ossification that results in disproportionate (short-legged) dwarfism. It is most frequently seen in **cattle (Angus, Hereford)** and **dogs (Alaskan malamute)**. In chondrodysplastic animals, the membranous (appositional growth) is normal but endochondral growth is impaired resulting in disproportionate growth of the skeleton. There are lethal and non-lethal forms of the disease. Although numerous forms of chondrodysplasia (dwarfs) have been described in human beings, few types are reported in animals. Disproportionate growth is considered normal in chondrodystrophoid breeds of dogs such as the Bull Dogs, Pekingese, Basset, and Dachshund. **Caution:** Chondrodysplasia (abnormal endochondral ossification) should not be confused with Dyschondroplasia in which the primary acquired lesion is the necrosis of cartilage (to be discussed in diseases of joints). Unfortunately some textbooks still use chondrodysplasia (congenital) and dyschondroplasia (acquired) as synonyms.

Osteopetrosis (petros=rock) is an inherited disease in which defective osteoclasts fail to reabsorb and remodel the fetal bone (primary spongiosa). This failure in resorption results in increased bone density with concurrent reduction of medullary spaces. Since there is no space for the bone marrow to grow, animals with Osteopetrosis often exhibit aplastic anemia. Osteopetrosis sporadically occurs in dogs, pigs, sheep horses and cattle (Angus), as well as in human beings. On cut surface, bones with Osteopetrosis appear diffusely solid. Paradoxically, affected bones have a notable propensity for pathological fractures.
**Congenital Cortical Hyperostosis of Pigs** affects long bones and is characterized by exaggerated appositional (periosteal) bone growth. Affected limbs appear swollen because of excessive deposition of radiating trabecula on the periosteal surface and edematous because blockage of lymphatic circulation. Most piglets with congenital cortical hyperostosis are born dead or die within hours. The joints are normal.

**LOCALIZED MALFORMATIONS**

**Limbs (Appendicular Skeleton):**
- **Amelia:** Absence of a limb(s).
- **Hemimelia:** Absence of the distal half of a limb(s).
- **Phocomelia:** Absence of proximal portions of the limb(s) [seal].
- **Peromelia:** Absence of distal portions of the limb(s)
- **Micromelia:** Small limbs
- **Syndactylyia:** Fusion of digits.
- **Polydactylyia:** Supernumerary digits
- **Others...**

**Vertebræ (Axial Skeleton):**
- **Lordosis:** Ventral deviation of a vertebral column.
- **Kyphosis:** Dorsal deviation of a vertebral column.
- **Scoliosis:** Lateral deviation of a vertebral column.
- **Kyphoscoliosis:** Dorsolateral deviation of a vertebral column.

**LOCALIZED DEFORMATIONS**

**Angular limb deformities** are important in horses and characterized by lateral deviation of the distal portion of one or more limbs. Sometimes this problem is present at birth, while in others it develops later in life. There are multiple causes including:
- Malposition *in utero*
- Joint laxity
- Hypothyroidism (congenital goiter)
- Trauma (ischemia or reduced blood supply)
- Malnutrition
- Secondary to defective endochondral ossification.

**METABOLIC BONE DISEASES**
*(Nutritional, Toxic or Hormonal Osteodystrophies)*
Overview of Metabolic Bone Diseases:

- The same disease could have different etiology.
- The same etiology could produce different disease.
- One disease could progress to another disease.
- Two bone diseases could be present simultaneously.
- Bone disease usually has multifactorial etiology; etiologic diagnosis is difficult.
- There are notable differences among animal species.

**Bone mass** results from the balance between **formative (deposition)**, **resorptive** and **resting states**. In human beings, the peak of bone mass occurs around the age of 30.

Remodeling of bones is a constant undertaking, from birth to old age. Many skeletal diseases occur when there is an alteration in the equilibrium between deposition and resorption of bone tissue.

**Osteopenia** is a term used to denote loss of skeletal mass or too “little bone” regardless whether the remaining bone tissue has a normal composition or not. Hormones produced by pituitary, the thyroid, gonads, adrenal are also involved in the metabolism of bones.

