DISEASES OF BONES-JOINTS-MUSCLES

DISEASES OF MUSCLES

DISTURBANCES OF GROWTH

1-Muscle Atrophy

- **Denervation atrophy**
- **Disuse atrophy**
- **Atrophy caused by endocrine disease (hypothyroidism and hypercortisolism)**
- **Atrophy caused by cachexia, aging**
- **Atrophy caused by congenital myopathy**

2- Muscle Hypertrophy

- ***Physiologic hypertrophy***
- ***Compensatory hypertrophy***

Muscle atrophy

- Muscle atrophy can refer to reduction in overall muscle mass.
- Reduction in mass most often reflects decreased myofiber diameter that can involve all fibers uniformly or that can selectively involve muscle fiber types.

Denervation atrophy:

- *Myofibers that have lost connection with peripheral nerves due to neuropathy or neuronopathy undergo rapid and severe atrophy due to denervation.*

- This form of atrophy has also been referred to in the somewhat contradictory terms "neurogenic atrophy.«

- It is asymmetrical (the hallmark of equine protozoal myeloencephalitis) gluteal atrophy in the horse, and radial or brachial paralysis in dogs and horses due to trauma.

- Lesions involving the ventral gray matter of the spinal cord or the ventral roots emerging from the spinal canal, and inherited or acquired peripheral neuropathies, are also common causes of denervation atrophy.

Disuse atrophy

- Disuse atrophy occurs due to decreased contractile activity of innervated muscle.
- Decreased muscular activity due to painful lameness, bone fracture or disease, or limb immobilization are most common.

Atrophy of cachexia:

- Atrophy of cachexia and malnutrition occurs when an animal is unable to supply enough dietary nutrients to maintain muscle; muscle proteins become the source of nutrients for the rest of the body.

Muscle Hypertrophy

- Hypertrophy can refer to the muscle as a whole or to increased diameter of myofibers.
- Overall muscular hypertrophy occurs due to physiologic increase in myofiber diameter due to exercise conditioning.
- This process of physiologic hypertrophy of fibers is accomplished by adding sarcomeres, by adding myofilamerits to the periphery of myofibrils, and by adding new myofibrils to the existing ones by a process of longitudinal splitting.

Regeneration and repair of muscle

- The ability of muscle to repair itself is remarkable considering its high specialization and the great length and great vulnerability of individual fibers.
- The ability to rapidly repair the damaged segment of a fiber, without apparent complication to the rest of the fiber, is without parallel in other cells of the body.
- The major participants in the regenerative sequence are macrophages from the blood, the satellite cells, because only they, within the muscle, have retained the capability for mitotic division, and the basal lamina, which acts as a very efficient scaffold.
- The integrity of the basal lamina determines from the very beginning how effective regeneration will be and whether the outcome will be regeneration of myofibers, fibrous replacement, or a mixture of the two.

Regeneration and repair of muscle

- An intact basal lamina effectively keeps myonuclei, satellite nuclei, and myoblastic cells inside.
- Macrophages dissolve and remove the debris; neutrophils disappear unless infection complicates the process.
- Removal of sarcoplasmic debris leaves some space enclosed within the collapsing sarcolemma; and proliferating satellite cells are seen in the sarcolemmal tube.
- These cells are now termed myoblasts.
- Myoblasts increase in number until a critical myoblastic mass is reached.

Portals of Entry and Pathways of Spread into the Muscular System

DIRECT

- Penetrating wounds
- Intramuscular injections
- Bone fracture causing trauma to adjacent muscle
- External pressure causing crush injury

HEMATOGENOUS

- *Bloodborne pathogens, toxins, autoantibodies, and immune complexes*
- *Cytotoxic lymphocytes causing immune-mediated damage*
- *Other inflammatory cells*

Ischemic Muscle Necrosis

It emerges as 4 different syndromes:

1. **Vascular occlusion syndrome:**

- Occlusion of major arteries such as aortic-iliac thrombosis ("saddle thrombi") can also cause ischemic muscle necrosis.

Ischemic Muscle Necrosis

2. Compartment syndrome

- Muscles that are surrounded by either a heavy aponeurotic sheath or by bone and sheath are vulnerable to ischemia when muscle fibers are subjecte to moderately vigorous but not exhaustive contraction.
- This syndrome occurs in well-conditioned athletes.
- It occurs in the supracoracoid muscles of some breeds of broiler chickens and in some breeds of turkeys.
- The so-called *spontaneous rupture of the gastrocnemius muscle of Channel Island breeds of cattle* may represent an example of compartment syndrome leading to ischemia and subsequent rupture.

Ischemic Muscle Necrosis

3. Downer syndrome:

- Most of the domestic species share a muscle ischemia syndrome that is initiated by external pressure of objects or by pressure created by the weight of body, torso, or head on a limb tucked under the body for prolonged periods.

4. Muscle crush syndrome:

- This form of muscle ischemia has characteristics in common with downer syndrome.
- It is usually initiated by acute accidental trauma, often including bone fracture.

NUTRITIONAL MYOPATHY

*(nutritional muscular dystrophy, **white muscle disease,** stiff-lamb disease)*

- Nutritional Muscular Dystrophy is a disease caused by a deficiency of selenium and vitamin E in dietary intake.
- The nutritional deficiencies are principally selenium and vitamin E.
- The adult disease affects animals fed marginal quality rations, such as turnips or poor-quality hay, and can appear as clinical or subclinical disease in animals in very poor condition.
- Nutritional myopathy is a problem around the world but it occurs most often in those countries with intensive livestock agriculture operations.

White Muscle Disease

- This condition often affects young ruminants, such as calves and lambs.
- They infrequently affect carnivores and foals.
- Adult and even older animals can be affected.

Pathogenesis:

- Soils that contains low levels of selenium produce forages and grains that are deficient in selenium.
- Similarly, if the forage is of low quality or is not stored properly it may be deficient in vitamin E.
- If an animal consumes this type of diet without additional supplementation they become susceptible to this disease.
- Selenium and vitamin E are antioxidants therefore, deficiencies of these nutrients leads to oxidative damage to cells within the body.
- In many cells, vitamin E- and selenium-containing enzymes are required as physiologic antagonists to a group of chemically varied substances known as free radicals.

Pathogenesis:

- Selenium is an essential factor.
- The lipid peroxides are reduced to lactic acid by means of Gulutation peroxidase.
- Harmful effect on the cell membrane is prevented.
- Vitamin E is an antioxidant. It prevents the formation of high concentrations of peroxide from fatty acids.
- If selenium and vitamin E are absent, the peroxide damages the cell membrane, then hyaline degeneration and necrosis develop.
- Free radicals may initiate cellular injury by causing peroxidation of membrane lipids and by causing physicochemical damage to protein molecules including those of mitochondria, endoplasmic reticulum, and cytosol.
- In the formation of the disease, vitamins A, C and some amino acids are also considered to be inadequate.

White Muscle Disease

Cattle:

- Nutritional myopathy occurs, sometimes in endemic proportions, in calves, mostly of beef type and 4-6 weeks old.
- It is also common in animals up to 6 months of age and occurs sporadically in older cattle.
- The disease is often related to poor-quality feed.

White Muscle Disease

- ***Postmortem lesions in calves*** *are usually dominated by marked mineralization of necrotic skeletal and/or cardiac muscle.*
- *When* the heart is extensively affected, intercostal muscles and the diaphragm are usually also affected, but other skeletal muscle lesions may not be widespread.
- *Heart lesions in calves usually involve the left ventricle more than the right.*
- Small lesions just under the epicardium or endocardium may appear as scattered white "brush" strokes.
- The mineralized lesions are creamy white and opaque. Small streaks of hemorrhage may also be seen.

