Metabolic Bone Diseases

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**METABOLIC BONE DISEASES**

**Metabolic bone diseases** are systemic bone disorders of various etiologies including **dietary** (nutritional), **hormonal** and **toxic**.

The best known metabolic bone diseases are **rickets, osteomalacia, osteoporosis and fibrous osteodystrophy**.

The most common toxic osteodystrophies are **hypervitaminosis A and D, osteofluorosis and lead poisoning**.

The fundamental problem in metabolic bone diseases is an imbalance between bone formation and resorption in the normal remodeling process of bones.
Osteoporosis. Normal (n) vs. osteoporotic (o).

Notice the loss of trabecular bone characterized by an enlarged medullary space and thinner cortices. As you may expect, the bones are fragile but not soft as with rickets, osteomalacia or osteodystrophia fibrosa.

The basic problem in osteoporosis is a negative balance between formation and resorption of bone leading to reduction of bone mass. A simple definition of osteoporosis is “there is little bone, but what bone there is, is normal.” Osteoporosis is also referred to as bone atrophy.
Osteoporosis.

Note the reduced trabecular bone in the metaphysis with some visible cavitations in the diaphyses. There are also thin cortices and an enlarged medullary cavity.

Causes of osteoporosis include starvation, parasitism, chronic wasting diseases, deficiencies of calcium and copper, hyperadrenocorticism, and prolonged administration of steroids. It also results from physical inactivity (disuse atrophy of bone) and senility. Osteoporosis is an important disease in human beings, particularly in older women (postmenopausal osteoporosis).

(See also figure 10-11 in Thomson's book).
Bilateral pathological fractures. Bovine.

Note the bilateral femoral fractures. These bones had thin cortices and reduced trabecular bone. Pathological fractures are commonly seen in animals with osteoporosis, rickets and osteomalacia.

Osteoporotic bones are fragile but not soft as with rickets, osteomalacia or osteodystrophia fibrosa.

Osteoporosis is difficult to evaluate grossly unless it is a severe case in which a significant bone mass has been lost.

Note the deformation of the forelegs and enlarged carpal joints. The deformity is due to softening of bone in addition to weight bearing when the animal stands.

Gross lesions in rickets are typically characterized by an abnormal widening of the “growth cartilage” (growth plates), bone softening, deformations, and swelling of the cartilaginous joints.

The enlargement of the carpal joints is due to the accumulation of noncalcified cartilage at the site of endochondral ossification.

See figure 10-19 in Thomson's book.
Rickets. Porcine.

Note this pig attempting to avoid placing on its limbs in order to avoid pain.

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

In human rickets, enlargement of the costochondral joints is prominent forming the so-called rachitic rosary.
Rickets.

A sagittal section of a rachitic long bone.

Note the irregular thickening of the growth plate.

In growing animals, endochondral ossification occurs when cartilage proliferates, matures, becomes hypertrophic and finally degenerates and becomes mineralized forming woven bone. In rickets, chondrocytes proliferate but do not mature and degenerate properly, thus cartilage is retained and accumulates in bones.
**Rickets. Normal versus rachitic growth plates**

Note the homogenous thickness in the normal bone while the rachitic bone shows a severe focal thickening of the growth plate.

Thickening of the growth plate can be detected by gross or radiological examination.
Rickets. Histology

Normal vs. affected growth plates.

Notice the abnormal retention and lack of mineralization in the growth cartilage in the animal with rickets (left picture). Unmineralized osteoid appears pink.

Microscopically, bones show a failure in mineralization of osteoid and the retention of cartilage matrixes which had failed to mineralize.
Osteomalacia.  Bovine.

Note the deformity of the forelegs with lateral deviation of the radius and ulna.

As in rickets, bone deformities and abnormal limb curvatures in osteomalacia result from bone softening and weight bearing.

The accumulation of non-calcified cartilage in the growth plate is not seen in osteomalacia since this is a disease of mature animals in which the growth plate has already closed.

The etiology of osteomalacia is similar to that of rickets in that deficiencies of phosphorus and vitamin D are major contributors.
Osteodystrophia Fibrosa. Equine.

Note the extreme swelling and deformity of the nasal bones. In osteodystrophia fibrosa cranio-facial bones are more severely affected.

Osteodystrophia is a metabolic bone disease characterized by increased osteoclastic resorption of bone and replacement by fibrous connective tissue due to prolonged and excessive secretion of a parathyroid hormone (PTH).

Osteodystrophia fibrosa in horses is commonly associated with diets rich in phosphorus and low in calcium as found in bran. Hence, the disease in horses is often referred to as "bran disease."
Osteodystrophia Fibrosa. Goat.