<table>
<thead>
<tr>
<th>METABOLIC BONE DISEASES</th>
<th>Causes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficient or Excessive:</td>
<td>• Nutritional (Vit. A, C, D, Ca, P, F, Pb)</td>
</tr>
<tr>
<td>• Production of bone matrix (osteoid)</td>
<td>• Hormonal (PTH, estrogen, thyroid, adrenal, etc)</td>
</tr>
<tr>
<td>• Mineralization of bone matrix</td>
<td>• Toxic: Lead, fluoride, etc)</td>
</tr>
<tr>
<td>• Resorption of bone</td>
<td>• Mechanical (disuse atrophy)</td>
</tr>
</tbody>
</table>

The fundamental underlying problem in metabolic bone diseases is an imbalance in the modeling or remodeling processes.

<table>
<thead>
<tr>
<th>The best-known metabolic bone diseases are:</th>
<th>The most common toxic osteodystrophies are:</th>
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</thead>
<tbody>
<tr>
<td>• Osteoporosis</td>
<td>• Hypervitaminosis A in cats</td>
</tr>
<tr>
<td>• Rickets</td>
<td>• Hypervitaminosis D</td>
</tr>
<tr>
<td>• Osteomalacia</td>
<td>• Osteofluorosis</td>
</tr>
<tr>
<td>• Fibrous Osteodystrophy</td>
<td>• Lead poisoning</td>
</tr>
</tbody>
</table>

**OSTEOPOROSIS**

**Osteoporosis**: (syn. bone atrophy, Osteopenia). The fundamental problem in osteoporosis is a negative balance between the formation and resorption of bone leading to a reduction of bone mass. A simple definition of osteoporosis is “there is little bone, but what bone there is, is normal.” It is difficult to evaluate osteoporosis grossly unless it is a rather severe case. Grossly, there is reduction in the thickness of cortical bone and reduced number of trabecula in cancellous bone. As result of loss of trabecular bone the medullary cavity appears enlarged and there are increased fragility and predisposition to pathological fractures.
OSTEOPOROSIS

**Most common causes of osteoporosis:**

<table>
<thead>
<tr>
<th>Starvation</th>
<th>Parasitism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic wasting diseases</td>
<td>Calcium and copper deficiencies</td>
</tr>
<tr>
<td>Hyperadrenocorticism, and prolonged administration of steroids. It also results from physical inactivity (disuse atrophy of bone)</td>
<td>Senility. It is common in human beings, particularly in older women (postmenopausal osteoporosis).</td>
</tr>
</tbody>
</table>

RICKETS

**Rickets** is a metabolic bone disease of complex etiology affecting growing bones (softening of bones in young, growing animals). The pathogenesis involves two main processes:

- Defectivem mineralization of:
  - Osteoid
  - Growth Cartilage (endochondral ossification)

As a result, bones become soft and the areas of endochondral ossification appeared swollen (i.e., rachitic rosary in costochondral joints in human beings).

The etiopathogenesis of rickets is multifactorial but typically involves vitamin D or phosphorus deficiencies. Rickets is commonly seen in animal housing facilities where there is little sunlight, or in areas where the soil is deficient in phosphorus.

**Gross lesions** are typically characterized by an abnormal widening of the “growth cartilage” (growth plates), bone softening and deformations, and swelling of the cartilaginous joints. **Microscopically**, bones show failure of mineralization of osteoid and retention of immature cartilage matrixes that had failed to mineralize.

**Osteomalacia** (softening of bones in grown animals) is the same disease as rickets; however, this metabolic bone disease occurs in grown animals whose growth plates have already closed.
The etiopathogenesis is similar to rickets in that it is a failure in the calcification of osteoid during the normal remodeling of bone associated primarily to Vitamin D or P deficiencies. Unmineralized osteoid is resistant to osteoclastic activity and accumulates in the bones. The bones are soft and deformed. Histologically, there is accumulation of unmineralized osteoid. Pathological fractures are common sequels to osteomalacia.

FIBROUS OSTEODYSTROPHY

Osteodystrophia Fibrosa (Fibrous osteodystrophy): It is a metabolic bone disease characterized by increased osteoclastic resorption of bone and replacement by fibrous connective tissue. It results from prolonged and excessive secretion of a parathyroid hormone (PTH). Excessive secretion of PTH (hyperparathyroidism) could by primary or secondary.