White Muscle Disease

- **Lungs** are often filled with pink frothy fluid and an excess of fluid may be present in the thorax indicating heart failure.
- Acute pneumonic changes sometimes develop as a complication of pulmonary edema.
- *In those cases where skeletal muscle lesions predominate, the most extensive lesions can be found in the large weight-bearing muscles of the thigh and shoulder,* but many others are affected and the lesions are bilaterally symmetrical.
- Suckling animals often have extensive lesions in the *highly active tongue and neck muscles,* and occasionally in the voluntary muscles of rectum, urethra, and esophagus.
- Affected muscles are pale, irregularly opaque and yellow to creamy-white.

Sheep and Goats

- *Nutritional myopathy in* **sheep** *is probably more prevalent in more areas of the world than the disease in cattle.*

- The names white muscle disease, rigid lamb disease, and stiff lamb disease were coined to describe the most frequently encountered clinical patterns **in 2-4-week-old lambs**, which very often are spring lambs, recently turned out onto the first green pasture.

- Thus, in various parts of the world, the disease has been precipitated by stress from bad weather, prolonged winter feeding, subsistence on root crops, or forced activity, as well as feeding on stubble, legume pastures, dry pastures, and pastures with too much copper.

Sheep and Goats

- Deficiency in sheep is attributed to deficiency of vitamin E or selenium, but seldom of both.
- Bilaterally symmetrical lesions of the thigh muscles may occur but they may predominate in or be confined to the intermediate head of the triceps, or the tensor fascia latae.
- **Microscopically,** the changes seen in affected muscle over a period of several days follow the expected sequence of necrosis, mineralization, phagocytosis, and regeneration characterized by satellite cell proliferation and myoblastformation.

Sheep and Goats

- In lambs, the disease typically occurs between 3 to 8 weeks of age, but may occur in older lambs as well.
- Progressive paralysis occurs, which is evident through the following symptoms: arched back, difficulty moving and an open shouldered stance.
- Cardiac failure may occur in two forms: sudden heart failure or gradual cardiac failure characterized by lung anemia that causes death due to suffocation.

Pigs

- *Nutritional myopathy in swine has been reported as a spontaneous disease wherever intensive pig rearing is practiced,* but particularly in northern, central and eastern continental Europe, the UK, the US, and Canada.
- Classical lesions involving only skeletal muscles are less common than some of the other expressions of porcine vitamin E/selenium deficiency such as hepatosis dietetica and mulberry heart disease.
- *Systematic microscopic study of muscles has revealed a much higher incidence of muscle lesions than was thought to exist.*

Microscopically;

The appearance of the lesions is similar to that of calves; however, calcifications are much more severe.

- **Microscopic findings:**
- **- calcification,**
- **- satellite cell proliferation and**
- **- myoblastic regenerative repair**

Muscle repair is examined in 3 periods.

1. **In the acute period**, The findings related to hyaline degeneration and necrosis are noteworthy.

- The muscle cells are bulging, lost in stripes and have a rough, eosinophilic appearance.
- This is Zenker degeneration (Hyaline degeneration).
- At the end of this period, the core forms picnose and karyorhexis.
- The coagulation necrosis (Zenker's necrosis) occurs when the muscle cells appear completely homogenous pink (eosinophilic) appearance.

2.Subacute period is a resorbive period.

- Necrotic muscle cells are phagocytosed by macrophages from the region (intersititium with monocytes from the blood and histiocytes located in the capillar vein).
- In addition, there are small amounts of neutrophil leukocytes, eosinophil leukocytes and lymphocytes in the region.

3.Subacute period follows the period of regeneration and reparation.

a) Regeneration:

- If the sarcolemma remains intact, the nuclei in the inner part of the sarcolemma grow, the vesicular shape becomes (active) and divide.
- Thus, multinucleated cells are formed.
- Then the cells around the core are separated and the new cells are shaped (the sarcoma around the nucleus is considered to be the sarcoma).
- The appearance of multinucleated muscle cells indicates regeneration.

b) Reparation:

- It forms the chronic period.
- If the sarcolemma is destroyed by necrosis, regeneration does not occur.
- The necrosis portions are cleaned as above.
- Afterwards, the cleaned areas are filled with connective tissue (fibroblast, fibrocyte) accompanied by capillary vessels from the interstitial region and granulation tissue is formed.
- Other cells such as monocytes, histiocytes, lymphocytes can also be seen in the granulation tissue.
- Over time, collagen yarns are formed and granulate tissue is formed alongside the scar tissue.
- In addition, dystrophic calcification is seen in some muscle strands that are necrotic in the area.

TOXIC MYOPATHIES

- **Ionophore toxicity (*monensin, lasalocid, salinomycin, narasin, and maduramicin*)**
- ***Plant toxicity***
  - ***Cassia spp. toxicity- ruminants***
  - ***Cassia spp. toxicity- swine***
  - ***Gossypol toxicity***

Monensin Toxicity

- Monensin, an antibiotic produced by the fermentation of Streptomyces cinnamonensis, has a growth-promoting effect in ruminants.
- It is an efficient coccidiostat in birds and other animals.
- Many episodes of monensin poisoning have been caused by mixing errors in packaged, pelleted, commercial animal feeds.
- It has put hundreds or thousands of animals at risk.
- Clinical signs of lethargy, stiffness, muscular weakness, and recumbency occur within 24 hours.

Monensin Toxicity

- Horses in the early stages, to show marked signs of colic, apprehension, shifting or fidgeting, sweating, myoglobinuria, and muscle tremors.
- Dogs show apprehension and progressive weakness.
- Myofiber nuclei and satellite cell nuclei as well as endomysial cells apparently survive acute toxicity, and the early stages of regeneration.
- Myocardial lesions in monensin toxicity are not reparable.

Cassia spp. toxicity- ruminants

- In the southern USA, mature cattle and goats on pasture may ingest the beans or coffee senna plant.
- Animals develop diarrhea, show evidence of weakness, and display a swaying, stumbling gait that is related to the developing muscle lesions.
- The disease progresses rapidly and most of the animals affected become recumbent and develop myoglobinuria.
- Postmortem lesions in recumbent animals consist of ill-defined pallor of much of the muscle mass.
- Histologic changes are typically monophasic multifocal myopathy.

Gossypol Toxicity

- *Gossypol is a yellow, pigmented, polyphenolic substance present in cottonseeds.*
- It is toxic to **swine**, and toxicosis occurs when swine are fed cottonseed cake or meal at a concentration of 10% or more of rations to which it is added as a protein supplement.
- The toxic effects are **cumulative.**
- Gossypol is toxic to experimental lambs and calves at concentrations of less than 450ppm in the feed (the level of free gossypol permitted in human and some animal foods).

Gossypol Toxicity

- Lesions are present in several organs, including the heart, skeletal muscles, liver, and lungs, and death is due to cardiac failure, which causes fluid accumulation in body cavities.
- Histologically, segmental necrosis of skeletal muscle and myocardium is present, the liver has centrilobular necrosis and the lungs are congested and edematous.
- Affected animals are pot-bellied and poorly grown, and most die acutely.

EXERTIONAL MYOPATHIES

- **Exertional myopathy is indicative of myofiber damage occurring due to exercise stress.**

- The initiation of abnormal excitation-contraction coupling, inadequate energy metabolism, ionic imbalance, or simply the mechanical stresses occurring during contraction are thought to lead to myofiber damage of predisposed muscle.

