Musculoskeletal System

Robert E. Schmidt, DVM, PhD
Zoo/Exotic Pathology Service
Davis, California, USA

Skeletal Muscle

A. **Embryology**

1. Clonable myoblasts appear on or about day 3 in-ovo
2. Myogenesis involves fusion of spindle-shaped uninucleated myoblasts.

    a. These eventually form mature muscle fibres.

3. Projections extend from myotubules and attach cells to each other.
4. Thick myosin [15-16nm] and thin actin [5-6nm] filaments are synthesized by clusters of ribosomes in muscle cell cytoplasm.

    a. Extent of synthesis increases following fusion of myoblasts.
    b. During growth of myotubules there is progressive organization of myofibrils until most of the cell has cross striated pattern similar to adult skeletal muscle.

5. Sarcoplasmic reticulum develops in isolated portions from rough endoplasmic reticuluml during earliest myotube stage.

    a. Connect during development and form a network around contractile filaments.

6. Transverse tubules [t-tubules] develop more slowly than sarcoplasmic reticulum.

    a. They are formed by invagination of the surface of myotubes and gradually project into myotube and contract the sarcoplasmic reticulum.

7. Growth of muscle and differentiation of fibre types.

    a. Individual fibres increase in length by addition of new sarcomeres and in breadth as number of myofibrils increases.
    b. Growth is dependent on contractility
    c. Most muscles contain a mixture of fibre types.

        i. five major types classified morphologically and biochemically.

            - twitch fibres-3 subtypes
            - tonic fibres-2 subtypes

8. Striated muscle derived from paired somites [neck, trunk, limb] or mesenchyme of the branchial arches [head and neck].

    a. Sclerotome migrates from a somite to form a vertebra leaving the myotome {muscle plate].

        i. myotome thickens and differentiates into myoblasts.

    b. At the beginning of differentiation the nucleus is central in a fibre surrounded by granular cytoplasm that gives rise to myofibrils. Nuclei eventually forced to the surface by newly forming fibrils.

9. During morphogenesis muscle fibres aggregate into groups that make up the individual muscles.

    a. Muscle fibres change direction and muscle primordia migrate to distant locations.
    b. successive myotomes fuse into composite muscles and longitudinal splitting of myotomes may take place.
    c. Tangential splitting and degeneration of myotomes may occur.

B. **Anatomy**

1. *Gross Morphology*

    a. A muscle is comprised of muscle fibres that are parallel to each other. It can be considered as a collection of sarcomeres arranged in series and in parallel.
    b. Fibre length is usually just long enough to permit the required amount of shortening and force development.
    c. Major fibre types:

        i. red and white-differentiated by myoglobin content.
            - red fibres fatigue slowly, white quickly.

        ii. twitch and tonus-differentiated by pattern of innervation, sarcotubular system and other cytologic features. refers to fast and slow fibres respectively.
        iii. sarcotubular system of twitch fibres is well developed but in tonus fibres it is reduced.
        iv. differences in fibres are speed of contracting and relaxation, and the rate of fatigue and propagation [depolarization] ability of the membrane.

2. *Histologic structure.*

    a. Elongated cell with tapered or blunt ends. 1-40 mm long and 10-100um in diameter.
    b. Cells are multinucleated and striated. Nuclei located near the periphery of the cells.
    c. Cross striations are perpendicular to the fibre long axis-I and A bands, and Z lines.

d. The unit of contractility is the sarcomere which includes the myofilaments contained between adjacent Z lines.
e. Myofibrils contain actin and myosin.

i. actin is in thin filaments 5 nm in diameter, and myosin is 10nm in diameter.

3. *Muscle-bone systems*

a. One joint muscles-span one articulation.
b. Two joint muscles-most of the important strong muscles of birds. They span 2 articulations between their origin and insertion.
c. Special systems.

i. linkage systems-muscles serve as ligaments-are found in skeleton where some separation between bones is required or some tensile force is necessary; instead of simple resistance to the load as placed on a ligament.
ii. rigid struts-combination of muscle and bone. are rigid only when the muscle contracts.
iii. shock absorbing mechanisms-muscles may redistribute force or provide a torque to resist external torque.