- **Secondary hyperparathyroidism** is the most common and can be classified as:
  - The fundamental mechanism is a reduced concentration of calcium in the plasma with a relative increase in phosphorus.
  - **Nutritional hyperparathyroidism** results from a low-calcium-high phosphorus diet.
  - **Renal hyperparathyroidism**, there is failure to eliminate P in the urine, which causes hyper-phosphatemia. Whether it is nutritional or renal hyperparathyroidism, excessive secretion of PTH promotes bone reabsorption through osteoclastic activity. Bones, particularly those of the head, become swollen, soft (loose teeth), deformed and prone to pathological fractures. Osteodystrophia fibrosa is commonly seen in horses with bran disease (nutritional), and in dogs (rubber jaw) and cats with renal disease (renal osteodystrophy). It is also important in captive primates and reptiles (pet iguanas) and sporadic in pigs, goats and cattle with nutritional imbalances.

Toxic Osteodystrophies

- **Lead poisoning** interferes with osteoclastic activity. Osteoclasts contain typical acid-fast inclusions. Lesions are subtle and consist of Increase bone density in the metaphyses.

- **Osteofluorosis** results from a chronic ingestion of high concentrations fluorides present in the water, plants, and rocks of some geographical regions. Affecting only herbivorous animals, fluorosis interferes with the normal metabolism of bones and teeth, particularly in fetuses and growing animals. In cattle fluorosis only occurs when the concentrations of fluoride reach more than 2,500 ppm in bones. Growing bones (metatarsal, mandibles, the pelvis) become thickened due to excessive periosteal ossification. In addition, Osteofluorosis produces rickets-like lesions in bones, and a notable softening and discoloration of teeth, referred to as odontofluorosis. Soft, black teeth with excessive
wear and tear of the occlusal surfaces characterize Odontofluorosis.

**Hypervitaminosis-A** causes a toxic osteodystrophy in cats, and to a lesser extent in calves and piglets. When cats are fed livers of grazing bovines, or any other feed with excessive vitamin A, the periosteal surfaces of vertebrae become roughened causing a syndrome known as *deforming cervical spondylosis*. Affected vertebrae have abundant exostosis and eventually fuse producing vertebral ankylosis. Although the pathogenesis of hypervitaminosis A poorly understood, it has been reported that high levels of retinoid and other vitamin A metabolites stimulate osteoblastic activity.

**BONE REACTION TO INJURY**

### Necrosis (osteosis)

- **Grossly:** Softening, discoloration  
- **Histologically:** Empty lacunae, resorption.

#### Possible sequelae to bone necrosis:

- Necrosis ➔ resorption ➔ woven bone ➔ mature bone
- Necrosis ➔ resorption ➔ woven bone ➔ scar (callus)
- Necrosis ➔ sequestrum (no resorption)
- Necrosis ➔ resorption ➔ inflammation ➔ proliferation (exostosis)

- **Sequestrum:** A piece of necrotic bone isolated from the remaining viable bone.
- **Involucrum:** A dense collar of bone surrounding sequestrum.
- **Bone proliferation:** Exostosis, enostosis, hyperostosis (Chronic periosteal injury ➔ bone proliferation).

**Aseptic Bone Necrosis** is common in human beings but relatively rare in domestic animals. It is thought to be the result of bone ischemia. Aseptic bone necrosis is microscopically characterized by empty lacunae with little inflammation. **Aseptic necrosis of the femoral head** is an important entity in dogs.

**Bone Fractures and Repair:** A common occurrence (trauma) or as a result of weak bones (pathological fracture). Fracture ➔ hematomas ➔ necrosis ➔ resorption ➔ periosteal and mesenchymal cell proliferation ➔ cartilage ➔ woven bone ➔ lamellar bone ➔ callus. (Please read Applied Veterinary Histology by Banks, 3rd Ed, 1993 pp 216-218).
OSTEITIS, OSTEOMYELITIS, PERIOSTITIS, PANOSTEITIS.