Note the severe swelling and deformity of the facial bones due to the accumulation and proliferation of connective tissue.

Because of osseous softening in the maxillary and mandibular bones, the teeth become rather loose.

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.
Osteodystrophia Fibrosa. Dog (Rubber Jaw).

In dogs this disease is commonly associated with chronic renal disease (secondary hyperparathyroidism due to renal failure).

Renal osteodystrophy is due to the inability of the kidneys to excrete P. Excess P in blood and a relative reduction of blood Ca\(^{++}\) (hypocalcemia) activate parathyroid glands to secrete PTH. This hormone is hypercalcemic since it removes Ca\(^{++}\) from bones via osteoclasts (osteoclastic osteolysis) and osteocytes (osteocytic osteolysis). PTH also increases absorption of Ca\(^{++}\) in the intestine. In addition, animals with renal disease are unable to activate Vitamin D\(_3\) in kidneys.
Osteodystrophia Fibrosa. Pig

Note the swollen gums and missing teeth. Deformation of the facial bones is due to resorption of bone and an excessive deposition of connective tissue. Dental alveoli are weakened and teeth become loose.

Osteodystrophia fibrosa / Iguana

Osteodystrophia fibrosa is extremely common in captive reptilians. Even with a good feeding practice, animals in captivity often develop secondary hyperparathyroidism. The pathogenesis of Osteodystrophia fibrosa in captive reptiles is the same as in domestic animals.
Note the swollen gums and missing teeth. This disease is common in primates kept in captivity due to dietary imbalances particularly when there is a calcium deficiency and an excess of phosphorus.

A lack of exposure to ultraviolet (sunlight) is another contributing factor.

Note the angular deformity of the forelimb. This bone would be rather soft to the point that it can be cut with a knife. A cross section of this bone is shown in next slide.
Osteodystrophia Fibrosa. Primate

A cross section of long bones.

Note the marked swelling and deformation of the bones with extensive proliferation of fibrous tissue. Fibrous tissues fills most of the medullary space.

Osteodystrophia fibrosa is also known as "osteitis cystica fibrosa" in human medicine due to formation of numerous cysts in affected bones as seen in this primate. Cysts are only occasionally seen in domestic animals.

Osteodystrophia fibrosa may be reversed if the cause is removed.
Osteodystrophia Fibrosa.

An histologic section stained (Hematoxylin-eosin stain). Note the bone resorption characterized by Howship lacunae (white arrows) containing osteoclasts (arrowheads) and extensive replacement of bone with fibrous connective tissue (ct).

Histologic sections stained for connective tissue (Masson-Trichrome stain). Note the reduced number of trabecular bone (red) and extensive deposition of fibrous connective tissue (blue).

In severe cases there is no need to decalcify the bone samples to cut histological sections.
Osteodystrophia Fibrosa / Parathyroid adenoma

It is imperative to check the parathyroid glands and kidneys in any animal with Osteodystrophia fibrosa.

In this dog the parathyroid (PA) was reported to be adenomatous and presumably actively secreting large amounts of PTH. A normal parathyroid gland would be approximately one fifth of this size.

Primary hyperparathyroidism is relatively rare in domestic animals. Most veterinary cases are due to secondary hyperparathyroidism as a result of nutritional imbalances or due to renal diseases with impairment in the excretion of phosphorus.

See figure 6-35 Thomson's book (endocrine section).
**Odontofluorosis. Bovine.**

Note the dark discoloration, excessive and abnormal wear pattern in the incisive teeth.

Affecting only fetuses and growing herbivorous, fluorosis interferes with the normal metabolism of bones and teeth.

See figure 1-16 Thomson's book (Alimentary chapter).
**Osteofluorosis. Bovine.**

A cross sectional view of normal (n) and affected metatarsal bones (f). Note the increased thickening of cortical bone due to new periosteal bone formation (red line).

Osteofluorosis results from a chronic ingestion of fluorides present in water, plants and rocks in some geographical regions.

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.
**Vitamin A toxicity. Feline.**

Note the extensive hyperostosis and deformation of the periosteal surfaces of the bones.

The vertebrae are commonly affected in cats with vitamin A toxicity and in severe cases the periosteal proliferation results in vertebral fusion. This fusion of contiguous bones is referred to as ankylosis.

Cats are highly susceptible to vitamin A toxicity. It develops frequently when cats are fed livers from grazing cattle which are rich in Vitamin A. Also when animals are given excess vitamin A supplement.

Although the pathogenesis is poorly understood, it has been suggested that high levels of retinoid and other vitamin A metabolites stimulate osteoblastic activity.