C. **Structure/function relationships**

1. *Sarcomere-longitudinal segmental unit of the muscle fibre.*

a. Bounded by the sarcolemma and 2 disks/bands.
b. Join end-to-end to form the fibre.
c. Cross bridges occur between thick and thin filaments.

i. the bridges provide tension-developing and shortening mechanisms of muscle contraction.
d. As the sarcomere shortens or is stretched the thin filaments slide relative to the thick filaments.

2. *Muscle fibre.*

a. Made up of sarcomeres and bounded by a single continuous sarcolemma.

i. sarcolemma transmits stimuli from motor end-plate to all parts of the fibre as a propagated action potential.

3. *Muscle*

a. Comprised of numerous fibres parallel to each other.
b. Maximum tension depends on the number of sarcomeres arrayed in parallel, and the properties of the sarcomere.

i. cross section area of all sarcomeres is proportional to the maximum muscular force.

ii. the 2 most essential gross morphologic parameters are fibre length and number of fibres.
iii. fast twitch glycolytic populations of muscle fibres probably reduce force and power for takeoff and landing, while fast-twitch oxidative-glycolytic populations are used for sustained flight [power requirements reduced].
iv. oxidative fibres have significantly smaller size than anerobic fibres.

D. **Diseases**

1. *Congenital*

a. Muscular dystrophy [chicken and turkey]

i. irregular atrophy-fibres lost and replaced by fat.
ii. histologically there is an increased number of nuclei and fibre size is variable.
iii. genetic basis.

b. Arthrogryposis

i. contracture of joints secondary to failure of proper muscle development-atrophy of muscles in turn secondary to congenital neurologic problems.
ii. muscle lost and replaced by fibrous tissue.
iii. the condition can also be secondary to congenital toxicity.

- alkaloids from plants such as tree tobacco, lupines and poison hemlock.

2. *Non-Inflammatory*

a. Atrophy

i. a common reaction to many problems including disuse, denervation, cachexia, local compression and senility.
ii. there is a decrease in fibre size and cross-sectional area-alterations of contractile elements-and shrinkage of plasma membrane leading to its' pulling away from the external lamina which becomes convoluted. the sarcoplasmic reticulum becomes more prominent.
iii. the most severe alterations are associated with denervation atrophy.

- secondary to spinal cord and peripheral nerve disease-trauma, neoplasms or inflammation.
- atrophy usually selective-only fibres innervated by damaged nerve fibres.

b. Steatosis

i. extensive increase in intramuscular fat, with replacement of myofibres.
ii. exact cause not known-possibilities include nutrition, metabolic disorder and genetic.

c. Hypertrophy

i. compensatory-may be physiologic [exercise] or secondary to muscle disease.

d. Trauma

i. haemorrhage edema and disruption of fibres present.

3. *Nutritional*

a. Vitamin E/Selenium deficiency. A diet high in rancid polyunsaturated fat destroys vitamin E.

i. usually seen in water birds but similar lesions can be found in many avian species.

b. grossly there are white streaks and patches in striated muscle.

i. Histologic changes include muscle fibre degeneration without inflammation.

- fibres swell and loose striations, eventually becoming shrunken and fragmented.

c. hepatic and central nervous system lesions may also be present.

4. *Stress/exertional rhabdomyolysis*

a. muscle necrosis leads to myoglobinuria.
b. histologically there is necrosis and hemorrhage.

5. *Endocrinopathies*

a. hyperthyroidism or hyperadrenocorticism may can lead to myofibre degeneration or atrophy.

6. *Toxic*

a. ionophores-used as coccidiostats and growth promoters.
b. gossypol
c. plants such as *Cassia* sp.

7. *Other*

    a. myasthenia gravis - congenital lack of acetylcholine receptors leads to muscle weakness-the condition may be associated with thymic hyperplasia.

        i. antibodies developed to nicotinic acetylcholine receptors-neuromuscular innervation interfered with.

    b. seen rarely in birds-has been associated with sudden death and no lesion other than hyperplastic thymus in an older bird.

    c. in some cases there can be megaesophagus and possibly some myofibre damage.