**Etiology:** Bacterial > mycotic > viral, parasitic; Severe trauma

**Course:** Generally chronic and progressive.

**Route of entry:** Hematogenous, extension, penetration.

**Main pathological types:**
- Destructive (osteolytic)
- Productive (sclerosis).

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Examples of Specific Forms of Osteomyelitis in Domestic Animals

**Bacterial:**

- **Hematogenous osteomyelitis** occurs commonly in farm animals following bacteremia or septicemia. Frequent bacteria isolated from septic osteomyelitis include *Salmonella* spp., *Arcanobacterium pyogenes, Staphylococcus aureus, Rhodococcus equi* and other pyogenic organisms. Omphalophlebitis is a common source of bacterial embolisms in neonates. Bacterial embolisms lodge primarily in the epiphyseal vessels of long bones. These infections are important in young foals where 70% of foals with joint-ill also have septic osteomyelitis. Septic arthritis will be discussed under joints.

- **Septic osteomyelitis in the vertebrae (spondylitis)** occurs commonly in pigs and sporadically in other species. Tail biting has been incriminated in the pathogenesis of bacterial spondylitis or spinal abscesses in pigs. Vertebral infections eventually involve the spinal cord causing spinal meningitis or weaken the bone predisposing to vertebral fractures. Posterior paralysis is a frequent sign of septic spondylitis. Grossly, the ventral bodies of affected vertebrae are swollen. On a cut surface, the vertebrae contain mucopurulent exudates (spinal abscesses).

- **Lumpy Jaw (mandibular osteomyelitis)** is a localized (unilateral) infection of the jaw caused by the opportunistic bacterium *Actinomyces bovis*. This soil-born organism penetrates through injured oral mucosa and extends deep into the bone where it causes a chronic pyogranulomatous osteomyelitis. The mandible becomes swollen, deformed and produces a fistula with purulent exudate containing *sulfur granules*. The macerated jaw reveals exuberant exostosis. Microscopically, there are confluent pyogranulomas containing typical aggregates of bacteria referred as “club colonies.” Since treatment is expensive and non-curative, most animals are sent to slaughter.

**Mycotic Osteomyelitis:**

**Systemic (Deep) Mycoses.** As their name implies, systemic mycoses are disseminated fungal
infections caused by dimorphic fungi such as *Blastomyces dermatitides*, *Coccidioides immitis* and *Cryptococcus neoformans*. These fungi disseminate, through the blood and lymphatic systems, to many tissues including bones. Systemic mycoses cause a chronic granulomatous osteomyelitis with the typical periosteal exostoses.

**Viral Osteitis:**

Bone diseases caused by viruses are uncommon and not that important in domestic animals. The following viruses are reported to affect the bone in domestic animals:

- CAV-1 (Canine hepatitis)
- Canine Morbillivirus (Distemper)
- Feline Leukemia Virus
- Bovine Virus Diarrhea (BVD).

Lesions in other organs caused by these viruses are more relevant, clinically and pathologically, than those present in bones.

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**Hypertrophic (pulmonary) Osteopathy** is a condition sporadically reported in human beings (*Marie’s Disease*) and domestic animals, especially dogs. The pathogenesis is not clear but usually is accompanied by intrathoracic space-occupying mass (tumor, abscess). A change of the blood flow in the extremities has been postulated as the underlying mechanism of periosteal exophytoses. However, more recent studies suggest that pulmonary anastomoses (arterioles-venules) allow circulating megakarocytes to bypass the lung, reach the periosteal surface and induce periosteal growth. Interestingly, tumors of the urinary bladder and ovaries have also been associated to hypertrophic pulmonary osteoarthropathy. Bone changes are always bilaterally symmetrical characterized by multiple focal to coalescing osteophytes that affect primarily the appendicular skeleton.

**Craniomandibular osteopathy** ("Lion jaw") is a localized bone disease of unknown etiology in dogs. It is mainly seen in West Highland White and Scottish Terriers. Lesions affect only the head, are bilaterally symmetrical, and self-limiting. Affected dogs have a swelling of the temporo-maxillary region and mandibles. Grossly and radiographically, there are proliferative changes in the temporal, mandibular and maxillary bones causing bony bridging on the periosteal surface.

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**The End**

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