- Historically, the syndrome of passage *of myoglobin-pigmented urine (myoglobinuria)* was recognized long before it was determined that massive *skeletal muscle necrosis (rhabdomyolysis)* was the cause.

Exertional myopathy (rhabdomyolysis) in the horse (azoturia, *black water,* ***paralytic myoglobinuria, Monday-morning disease****, setfast, and tying up)*

- Muscle injury severe enough to result in myoglobinuria, profound weakness, and recumbency is common in heavy horse breeds, hence the terms azoturia, black water, and paralytic myoglobinuria.

- Exertional myopathy in light horse breeds is typically less severe, resulting in episodic muscle pain, sometimes associated with swelling, and reluctance to move, hence the names set fast and tying up.

Exertional myopathy (rhabdomyolysis) in the horse

- The most common cause of exertional rhabdomyolysis in many breeds of horses, including Quarter Horse, Warmblood, draft, Arabian, Standardbred, Tennessee Walker, Morgan, and Welsh pony-related breeds.
- Etiologies proposed for equine exertional rhabdomyolysis have included muscle lactic acidosis, hypothyroidism, electrolyte imbalance, and vitamin E and/or selenium deficiency.
- Only electrolyte imbalance, in particular hypokalemia, is still considered possible.

Exertional myopathy (rhabdomyolysis) in the horse

- Almost all horses with recurrent exertional rhabdomyolysis respond positively following a diet change to one that is high in fat, high in fiber, and low in starches and sugars.
- *Weakness and~or pain in the hindlimbs occur suddenly,* and the animal soon becomes unable or very reluctant to move.
- This may be accompanied by sweating and generalized tremors.
- The affected muscles, which are typically those of the *gluteal, femoral, and lumbar groups,* may be swollen and board-like in their rigidity.

Exertional myopathy (rhabdomyolysis) in the horse

- *Muscles may be moist, swollen, and dark, and streaks of pallor may be visible in the more extensively involved muscles.*
- *Myoglobinuria* can appear early in the disease, causing **dark red-brown discoloration of the urine**.
- That is often a prelude to death from **myoglobinuric nephrosis.**
- Damaged fiber segments generally undergo hypercontraction and hyaline degeneration followed by coagulative necrosis.
- Mineralization is not typically seen.

Capture Myopathy

- Exertional myopathy occurring in wild animals following capture and/or immobilization, an entity known as "capture myopathy."
- Clinically affected animals can exhibit dyspnea, weakness, muscle tremors or muscle rigidity, hyperthermia, collapse, and, often, death.
- Cardiac lesions, when present, are most often acute, although animals that survive capture myopathy may die acutely at a later date due to myocardial fibrosis.
- Myoglobinuric nephrosis may be seen.

MYOSITIS

- **Myositis** means inflammation of muscle.
- The cause of myositis is often not evident except in the obvious cases.
- **Suppurative myositis**
- **Malignant edema (gas gangrene)**
- **Blackleg**
- **Pseudo-blackleg**
- **Granulomatous myositis➔**
- ***Staphylococcal granuloma***
- ***Roeckl's granuloma of cattle***

Suppurative myositis

- Abscesses in muscle may sometimes be hematogenous in origin, but more often they result from ***inoculation*** (penetrating wound, contaminated injection, contamination of surgical site or laceration), or **by *extension from a suppurative focus*** in adjacent structures, such as joints, tendon sheaths, or lymph nodes.

- The most common causes of abscesses in muscle are *Arcanobacterium (Actinomyces, Corynebacterium) pyogenes* in cattle and swine, *Corynebacterium pseudotuberculosis* in sheep, goats, and horses, and *Streptococcus equi* in horses.

Suppurative myositis

- The early stage consists of local, ill-defined, cellulitis.
- Healing may take place after this with a minimum of scarring, or it may proceed to the formation of a typical abscess with a liquefied center, a pyogenic membrane, and an outer fibrous sheath.
- The lesion may slowly organize if it is effectively sterilized, expand if it is not or, alternatively, fistulate to the surface, collapse, and heal.

Malignant edema (Gas Gangrene)

- The muscles are highly susceptible to bacteria of the genus Clostridium, when they proliferate, are highly *toxigenic and cause extensive necrosis of muscle, with blood-stained edema and the formation of gas.*
- *Death occurs as a result of systemic intoxication.*
- *Since the pathogenic clostridia are frequently found in soil and feces, any contamination of an open wound is likely to introduce those potential pathogen.*

Malignant edema (Gas Gangrene)

- These bacteria (Clostridium) are gram-positive bacilli, to a greater or lesser degree anaerobic.
- They exist in the environment as resistant spores.
- Germination of the spores and vegetative growth requires fairly precise local conditions, chiefly a low oxidation-reduction potential and an alkaline pH.
- These conditions are best produced by deep penetrating wounds and the lesions that result from the activity of the anaerobes are called *"malignant edema,""gas gangrene"* and *" anaerobic cellulitis."*

Malignant edema (Gas Gangrene)

- **The species of the genus Clostridium that are of most importance as the agents of gas gangrene are**
- ***C. septicum, C. perfringens type A, and C, C. novyi type A, C. chauvoei, C. sordelli***
- **These organisms not only cause gas gangrene, which is usually a mixed infection,**
- ***C. chauvoei* - bacterial myositis – blackleg in ruminants.**
- ***C. novyi* - black disease,**
- ***C. septicum – braxy,***
- ***C. perfringens - the clostridial enterotoxemias***

Malignant edema (Gas Gangrene)

- Ruminants, horses, and swine are highly susceptible to these infections.

- Since deep wounds are the ones most suitable to the development of gas gangrene, the common causes of such susceptible wounds in animals are castration, shearing, penetrating stake wounds, injuries to the female genitalia during parturition and, especially in swine, inoculation sites.

Malignant edema (Gas Gangrene)

- The distinctive characteristics of these local infections are:
- *severe edema,*
- *the formation of gas bubbles that give crepitation,*
- *discoloration of the overlying skin,*
- *coldness of the affected part, and,*
- *in particular, the constitutional signs of profound toxemia with prostration,*
- *circulatory collapse, and*
- *sudden death.*

Malignant edema (Gas Gangrene)

- Malignant edema is more typically a cellulitis than a myositis, and the muscles may escape significant injury even in fulminating, highly toxigenic infections of the sort that are fatal in 48 h.
- One factor that is probably of much importance in determining whether the inflammation will be confined to the connective tissues (malignant edema) or will directly involve muscle (myositis) is the adequacy of the blood supply to the muscle.

Malignant edema (Gas Gangrene)

- If the muscle is devitalized by the initial trauma, or subsequently as a result of toxic injury to the blood vessels, the development of true gangrene is in order;
- in this manner, **malignant edema or anaerobic cellulitis may develop into gangrene**.

Blackleg

(Black quarter and Emphysematous gangrene)

- Blackleg is a gangrenous myositis of ruminants caused by ***C. chauvoei*** and characterized by the activation of latent spores in muscle.
- **This definition of blackleg separates it from gas gangrene.**
- Blackleg in cattle primarily affects animals **9 months to 2 years of age.**
- It affects animals in good condition, and often selectively causes death in the best-grown or best-fattened animals in a group.
- Blackleg is chiefly a disease of pastured animals with a tendency to be seasonal in summer.

Blackleg

- Blackleg, in spite of a worldwide distribution, peculiarly localized to regions, and within regions to farms.
- The muscle lesion produced is not distinctive for the blackleg pathogenesis, nor is the presence of ***C. chauvoei*** **in a typical gangrenous lesion,** because *C. chauvoei* can also be a wound contaminant.
- *C. septicum* proliferates rapidly after death while C. chauvoei does not.