8. *Inflammatory-influx of inflammatory cells and fluid. Abscess formation possible*.

    a. Infectious

        i. Bacterial-clostridial possible following local trauma, or due to septic localization.
        ii. Parasites

            - larval migrans-nematodes and arthropods.
            - protozoa-localization of sarcocystis leads to necrosis, inflammation and myodegeneration
            - if few organisms, may not be visible grossly.
            - eventually cysts will form and inflammation will subside.
            - large protozoal cysts in the striated muscle may be grossly visible as white foci-most commonly seen in wild ducks.

        iii. Mycotic infections

            - local extension from air sacs, or due to systemic localization-most common in immunosupressed birds, or overwhelming infections.
            - grossly nonspecific areas of necrosis and possible abscess formation.
            - histologic specificity due to finding fungal organisms.

    b. Non-infectious

        i. trauma-exact reaction may depend on type.
        ii. immunologic-not specifically reported in birds.

9. *Neoplasia*

    a. Rhabdomyosarcoma. Reported in birds but rare.

        i. comprised of striated muscle-if well enough differentiated cross striations may be visible on light microscopy.

b. Granular cell tumors??

i. seen in pet birds. exact cell type of origin not known but probably not myoblastomas as previously thought.
ii. large cells with PAS positive granules in cytoplasm.

c. Lymphosarcoma [Marek's in appropriate species]

i. Usually a diffuse infiltrate of poorly differentiated lymphoid cells-one of the few tumors that will commonly invade skeletal muscle.

d. fibromatosis-proliferation of fibroblasts within skeletal muscle-variable anaplasia.

i. caused by avian leukosis viruses

e. malignant melanoma-cells usually pigmented but amelanotic types seen.

f. metastatic tumours not common.

Tendons and ligaments

A. Physical damage-trauma, separation etc.

B. Inflammation-tendon sheath etc.

1. Infectious-mycoplasma, bacteria and reovirus[as extension from arthritis].

a. infiltrate pleocellular and there may be fibrin present-organisms may or may not be seen.

2. Non-infectious-trauma, immunologic.

a. infiltrate usually mononuclear.

C. Neoplasia-tendon sheath sarcomas possible.

Bone

A. Embryology

1. Two types of bone-membranous and cartilage.

a. Membranous develops in mesenchymal sheets-bones of the face and cranial cavity.
b. Cartilage-replaces provisional cartilage skeleton. All bones except face and cranium.

2. Only one mode of histogenesis.

    a. Bone matrix laid down by osteoblasts-osteoid becomes impregnated with calcium slats and osteoblasts are trapped in lacunae.

        i. osteoblastic activity influenced by hormones of the pituitary, thyroid and parathyroid glands.
        ii. deposition of calcium salts regulated by alkaline phosphatase produced by osteoblasts.

3. Development of membrane bones

    a. Bone preceded by a dense blastemal membrane.

    b. At well vascularized points intramembranous ossification begins.

        i. osteoblasts appear and deposit bone matrix.
        ii. expanding spicules unite into trabeculae.
        iii. entire primordium becomes enclosed within a periosteum.

4. Development of cartilagenous bone

    a. Endochondral bone formation.
        i. in centres of hyaline cartilage bone cells multiply, form radial rows and enlarge.
        ii. calcium is deposited in the matrix.
        iii. cartilage and part of calcified matrix disintegrates leading to primordial marrow cavities which are invaded by vascular primary marrow tissue.

    b. Periosteal bone formation.

        i. compact bone develops from periosteum around cartilage.

5. Bone growth

    a. Membranous bones increase laterally by marginal ossification.

    b. Both types of bone grow in thickness by deposition of peripheral periosteal-formed matrix accompanies by central resorption-the shaft becomes hollow.
    c. Increase in length due to continued development of the cartilagenous epiphyseal plate. New cartilage develops and is replaced by bone matrix.-continues until adult length is reached.

B. **Anatomy**

1. Histologic structure.

a. Compact bone

i. is comprised of calcified bone matrix deposited in layers or lamellae that are 3-7um thick.
ii. uniformly spaced throughout the matrix are cavities called lacunae, each filled by a bone cell [osteocyte].
iii. radiating from the lacunae in all directions are canaliculi that penetrate the interstitium of the lamellae and anastomose with canaliculi of adjacent lacunae.
iv. there are 3 common lamellar patterns.

- concentric around vascular channels within the bone to form cylindrical units called Haversian systems or osteons-4-20 lamellae
- between Haversian systems are angular fragments of lamellar bone ,of variable size and shape, called interstitial systems
- the limits of Haversian and interstitial systems demarcated by cementing lines.
- at the external surface of the cortical bone beneath the periosteum, and interior beneath the endosteum are lamellae that extend around much of the shaft circumference-called inner and outer circumferential lamellae.

v. there are two categories of vascular channels based on orientation and relation to the lamellar structure.

- longitudinal in the centres of Haversian systems are Haversian canals that contain 1 or 2 vessels in loose connective tissue.
- transverse channels connecting haversian systems, surface and marrow cavities are called Volkmann's canals.

b. Spongy bone

i. composed of lamellae with lacunae embedded in interstitial substance.
ii. trabeculae are relatively thin and usually not penetrated by blood vessels.
iii. no complete Haversian systems-cells are nourished from the free endosteal surface via canaliculi.

c. Periosteum

i. has an inner layer of osteoblasts in direct contact with bone.

- in adults these are in resting form and are similar to other spindle-shaped connective tissue cells.

ii. the outer layer is acellular dense connective tissue containing blood vessels-branches of these vessels traverse the deeper layer and enter Volkmann's canals.
iii. bundles of collagenous fibres from the outer layer penetrate inward through outer circumferential lamellae and interstitial systems, and anchor the periosteum to the bone.

d. Endosteum

i. thin connective tissue layer lining the walls of cavities that house the marrow.

- has both osteogenic and hematopoietic potential.

e. Osteoclasts

i. attach to bone surface and resorb bone by secreting protons into a subosteoclastic compartment.
ii. a functional Cl-/HCO3 anion exchanger is present in the osteoclast-localized to the plasma membrane not attached to the bone surface.

f. Epiphyses

i. four zones from epiphysis to medulla-proliferation, prehypertrophy, hypertrophy and ossification.
ii. cytologic organization the same in altricial and precocial birds.
iii. functionally heterogeneous cell types present-each play a different role in cartilage calcification.

2. Gross Bone Structure

a. Spongy bone is a lattice of branching spicules that comprises a system of interconnecting spaces containing bone marrow.
b. Compact bone-a solid continuous mass with spaces only seen microscopically.
c. Long bones-consist of a thick-walled hollow cylinder with central medullary cavity that contains marrow [diaphysis].

i. epiphyses at the end of the shaft consist of spongy bone covered by a cortex of compact bone.
ii. in growing animals the epiphysis and diaphysis are separated by the cartilagenous epiphyseal plate-united with the diaphysis by columns of spongy bone called the metaphysis.
iii. bone is covered by periosteum and the marrow cavity is lined by endosteum.

d. Flat bones-have surface layers called inner and outer tables with middle layer of spongy bone called the diploe.

i. the inner lining of the cranium is the dura mater.

3. Special features of avian bone.

a. Single ear ossicle [columella/stapes].
b. Most birds have uncinate processes on the ribs-a feature shared with reptiles.
c. The “ankle” is an inter tarsal-not tibiotarsal-joint.
d. There is a backward slant to the pubic bones [as in some dinosaurs].
e. Portions of the marrow are replaced by air sacs.
f. The main bones of the skull and pelvis are fused-also some back vertebrae in certain species.

- leads to a reduction of carpal, metacarpal, tarsal and metatarsal bones.