Pathogenesis

- *The infection is acquired by the ingestion of spores,* and either these spores, or spores produced following one or more germinative cycles in the gut, are taken across the intestinal mucosa in some way.
- Macrophages may be responsible for this passage, but it may be possible for the spores to enter natural or transient apertures at tips of villi or in lymphoid crypts or be taken in by lymphoepithelial cells of the ileal domes by endocytosis.
- *Spores are distributed to tissues where they may be stored for long periods in phagocytic cells.*

Blackleg

- *The latent spores in muscle are stimulated to germinate when a local event creates muscle damage or low oxygen tension.*
- Color and watery exudate drips from cut surfaces.
- *The odor which emanates from the muscle is sweet and butyric, like rancid butter.*
- The initial bacterial lesion in blackleg is cellulitis with copious edema and hemorrhage.
- Degeneration of the muscle fibers is caused by both diffusing toxin and injury to blood vessels.

Blackleg

- Gangrenous lesions expand longitudinally with the long axis of muscles more readily than in a lateral direction, but "skip" areas may create necrotic zones that are highly irregular in contour.
- The expansion is enhanced by the edema fluid between fibers.
- The exudate and gas bubbles separate bundles of fibers and individual fibers.
- These undergo necrosis with preservation of striations in the center of the focus, and fatty and granular degeneration towards the periphery.
- Leukocytes are sparse, being destroyed by diffusing toxins.

- The lesions of blackleg are usually found in the large muscles of the pectoral and pelvic girdles.
- They may be found in any striated muscle including the myocardium.
- Lesions in the crura of the diaphragm and in the tongue are quite common.
- <u>The other lesions;</u>
- Severe parenchymatous degeneration of liver, kidney, and endocrine glands,
- Fibrinohemorrhagic pleuritis
- Emphysematous myocarditis and necrosis
- Fibrinohemorrhagic pericarditis

Staphylococcal granuloma

- Chronic granulomas of muscle or connective tissue caused by staphylococci, and referred to as **botryomycosis**
- They occur, particularly in the *horse and pig.*
- Infection by ***Staphylococcus aureus***
- **In horses, lesions are most frequent on the neck and pectoral region ("breast boils"), while in the pig, castration wounds and the mammary glands are the most common sites.**

Staphylococcal granuloma

- The lesion begins as a microabscess around a small colony of organisms and progresses rapidly, sometimes to a very large size.
- The fully formed granuloma is a hard, nodular, gray-white mass of dense, fibrous tissue, irregularly cavitated by small abscesses.
- The abscesses may be joined by tracts or they may fistulate to the surface.
- They contain a small quantity of thick, orange-yellow pus, which in turn contains minute granules.
- Variable numbers of neutrophils, lymphocytes, and plasma cells are present in the loose fibrous tissue outside of the club colony.

PARASITIC DISEASES

- *Trichinellosis*
- Sarcocystosis
- Eosinophilic myositis of cattle and sheep
- Toxoplasma and Neospora myositis
- Cysticercosis
- Hepatozoonosis
- Chagas' disease (American trypanosomiasis)

Trichinellosis

- Muscle is the habitat for encysted larvae of the nematode Trichinella spp., which may survive there for many years.
- Trichinellosis is a zoonotic disease.
- The muscle belongs to the animal that earlier harbored the adult worm in its duodenum.
- Since animal-to-animal transmission of infection is accomplished by the consumption of infected muscle.
- Man, dogs, wild Canidae, cats, wild Felidae, pigs, rats, mustelids,bears, raccoons, and mice become hosts to the adult and their persistent larvae.
- Horse and birds may become infected when muscle tissue is included in their feed.

Trichinellosis

- Humans become infected when they consume uncooked or incompletely cooked meats.
- **The parasitic cycle for T. spiralis begins with ingestion of infected meat fibers.**
- Gastric juices liberate the encysted larvae.
- Maturity is reached in about 4 days following ingestion, the adults copulate and the male dies.
- The ovoviviparous females penetrate via the crypts of Lieberkuhn to the submucosal lymphatics where they deposit 0.1 mm long larvae into lymph vessels.

Trichinellosis

- Usually parasitic infestations of muscle are asymptomatic.
- **Heart muscle is sometimes involved, but not heavily; the muscles most involved are tongue, masseter and laryngeal muscles, diaphragm, intercostal muscles, and muscles of the eye, but no striated muscle is exempt.**
- Within the muscle fiber, the larva grows, coils and enlarges a segment of the host muscle fiber, which is induced to develop some unusual changes as the "nurse cell."
- Nuclei enlarge, myofibrils are greatly reduced, the basal lamina is very greatly increased in its thickness and number of folds around the affected segment of muscle fiber, and the sarcoplasmic reticulum, which is in intimate contact with the worm, proliferates.

Trichinellosis

- On routine microscopic examination of muscle, larvae lie in bulging glassy segments of muscle fiber that may be loosely encircled by eosinophils, and in due course, by a scattering of lymphocytes, plasma cells, and macrophages.
- If the parasitized muscle segment degenerates, the larva is exposed and soon dies to become the center of a more acute inflammatory, but still predominantly eosinophilic, reaction.
- Segments of muscle fiber adjacent to the encysted larva may show evidence of degeneration or subsequent regenerative repair with basophilia and centrally located nuclei.

Cysticercosis

- A few have a special predilection for skeletal muscles and myocardium.
- **Taenia solium:**
- resident in the intestinal tract of humans.
- The larvae usually develop in the pig or wild pig.
- Most of the larvae in the pigfind their way to heart, masseter, tongue, or shoulder muscles.
- **Taenia saginata:**
- resident in the intestinal tract of humans.
- larval form (Cysticercus bovis) infests heart and masticatory muscles in cattle.
- **Taenia ovis:**
- found in dogs and wild carnivores,
- larval form, has a cysticercus (Cysticercus ovis) that develops in the heart and skeletal muscles of sheep and goats.

Sarcocystosis

- Sarcocystis spp. are protozoal parasites of animal muscle that in many respects resemble coccidia, the main difference being their obligatory development in two hosts.
- The sexual stages develop in a predator host, while the asexual phases develop in the prey animal.
- Histologically, Sarcocystis organisms are rarely accompanied by an acute inflammatory reaction, and schizonts in endothelial cells cause little or no evidence of endothelial cell destruction.

Eosinophilic myositis of cattle and sheep

- Eosinophilic myositis is a relatively rare condition in cattle and sheep of all ages that has some significance for meat inspection because the lesions are usually discovered in skeletal muscle and myocardium of animals slaughtered for human consumption.
- Eosinophilic myositis in sheep and cattle may be caused by degeneration of Sarcocystis spp.
- **The gross lesions** of eosinophilic myositis in cattle are characteristic, being well-demarcated, green, focal stripes or patches that fade to off-white when exposed to air.
- Individual lesions may be 2-3 mm to 5-6 cm in diameter.
- **Histologically,** The reaction is characterized by large numbers of eosinophils, and it is these that impart the green color to the lesion.

Toxoplasma and Neospora Myositis

- ***Neospora Caninum Toxoplasma Gondii***
- *Two* apicomplexan parasites, *Toxoplasma* and *Neospora,* produce myopathy in several species.
- Toxoplasma gondii infections, particularly in puppies and kittens, or in any species of farm animal naturally immunosuppressed, or in animals on immunosuppressive therapy, may massively involve skeletal muscle fibers.
- Myositis with mononuclear leukocytic infiltration, myofiber necrosis, and myofiber atrophy is accompanied by polyradiculoneuritis.