C. Structure/Function Relationships

1. Growth

a. Many long bones have 3 ossification centres.
b. Growth plates-cartilage of the original bone model is reduced to the articular surfaces and a plate between the epiphyseal and diaphyseal centres.
   i. proliferative zone of the growth plate adds new cartilage cells to the epiphyseal and diaphyseal ossification centres simultaneously
   ii. eventually epiphyseal osseous replacement overrides the capacity of the cartilage on the epiphyseal side of the plate and the growth plate contributes cartilage only to the diaphyseal centre.
   iii. continued diaphyseal elongation results from growth plate interstitial growth-the epiphysis is moved further from the centre of the diaphysis.
c. Effects of hormones
   i. estrogens and testosterone inhibit linear growth by accelerating metaphyseal osseous replacement and inhibiting proliferative chondrocytes.
   ii. glucocorticoids inhibit skeletal development and retard secondary ossification centres.
   iii. growth hormone regulates the mitotic rate of proliferative chondrocytes [excess can lead to gigantism]
   iv. thyroxine [T4] is necessary for chondrocyte proliferation and maturation-it also affects the proliferation of osteogenic cells of the primary and secondary spongiosa.
   v. hormonally active form of vit d3 generates many of the biologic responses, including effects on osteoblasts and chondrocytes as well as stimulation of osteoclast production.

2. Support

a. bone has strength against compressive, shearing and tensile forces.

   i. when bone is subjected to these forces it may be stressed or moved.

ii. almost all stressing forces are asymmetrical and produce bending movements.
- there is an apparent correlation between load carried and the cross sectional geometry.
- the magnitude of stress is high at the periphery of a cross-sectional area, but low in the middle.

iii. strength of the bone [breaking point] is dependent on the maximum stress, and strength of the bone to withstand the stress.

- strength can be increased by organizing the material [boney trabeculae] so that the amount present at any spot is proportional to the stress-distribution of trabeculae follows stress patterns.
- maximum stress at the periphery is resisted by compact bone and by increasing the bone diameter.

iv. shape of many bones is correlated with the necessary distribution of material to withstand stress.
- bills are rounded
- curvature of sternum and synsacram correspond to stress pattern.

v. stress can be reduced by relocating to another part of the bone or another bone [skull roof to base].

3. Egg shell formation

a. The shell gland transports 2.0-2.5g of calcium within 15 hours for calcification of a simple egg.
i. at the rate of calcification circulating Ca would be depleted in 8-18 minutes.
ii. Calcium is replenished by intestinal absorption and bone mobilization.
- relative importance depends on dietary Ca concentration - hens consume 25% more feed on days when shell formation occurs.
- if dietary concentration of Ca is 3.56%k or high it can supply needs-if 1.95% bone supplies 30-40% and if there is minimal Ca in the diet the bone is the primary source.
- much of shell formation is at night when the Ca content of the GI tract is decreasing-bone is an important source of Ca in the early morning.

b. Vitamin D plays an important role
i. renal 2,5 dihydroxy-D3-1-hydroxylase activity increases prior to egg laying-corresponds to increase in total plasma calcium.

c. Calcium metabolism from medullary bone
i. forms along the endosteal surface and grows with a system of interconnecting spicules that may fill the medulla.

- in females Ca forms in fluid 10 days before egg laying.

ii. during the cycle of ovulation/ovipositioning, periods of medullary bone formation alternate with periods of depletion.
- if there is a low Ca diet, the bone cannot replenish and cortical bone is eroded, while medullary bone remains fairly constant.

Cartilage

1. It is present during development, but in the adult is seen primarily in articular pads.

   a. act as shock absorbers since cartilage deforms under stress.
   b. some articular pads may be formed of fibrocartilage which is stronger against shearing and compressive stress.

Ligaments and Tendons

1. Elastic ligaments-little is known about their distribution and composition in birds.

2. Collagenous ligaments-are flexible but inextensible.

3. There are two main groups of ligaments-articular and linkage.

   a. Articular bind bones together and prevent stress from disruption articulations, as well as fixing the type and extent of movement of 2 bones at an articulation.
   b. Uncommon and restricted to the head-they may span 2 or more joints.

4. Tendons

   a. Connect muscles to bones.

      i. reduces the amount of bone surface used for attachment.
      ii. allow muscles to cover a long distance between origin and insertion without requiring excessive muscle length.
      iii. permit location of muscles in favorable positions away from the site of action.

   b. Must be stronger than muscles to transmit force developed by the muscles.
   c. Must be flexible.

Articulations [joints]

1. Diarthroses have a joint cavity.

2. Synarthroses - a continuous intervening substance is present between bones.

   a. Synostosis-the intervening material is bone.
   b. Synchondrosis-the material is cartilage.

c. Syndesmosis-the material is fibrous tissue.

3. Joints allow movement between bones and serve as the centre of rotation of bones.

Diseases/Lesions of Bone

1. General reactions to injury.

   a. Direct physical injury-leads to osteoblastic proliferation [from the osteogenic layer of the periosteum] and new bone formation.

   b. Disuse-increased resorption and inhibition of bone formation.

   c. Necrosis

      i. aseptic-secondary to neoplasia or vascular lesions.
      ii. septic-associated with osteomyelitis

   d. Neoplasia-bone, cartilage or marrow origin, as well as metastatic tumors.

   e. Fracture repair-similar to mammals.
      i. hematoma formation
      ii. mesenchymal cell proliferation-matures into osteoblasts and forms woven bone [callus-internal or external].
      iii. callus formation is influenced by O2 tension, mechanical tension and compression.
      iv. woven bone is replaced by lamellar bone.

2. Abnormalities of Development

   a. Can be genetic, adaptational or due to teratogens.

      i. long bone deformities-slow differentiation of cortical bone and weak distal metaphysis-the exact cause is not known.
      ii. chondrodystrophies

         - tibial dyschondroplasia-turkeys, chickens and ducks.

            * has been produced by copper deficiency, some toxins excessive cysteine and acidosis-but the mechanism is not completely understood.
            * abnormal mass of cartilage in the proximal end of the tibia.
            * the cartilage is not calcified [prehypertrophic]-there is a reduction in the number of growth-plate chondrocytes containing protein transforming growth factor beta 3-which is thought to be associated with the failure of chondrocyte hypertrophy.
               * there is an apparent defect in vascularization so that the supply of mineral ions and nutrients to cartilage is inadequate to support matrix vesicle

formation and subsequent mineralization.

* chondrocytes in growth-plate do not reach normal size and necrose prematurely.

- nutritional chondrostrophy-generalized disorder of growth of long bones.
  * linear growth impaired-mineralization and appositional growth not affected.
    * bones become short and joints enlarge
    * may have secondary varus or valgus leg deformity which can lead to severe gastrocnemius tendon displacement.
    * has been related to deficiencies of manganese, choline, biotin, nicotinic acid, zinc and pyridoxine.
    * histologically there is a lack and disorganization of chondrocytes distal from blood vessels in the zone of proliferation.

- osteochondrosis-three forms, osteochondrosis dissecans, physitis and subchondral bone cysts.
  * microscopic tears and degenerative changes in the avian growth plate and articular cartilage.
    * may predispose to epiphysiolysis.
    * there may be abnormal endochondral ossification.

iii. localized deformities include hemimyelia, syndactyly and polydactyly.

* are primary structural defects associated with localized problems during embryogenesis.
* deformities arise late in fetal life and are alterations in a previously normal structure.
* the cause is not apparent.

3. **Metabolic Bone Disease**

a. Osteoporosis [osteopenia]-a reduction of bone mass with the remaining bone normally mineralized. It is a failure of matrix formation.

i. reduced thickness and more porous cortical bone.
ii. trabecular bone thinner and eventually lost.
iii. bone easily fractured.
iv. not a simple loss of apatite and collagen-involves changes in the collagen molecule biochemistry.
  - increased hydroxylation and change in cross-link profile lead to increased turnover of collagen and increased bone fragility.
v. causes
  - starvation
  - calcium deficiency-may result in hypocalcemia with parathyroid hypertrophy and increased parathormone production leading to bone resorption.
  - reduced physical activity.