NEOPLASTIC DISEASES OF MUSCLE

- Primary tumors of striated muscle are uncommon.
- **Rhabdomyoma**
- **Rhabdomyosarcoma**
- **Leiomyoma**
- **Leiomyosarcoma**
- **Nonmuscle primary tumors of muscle**
- These tumors arise from supporting mesenchymal tissues of muscle. Malignant tumors are far more common than benign tumors.
- *Poorly differentiated sarcomas* and *giant cell sarcomas*
- *Hemangiosarcoma*
- *Malignant lymphoma*

DISEASES OF BONES

SKELETAL DYSPLASIAS

Generalized skeletal dysplasias

- The underlying defect may lie in the formation of cartilage, thus affecting all bones that form by endochondral ossification. Such disorders are referred to as chondrodysplasias.

- Achondroplasia is often used in place of chondrodysplasia to describe diseases characterized by disproportionate dwarfism.

Generalized skeletal dysplasias

- **Dexter/Bulldog type chondrodysplasia:**
- occurs in the Dexter and Holstein breeds, and possibly in Charolais and Jersey.
- They possess severe, relatively consistent, skeletal abnormalities.
- They have extremely short limbs, which are usually rotated, a domed head with retruded muzzle and protruding mandible, and a large ventral abdominal hernia.
- The tongue is of normal size so protrudes markedly, and the hard palate is absent.
- The shortened limb bones consist of mushroomshaped, cartilaginous epiphyses separated by a short, central segment of diaphyseal bone.

Generalized skeletal dysplasias

- **Telemark type chondrodysplasia:**
- is inherited as an *autosomal recessive trait* and, as such, the heterozygous parents are phenotypically normal.
- Affected calves are born alive but cannot stand, and die of suffocation shortly after birth.
- The lesions in Jerseys may include a short, broad head, deformed mandible, cleft palate, and short, spiraled limbs, but many calves have mild lesions.

Generalized skeletal dysplasias

- **Brachycephalic ("snorter") type:**
- dwarfism was common in the Hereford breed in North America and New Zealand, but also occurred in other beef breeds, especially the Angus.
- It is inherited as an *autosomal recessive trait.*
- Affected calves have a short, broad head with bulging forehead, retruded upper jaw and a slightly protruding mandible. The eyes are prominent and laterally displaced.
- The vertebral column is shortened and the ventral borders of individual vertebrae are flattened, a useful diagnostic feature visible radiographically in young calves.
- These anomalies in some cattle breeds are also observed **in pigs, dogs and cats.**

Localized Skeletal Dysplasias

- The legs mostly were affected.
- **Amelia:**
- Absence of legs
- **Hemimelia:**
- It is a defect in the middle part of a leg.
- It may be transversal or paraxial.
- There is no anterior-posterior leg bones or the radius-ulna tibia-fibula is aplasic.

Localized Skeletal Dysplasias

- **Syndactyly:** Fusion of digits
- **Polydactyly:** Presence of supernumerary digits
- **Ectrodactyly:** Partial or complete absence of a digit
- **Adactyly:** Absence of a digit
- **Dactylomegaly:** Abnormally large digits

Localized Skeletal Dysplasias

- **Head**
- Brachycephalic - Shortening of the head
- Brachygnathia - Abnormally short jaw (inferior or superior)
- Campylognathia - HareLip
- Palatoschisis - Cleft palate
- Prognathia - Abnormal projection of the jaw
- **Spine**
- Kyphosis - Abnormal dorsal curvature of the spinal column
- Lordosis - Abnormal ventral curvature of the spinal column
- Scoliosis - Lateral deviation in the spinal column

Metabolic Diseases of Bones

- Metabolic bone diseases, also referred to as **osteodystrophies,** are the result of disturbed bone growth, modeling, or remodeling due to either nutritional or hormonal imbalances.
- Metabolic bone diseases are traditionally classified as **rickets, osteomalacia, fibrous osteodystrophy,** or **osteoporosis.**

Adrenal Cortex

- Hyperadrenocorticism is the cause of osteoporosis.

OSTEOPOROSİS

- *Osteoporosis is easily the most common of the metabolic bone diseases,* both in man and animals. Rather than being a specific disease, *osteoporosis is a lesion characterized by a reduction in the quantity of bone, the quality of which is normal.*

- In effect, osteoporosis represents an imbalance between bone formation and resorption in favor of the latter, resulting in bone that is structurally normal but with reduced breaking strength.

OSTEOPOROSİS

- It shows marked fragility.
- It is especially common in farm animals.
- Most cases are of nutritional origin.
- Calcium failure in development is an important contributing factor.
- A few cases are due to an uncomplicated nutrient deficiency.

Etiologic Factors

- **Starvation induced osteoporosis:**

- Most cases of osteoporosis in animals, especially farm animals, are nutritional in origin and may be due to deficiency of a specific nutrient, such as calcium, phosphorus, or copper, or to starvation, where there is restricted intake of an otherwise balanced ration.

- The *effects of starvation* on the skeleton are greater in young growing animals than in adults.

- Growth of the skeleton is retarded and may cease during periods of starvation due to reduced production of bone matrix.

- **Disuse osteoporosis**
  - is a loss of bone mass due to muscular inactivity and reduced weight bearing.
  - It may be localized, following paralysis or fracture of a limb, or more generalized in association with prolonged recumbency or inactivity.
  - Bones that normally carry the greatest loads suffer the greatest proportional loss in mass from disuse.

- ***Senile osteoporosis***

- is common in humans and occurs in other animals, but *seldom appears as a clinical problem in veterinary medicine.*

- Insufficiency of active vitamin D metabolites

- The decrease in secretion of parathyroid hormone and sex steroids causes the decrease in physical activity.

- ***Gastrointestinal Parasitism Induced Osteoporosis***

- Osteoporosis is often present in animals with severe gastrointestinal parasitism, most likely *secondary to malabsorption.*
- *It is important for ruminants. The cause is parasitic (Trichostrongylus colubriformis) infestation.*
- **Corticosteroid-induced osteoporosis** is common in humans and its occurrence in animals may be underestimated.
- **Inflammatory bowel disease-induced osteoporosis**

- ***Calcium Deficiency Induced Osteoporosis***
- It can be experimentally. It is asymptomatic in adult animals.
- Generalized osteoporosis, and a tendency to fracture vertebrae, femurs, and phalanges, characterizes the condition.
- **The osteoporosis induced by calcium deficiency** is due to excess bone resorption as a result of increased **activity of parathyroid hormone** following a reduction in plasma-ionized calcium concentration.
- Both adult and growing animals, there is severe loss of cancellous bone, especially in bones with a high trabecular component such as vertebrae.

- **Phosphorus Deficiency Induced *Osteoporosis***
- Phosphorus deficiency produces osteomalacia in adults and rickets in growing animals, both under natural and experimental conditions.
- **Copper Deficiency Induced Osteoporosis**
- **a component of the enzyme lysyl oxidase**, *copper is required for the cross-linkage of collagen and elastin.*
- Impaired cross linkage of collagen in bone matrix most likely accounts for the increased bone fragility in copper-deficient animals.

Rickets and Osteomalacia

- It is convenient to consider these two diseases together as they have *a similar etiology and pathogenesis, differing only in the age at which they occur.*
- Rickets is a disease of the developing skeleton in young animals and is accompanied *by abnormal endochondral ossification at growth plates, in addition to defective bone formation.*
- Osteomalacia occurs only in adults and although there are no lesions associated with growth cartilages, *the bone changes are the same as those that occur in rickets.*
- Both diseases occur in all domestic animal species and wildlife.