- copper, phosphorous and vitamin D3 deficiencies.
- egg production/laying.

b. Rickets and osteomalacia-immature skeleton=rickets and mature=osteomalacia. These problems are due to a failure of mineralization of matrix leading to bone deformities and fractures.

i. *rickets* - a disease of bone and cartilage undergoing endochondral ossification.
- irregular thickening and misalignment of physeal chondrocytes, particularly the zone of proliferation.
  * thickening due to lack of mineralization-blood vessels and chondroclasts will not invade the physis and there is failure of removal of chondrocytes despite normal production.
- commonly caused by a deficiency of vitamin D, phosphorous or calcium, or an imbalance of calcium/phosphorous.
- excess unmineralized osteoid and fibrous tissue can accumulate.
- hypocalcemia can develop with vitamin D or calcium deficiency and secondary hyperparathyroidism may lead to fibrous osteodystrophy.
- grossly bones are soft and the metaphyses are flared-fractures may be present.
- histologically there may be retention of the cartilagenous core within the growth plate due to lengthening of the zone of hypertrophy.

ii. *osteomalacia*

- develops in new bone as remodeling occurs.
- no lesion in the physeal cartilage.
- gross changes similar to rickets.

c. Osteodystrophy Fibrosa

i. characterized by increased osteoclastic resorption of bone with replacement by fibrous tissue.

ii. due to primary or secondary hyperparathyroidism.
- primary-hyperplasia or neoplasia of the parathyroid.
- secondary
  * nutritional-diet low in calcium or and/or has excess phosphorous as in many all-seed diets.
    # increased phosphorous may interfere with intestinal absorption of calcium.
    # leads to decrease in serum ionized calcium and increase in parathormone.
  * renal-chronic severe renal disease leading to inability to excrete phosphate, inadequate production of 1,25 dihydroxy vitamin D and acidosis.
    # phosphate retention leads to hyperphosphatemia, hypocalcemia and increased parathormone excretion.

iii. *lesions*

* increased osteoclastic resorption of cancellous bone and proliferation of fibrous tissue.
* bones become soft and may bend-can also fracture or become deformed.
* growth plates normal unless there is also a vitamin D deficiency.

d. *Vitamin C Deficiency*

i. leads to arrested osteoblastic activity.
ii. spicules of calcified cartilage remain as only support for metaphysis-usually leads to fracture and hemorrhage.

e. *Vitamin A Deficiency-usually a result of inadequate diet*

i. vitamin A needed for osteoclast function-in deficiency there is a reduction in osteoclasts leading to an imbalance with osteoblasts and excessive bone production.
- in young animals [mothers may have been deficient] bone increases in size and can constrict cranial nerves in foramina leading to nerve damage.

f. *Polyostotic hyperostosis*

i. generalized medullary bone opacity radiographically - but histologically the excessive bone appears normal.

-cause not determined.

4. **Toxic Bone Disease**

a. Vitamin D

i. prolonged uptake can lead to osteosclerosis-can be secondary to increased absorption and intestinal mobilization as well as decreased urinary excretion.

- persistent hypercalcemia leads to lower PTH and elevation of calcitonin which stops bone resorption.
- there is direct stimulation of osteoblasts.
- bone matrix is woven and histologically stains basophilic [blue].

b. Lead

i. bound to the mineral phase of bone-leads to a “lead-line” which is a growth retardation lattice secondary to lead induced malformation of osteoclasts.

- osteoclasts may contain acid-fast inclusion bodies.

c. Vitamin A

i. excess leads to destruction of cartilagenous growth plates which become thin and irregular-results in osteoporosis in young animals and deforming cervical spondylosis in adults.

d. Fluorine

i. chronic toxicity results in osteopetrosis-bones become thicker and heavier and the marrow cavity is lost.

- trabeculae are dense and the periosteum is thickened at lower doses
- at higher doses there may be osteoporosis.

5. Degenerative Bone Disease

a. Poor fracture healing-all can lead to fibrous callus.

i. malnutrition
ii. loss of blood supply
iii. excessive movement
iv. infection

b. Ischemia

i. neoplasia-leads to interference with the vascular supply.
ii. primary vascular disease.
iii. infection
iv. trauma with or w/o fracture.
v. aseptic necrosis can be the result-the bone has a dry chalky appearance grossly.