Rickets and Osteomalacia

- The pathogenesis of both rickets and osteomalacia involves defective mineralization.
- Anything that interferes with the mineralization of cartilage or bone matrix may cause rickets or osteomalacia, but most cases in animals result from dietary deficiencies of either vitamin D or phosphorus.

- **Phosphorus Deficiency Induced *Osteomalacia***

- Phosphorus deficiency is well established as a cause of rickets and osteomalacia, although the exact mechanism is uncertain.
- Rickets and osteomalacia due to phosphorus deficiency are uncommon, but do occur in animals grazing pastures low in phosphorus.
- Signs of phosphorus deficiency develop slowly.
- Clinical disease is most likely to occur in cows where the deficiency is exacerbated by the extra demands of pregnancy or lactation.

- **Phosphorus Deficiency Induced *Osteomalacia***

- Such animals lose condition, develop transient, shifting lameness, and show an increased susceptibility to fractures.
- They may crave phosphorus-rich materials, and osteophagia and pica are characteristic signs of the deficiency.
- Fertility can be severely reduced and estrum may be irregular, inapparent, or absent.
- Hypophosphatemia develops early but also returns to normal rapidly if the animals are supplemented.

Vitamin D deficiency induced *Osteomalacia*

- Pre Vit. D3 (cholecalciferol) one of the important components of Vitamin D is formed in the skin.
- When the winter sun is at an angle of less than 30 degrees to the horizontal, the short-wavelength ultraviolet rays required for the activation of 7-dehydrocholesterol in the skin are reflected by the atmosphere and dermal synthesis of previtamin D 3 is impaired.

Vitamin D deficiency induced *Osteomalacia*

- Vitamin D deficiency may occur in grazing animals where the combination of relatively high latitudes and temperate climates allows them to be pastured for much of the year. Such conditions occur in parts of the United Kingdom, South America, New Zealand, and southern Australia.
- *It is likely that many grazing animals are vitamin D deficient for a period during the winter.*
- Sheep appear to be more susceptible to vitamin D deficiency than cattle, possibly because a dense fleece covers much of their skin.

HYPERPARATIROIDISM and BONE DISORDERS

- ***Fibrous osteodystrophy*** *(osteodystrophia fibrosa, osteitis fibrosa cystica)*

- Fibrous osteodystrophy is a relatively common metabolic bone disease characterized by extensive bone resorption accompanied by proliferation of fibrous tissue and poorly mineralized, immature bone.

- The pathogenesis involves persistent elevation of plasma PTH and the lesion can be considered to represent the skeletal manifestation of **primary or secondary hyperparathyroidism.**

Fibrous osteodystrophy

- Different animal species vary in their susceptibility to fibrous osteodystrophy and, to some degree, in the distribution of lesions.
- Horses, pigs, dogs, cats, ferrets, and goats are often affected, as are reptiles and New World nonhuman primates, but the disease is rare in sheep and cattle.
- In the **horse,** the disease occurs at any time after weaning but the prevalence, and possibly the susceptibility, declines after about the seventh year.

Fibrous osteodystrophy

- Horses require a calcium:phosphorus ratio of approximately 1:1.
- Diets in which the calcium:phosphorus ratio is 1:3 or wider, can result in osteodystrophia fibrosa depending to some extent on individual and familial susceptibility, and on alternative sources of calcium, such as drinking water.
- The condition usually occurs after maintenance for some months on diets consisting largely of grain, corn, and grain by-products such as bran, hence the term **"bran disease."**

Fibrous osteodystrophy

- **Primary hyperparathyroidism** *is usually the result of a functional parathyroid gland adenoma.*
- In primary hyperparathyroidism, autonomous secretion of PTH results in persistent hypercalcemia and hypophosphatemia, the latter reflecting increased urinary clearance of phosphate.
- The persistent hypercalcernia in primary hyperparathyroidism is generally accompanied by *polydipsia/polyuria, muscular weakness, and widespread mineralization of soft tissues.*
- Affected animals may succumb to the effects of *nephrocalcinosis* before the skeletal changes are severe enough to become clinically apparent.

Fibrous osteodystrophy

- **Secondary hyperparathyroidism** is a much more common cause of fibrous osteodystrophy in animals than primary hyperparathyroidism and *may be due to either chronic renal disease or a dietary imbalance of calcium and phosphorus.*
- PTH secretion is stimulated by a reduction in plasma-ionized calcium, whatever the cause, and if the stimulus persists then generalized bone resorption results.
- **Renal secondary hyperparathyroidism** occurs most often in dogs, and occasionally in cats, as a complication of chronic renal failure.
- Impaired glomerular filtration in animals with renal failure leads to progressive hyperphosphatemia due to reduced renal clearance of phosphate.

Fibrous osteodystrophy

- **Clinically;** Affected animals become depressed and may develop sudden lameness due to infractions of long bones or vertebrae, the latter resulting in paralysis.
- Signs of the disease are progressive and include reluctance to move, hindlimb lameness and incoordination.
- Early signs consist of minor changes in gait, stiffness, transient and shifting lameness, and lassitude.
- Loss of appetite with progressive cachexia and anemia develop later. The anemia may be due to depression of erythropoiesis by parathyroid hormone or its metabolites.

- *The most characteristic feature is bilateral swelling of the bones of the skull* including both the maxillae and mandibles, hence the term *"bighead'.*

- The *lesions of renal osteodystrophy in dogs are usually most severe in the bones of the skull.*

- As the disease progresses, there is accelerated resorption of cancellous bones of the maxilla and mandibles, occasionally resulting in soft, pliable mandibles (so-called "rubber jaw").

Nutritional Secondary Hyperparathyroidism

- *It may be due to a simple dietary deficiency of calcium, excess dietary phosphorus, or to a deficiency of vitamin D.*
- Vitamin D deficiency alone is also a cause of rickets or osteomalacia.
- Horses seem to be remarkably sensitive to the effects of high-phosphorus diets and relatively resistant to the effects of rations low in phosphorus.

Nutritional Secondary Hyperparathyroidism

- In practice, *nutritional secondary hyperparathyroidism is most often caused by diets containing low calcium and a relatively high concentration of phosphorus* and, with the exception of horses, affects young, rapidly growing animals.

- **In pathogenesis** increased plasma phosphate concentration, resulting from increased intestinal absorption of phosphorus, depresses plasma-ionized calcium and indirectly stimulates the release of PTH.

SCURVY

- **Scurvy** is a disease resulting from a lack of vitamin C (ascorbic acid).
- **Vitamin** C (ascorbic acid) is a co-factor for the enzymes prolyl and lysyl hydroxylase, which are required for the hydroxylation of proline and lysine during collagen synthesis, and is also an important antioxidant.
- In vitamin C **deficiency,** *there is reduction or failure in the secretion and deposition of collagen*.

SCURVY

- Most mammals synthesize ascorbic acid from glucose via glucuronic acid and gulonic acid.
- Some species, including humans, certain nonhuman primates, and guinea pigs, lack the hepatic microsomal enzyme L-gulonolactone oxidase and, in the absence of a dietar source of ascorbic acid, **develop scurvy.**

SCURVY

- **Gross lesions** are dominated by *sub-periosteal accumulations of clotted blood* around the shafts of the long bones, the scapulas, the bones of the head, especially the mandible, and on the ribs.

- The metaphyses are fragile, discolored by hemorrhage and separate easily from the adjacent physes.

- The bones are osteopenic and fragile.