- histologically there is death and loss of osteocytes, the marrow cells loose staining and vascular fibrous tissue invades the area.

6. Inflammatory Bone Disease

a. Osteomyelitis

i. usually infectious

- bacteria-wide variety, both aerobic and anerobic
- fungi, including aspergillus, candida and coccidioides or other deep mycoses.

ii. may be secondary to trauma, or hematogenous dissemination.
iii. birds tend to form granuloma that wall off infectious agents as there are no lysosomal enzymes in heterophils.

- grossly lesions are dry and caseous and usually non-draining.
- may not spread systemically but can become generalized if the bird is immunocompromised.

- bacterial toxins and ischemia can lead to bone necrosis and sequestra may form.

7. Proliferative Bone Disease

a. Exostosis/enostosis/osteophytes

i. deposition of woven bone can occur on peri-or endosteal surfaces as well as in trabeculae.

- variety of causes include infection, trauma and neoplasia.

b. Osteochondrosis

i. focal area of disordered endochondral ossification in a bone growth area that was normal.
ii. may be secondary to biomechanical forces and associated with ischemia or trauma.
iii. can occur in the epiphysis [articular or nonarticular] and the growth plate.

- nonarticular-sites of tendon and ligament attachment associated with excessive traction.
- articular cartilage-associated with chondrocyte necrosis and cartilage dissection.

c. Osteopetrosis

i. marked diaphyseal swelling of long bones due to massive growth of subperiosteal bone.
ii. can be caused by retroviruses that cause increased osteoblastic proliferation or decreased osteoclastic resorption.

- in birds osteoclasts appear to be in normal number-problem is due to what is a neoplastic proliferation of osteoblasts.

d. Neoplasia

i. Osteoma-large hard swelling in any location but often involving the skull or vertebrae.

- comprised of cancellous bone with marrow spaces.

ii. osteosarcoma-firm mass that histologically is comprised of fusiform/stellate-shaped cells and may have have osteoid and/or bone.

- parosteal -arises on the surface of bone with no marrow involvement.

iv. chondroma-firm mass comprised of well differentiated cartilage.
v. chondrosarcoma-poorly differentiated cartilage-will have mitotic activity histologically.

vi. osteochondroma-not sure if seen in birds-in mammals can be single or multiple.

- comprised of osteophytes with a cartilagenous cap.
- may be multiple in cats and caused by retrovirus.

vii. fibrosarcoma-can arise in medullary space-may be difficult to differentiate from osteosarcoma histologically.
viii. hemangiosarcoma-also seen in the medullary cavity.
ix. synovial sarcoma-has been reported in birds-histologically there is mucin and fusiform cells.-may be difficult to distinguish from air sac carcinoma of bone.
x. metastases/extensions.

- air sac carcinoma
- other carcinomas-may arise anywhere in body.

Diseases of the Joints

1. Congenital dysplasia

2. Luxation/subluxation

   a. Congenital
   b. traumatic

3. Inflammatory disease

   a. Infection

      i. bacteria including streptococcus, mycoplasma and reovirus.
      ii. all synovial membranes may be involved
      iii. acute cases-gross exudation and fibrin production - histologically there is an infiltration of heterophils and a few macrophages.
      iv. in chronic disease there is synovial hyperplasia and villus formation with fibroplasia-lymphocytes and plasma cells predominate-eventually there is granulation tissue formation.

   b. Articular urate deposition [gout].

      i. pleocellular inflammatory infiltrate including giant cells.
      ii. variable necrosis and deposition of amorphous or crystalline urates that leads to gross swelling and white chalky material in and around the joint.

   c. trauma-with or w/o foreign body penetration.

4. Hemorrhage-from trauma-possibly associated with “conure bleeding syndrome”.

5. Degenerative joint disease.

   a. Variety of causes.
   b. Leads to formation of cartilagenous flaps and free cartilage in the joint cavity.

c. Eventually there is formation of osteophytes and fibrosis in the periarticular soft tissue.

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