SCURVY

- **The most characteristic microscopic lesion of scurvy** is in the metaphysis.
- *Naked spicules of calcified cartilage, derived from the zone of provisional calcification in the growth plate, persist as a "scorbutic lattice«.*
- The layer of bone that is normally deposited on this cartilage framework by active osteoblasts is absent or deficient.
- Osteoblasts are sparse and appear to have lost their polarity.

Toxic Osteodystrophies/ Vitamin D Toxicity

- Vitamin D is essential for normal bone development, in particular mineralization of cartilage during endochondral ossification and of newly formed osteoid, but in excess, it is highly toxic.
- **Vitamin** D toxicity may result from accidental over-supplementation of young animals, ingestion of plants that contain the active form of the vitamin, or accidental ingestion of rodenticide containing cholecalciferol (vitamin D3).
- The potency of the latter toxin is illustrated by the fact that cats and dogs may be poisoned by ingesting the carcasses of poisoned rats.
- Cats appear to be more sensitive to vitamin D toxicity than dogs.

Toxic Osteodystrophies/ Vitamin D Toxicity

- Vitamin D appears to prevent postparturient hypocalcemia ("milk fever") in cows but mineralization of soft tissues may result, particularly in pregnant Jersey cows, and in this breed its use is contraindicated.
- The *mechanism of vitamin D toxicity* is related primarily to its effect on increasing calcium absorption from the intestine, mobilizing it from bone and reducing its excretion by the kidney.
- The end result is *hypercalcemia* together with *hyperphosphatemia,* which, if persistent, will lead to widespread mineralization of soft tissues, in particular the kidneys, gastric mucosa, lungs, endocardium, and arterial walls.

Hypervitaminosis D Lesions

- *The skeletal changes in hypervitaminosis D may be characterized by either sclerosis or rarefaction,* depending on the level of dietary calcium and the pattern of exposure.
- An early response in bone is widespread, intense osteoclastic activity.
- With continued administration, the matrix produced by osteoblasts accumulates, sometimes in large amounts and in a distinctive pattern.
- It often has a tangled fibrillary arrangement and appears somewhat mucoid, floccular, and intensely basophilic.

Hypervitaminosis D Lesions

- Initially, the maturation of the matrix is local and irregular in distribution, and is unrelated to normal patterns of osteogenesis.
- If toxicity is prolonged, the abnormal matrices continue to accumulate and virtually obliterate the marrow spaces.
- This produces a mosaic of basophilic and acidophilic matrix, and newly formed woven bone.

Hypervitaminosis D Lesions

- The *presence of abundant basophilic matrix is virtually pathognomonic for vitamin D toxicity* and is valuable diagnostically when plasma levels of the vitamin are not known.

- Necrosis of osteocytes occurs with high doses of vitamin D and groups of empty lacunae are often present in cortical bone and in the center of trabeculae.

Deficiencies and Excesses of Vitamin A

- Toxic injury of bones in excess and hard tissue disorders in deficiency occurs.
- Depending on the age and species of animal, and the duration and level of exposure to excess vitamin A, ***the manifestations of toxicity*** *may include physeal damage, osteoporosis, or the development of exostoses (osteophytes).*
- The physeal lesions of vitamin A toxicity are characterized by reduced chondrocyte proliferation and reduced size of hypertrophic chondrocytes, resulting in narrowing of growth plates.

Vitamin A Toxicity

- The **osteoporosis** of vitamin A toxicity is associated with decreased numbers of osteoblasts and fewer, thinner osteoid seams than normal.
- It is most severe in cortical bone and some of the membranous bones of the skull.

Fluoride Toxicity

- Fluoride is an essential trace element but, when present in chronic excess, is capable of inducing *characteristic dental and~or bony changes.*
- Fluorosis *is the term used to denote chronic fluoride toxicity.*
- *All* species are susceptible but *fluorosis is most common in herbivorous animals.*
- **Acute intoxication leads to gastroenteritis.**
- *Fluoride is removed rapidly from the blood, by renal excretion and deposition in bones and teeth.* A small amount is deposited in soft tissues.

Fluorosis

- Toxic levels may be obtained from subsurface waters, especially where *rock phosphate* is plentiful. Rock phosphates vary considerably in their fluoride content, and chronic poisoning has been observed in cattle and sheep given rock phosphates as "licks."
- Contamination of pastures adjacent to *mineral ore refineries* may also cause toxicity, either directly or by uptake of fluorine by plants.
- **The characteristic changes of severe fluorosis occur in teeth and bones and are accompanied by shifting lameness, loss of production, and a variety of nonspecific signs of debility.**

LESIONS

- **Dental lesions** develop only if intoxication occurs while teeth are in the developmental stages and enamel is forming.
- The mildest macroscopic evidence of dental fluorosis is the *presence of small foci with a dry, chalky appearance compared to the normal glistening surface of enamel.*
- In more severe cases, *all the enamel in affected teeth may be chalky, opaque and show various degrees of yellow, dark brown, or black discoloration, which is virtually pathognomonic for fluorosis.*
- Affected teeth show accelerated wear and may develop chip fractures. In chronic cases, they may be worn to the gum line.

LESIONS

- Lesions of similar severity should be present in teeth that develop simultaneously.
- These associations include the first incisor with the second molar, second incisor with the third molar, and the third incisor with the second premolar.
- Lesions in the second incisor must be severe before lesions are prominent in the third molar, and in general, incisor abrasion develops prior to molar abrasion.
- Lesions may develop in the fourth incisor in the absence of changes in other teeth.

LESIONS

- The bone lesions of fluorine toxicity, **osteofluorosis,** are generalized but not uniform and, in severe cases, are characterized grossly by the formation of periosteal *hyperostoses,* which give the macerated bones a chalky roughened appearance.
- Lesions occur first on the medial surface of the proximal third of the metatarsal and later on the mandible, metacarpals, and ribs.
- The pelvis, vertebrae, and other bones of the distal limbs are also affected.

LESIONS

- In chronically affected cattle, fracture of the digital bones in the medial claw is common, leading to lameness and a preference for affected animals to stand cross-legged.
- At *highly toxic levels,* the gross lesions of osteofluorosis occur rapidly.
- *In young, growing dogs and pigs, and presumably in other species, fluorine intoxication produces lesions, which, in many respects, resemble rickets.*

RESPONSE to MECHANICAL FORCES and INJURY

- The cells of bone tissue are capable of the same basic cellular responses as most other tissues, including *atrophy, hypertrophy, hyperplasia, metaplasia, neoplasia, degeneration, and necrosis*.

- Depending on the stimulus, the response may be localized or generalized but, in general, the magnitude of skeletal response is greater in young growing animals than in adults.

Fracture repair

- *Bone fractures are very common in animals* and occur either when a bone is subjected to a mechanical force beyond that to which it is designed to withstand, or when there is an *underlying disease process that has reduced its normal breaking strength.*
- The latter is referred to as a **pathological fracture** and unless the predisposing disorder is corrected then the repair process is unlikely to be successful.
- The possibility of a localized bone disease (e.g., neoplasia or osteomyelitis) or a generalized disorder (e.g., fibrous osteodystrophy or osteoporosis) should always be considered if bone fracture has occurred without evidence of trauma.

Fracture types

- Fractures are classified as **simple,** if there is a clean break separating the bone into two parts, or **comminuted,** if several fragments of bone exist at the fracture site.
- When one segment of bone is driven into another the fracture is referred to as an **impacted fracture,** and when there is a break in the overlying skin, usually due to penetration by a sharp fragment of bone, the fracture is referred to **as compound.**
- If there has been minimal separation between the fractured bone ends, and the periosteum remains intact, the lesion is classified as **a greenstick fracture.**
- An **avulsion fracture** occurs when there is excessive trauma at sites of ligamentous or tendinous insertions and a fragment of bone is torn away.

Process of fracture repair

There are three major phases of fracture healing, two of which can be further sub-divided to make a total of five phases:

1-Reaction

i. Inflammation

ii. Granulation tissue formation

2-Repair

iii. Cartilage callus formation

iv. Lamellar bone deposition

3-Remodeling

v. Remodeling to original bone contour

Process of fracture repair

- ***I.* Stage:**
- After bone fracture, blood cells accumulate adjacent to the injury site.
- Soon after fracture, blood vessels constrict, stopping further bleeding.
- Within a few hours, the extravascular blood cells form a clot called a hematoma that acts as a template for callus formation.
- These cells, including macrophages, release inflammatory mediators such as cytokines (tumor necrosis factor alpha (TNFα), interleukin-1 family (IL-1), interleukin 6 (IL-6), 11 (IL-11), and 18 (IL-18)) and increase blood capillary permeability.

Process of fracture repair

- ***I.* Stage:**
- Inflammation peaks by 24 hours and completes by seven days. Through tumor necrosis factor receptor 1 (TNFR1) and tumor necrosis factor receptor 2, TNFα mediates the differentiation of mesenchymal stem cell (originated from the bone marrow) into osteoblast and chondrocytes.
- Stromal cell-derived factor 1 (SDF-1) and CXCR4 mediate recruitment of mesenchymal stem cells.
- IL-1 and IL-6 are the most important cytokines for bone healing.
- IL-1 promotes formation of callus and of blood vessels.
- IL-6 promotes differentiation of osteoblasts and osteoclasts.

Process of fracture repair

- **II. Stage:**

- All cells within the blood clot degenerate and die. Within this area, the fibroblasts replicate.

- Within 7-14 days, they form a loose aggregate of cells, interspersed with small blood vessels, known as granulation tissue.

- Osteoclasts move in to reabsorb dead bone ends, and other necrotic tissue is removed.

Process of fracture repair

- **III. Stage:**
- Bony callous formation:
- The fibrocartilaginous callus is converted into a bony callus of spongy bone.
- It takes about two months for the broken bone ends to be firmly joined together after the fracture.
- This is similar to the endochondral formation of bone when cartilage becomes ossified; osteoblasts, osteoclasts, and bone matrix are present.

Process of fracture repair

- **IV. Stage:**
- Lamellar bone deposition. Remodeling.
- The process substitutes the trabecular bone with compact bone and forms lamellar bone tissue.
- **V. Stage:**
- Remodeling to original bone contour
- The bone regains its original form and function and the healing is complete.

Complications of fracture repair

- **Technical:**
- Delay or failure of treatment
- **Biological:**
- Delay and deficiency in tissue response
- Deformations and excessive callus formation
- The repair of compound fractures may be delayed by the development of bacterial osteomyelitis following contamination of the fracture site through the open skin wound.

Complications of fracture repair

- When it becomes chronic, large callus formation is seen.
- In chronic cases, fistulizations and pseudarthrosis (pseudo joint) are formed.
- **Pseudodarthrosis formation factors:**
- lack of adequate fixation
- osteomyelitis
- blood circulation disorder
- Pseudoarthrosis may also develop if soft tissues separate the fractured bone ends or if persistent infection inhibits callus formation.

OSTEOSIS

- Like any living tissue, *bone will die when deprived of its blood supply.* This is referred to as **osteonecrosis,** or the synonymous term **osteosis.**

- In animals, bone ischemia is most often associated with trauma, particularly fractures.

- It is mostly not recognized macroscopically.

- *Microscopically, zones of empty lacunae due to loss of osteocytes characterize necrotic bone.*

OSTEOSIS

- The prognosis is more favorable if the necrotic bone is at a site that is both sterile and has good collateral circulation, and the volume of necrotic bone is small.
- In such cases, a zone of granulation tissue develops at the interface between the necrotic and viable tissue.

Aseptic Necrosis of Femoral Head
Legg-Calve-Perthes disease

- This disease, characterized by avascular necrosis of the femoral head occurs with some frequency in dogs, especially smaller breeds (Miniature Poodles, West Highland white and Yorkshire Terriers etc).

- The disease is inherited as an autosomal recessive trait.

Aseptic Necrosis of Femoral Head
Legg-Calve-Perthes disease

- Clinically, the disease has an insidious onset, usually between 4 and 8 months of age, and is bilateral in approximately 15% of cases.
- There is no obvious sex or leg preference in dogs.
- In the clinic only lameness is seen.

Aseptic Necrosis of Femoral Head
Legg-Calve-Perthes disease

- *The osteonecrosis in Legg-Calve-Perthes disease is initiated by one or more episodes of ischemia.*
- Hyperemia at the beginning of the case, then necrosis develop.
- When the subchondral infarct is more extensive, *continued weightbearing leads to fracture and collapse of the necrotic trabecular bone and flattening of the femoral head*, predisposing to degenerative arthropathy.

INFLAMMATORY DISEASES OF BONES

- **Osteitis** is inflammation of bones.
- Inflammation of bones inevitably originates in vascular areas of either the medullary cavity or the periosteum and is referred to as either **osteomyelitis or periostitis respectively.**

Bacterial infections of bones

- Bacterial infections of bones are very common in animals, especially young horses and ruminants.
- Since the route of infection is *usually hematogenous,* most are centered on the medullary cavity and are referred to as osteomyelitis.

Bacterial infections of bones

Vertebral osteomyelitis

- Arcanobacterium pyogenes is the most common causative organism in vertebral osteomyelitis in most species.
- These include: Escherichia coli, Salmonella typhimurium, staphylococci, streptococci, and R. equi in foals;
- Tuberculosis in older horses;
- Fusobacterium necrophorum in calves;
- **Mannheimia (Pasteurella) haemolytica, E necrophorum, and staphylococci** in sheep;
- and Erysipelothrix rhusiopathiae, Brucella suis, staphylococci, and streptococci in pigs

Bacterial infections of bones

- **Localized bacterial periostitis➔** the feet of cattle with *F. necrophorum* ("footrot")
- **Atrophic rhinitis of pigs➔** *Pasteurella multocida*
- **Mandibular osteomyelitis➔** *Actinomyces bovis*

Actinomycosis

- **Mandibular osteomyelitis** is primarily a disease of cattle caused by *Actinomyces bovis,* but occasionally occurs in horses, pigs, deer, sheep, and dogs.

- In cattle, the disease is known as **actinomycosis** or **"lumpy jaw,"** and *the classic lesion is confined to the mandible.*

- *The* maxilia is rarely involved and the organism rarely spreads even to regional lymph nodes, which, although large and indurated, are not infected.

Actinomycosis

- A. bovis is probably an obligate parasite of the oropharyngeal mucosa in a number of animal species, and most infections involve the buccal tissues.
- The organism is not particularly virulent, and in most, perhaps all cases, the surface tissues must be injured by some other agent or by a foreign body for invasion to occur.
- The osteomyelitis follows direct extension of the infection from the gums and periodontium.
- Once in the bone, A. bovis causes **a chronic, pyogranulomatous inflammatory reaction**.

Actinomycosis

- Suppurative tracts permeate the medullary spaces leading to multiple foci of bone resorption and proliferation.
- Large sequestra do not develop, even when the cortex is invaded, probably because of the slow, progressive nature of the disease.
- Fistulae often extend into the overlying soft tissue and may discharge through the skin or mucous membranes.
- Periosteal proliferation is excessive and the bone may become enormously enlarged, the normal architecture of the mandible being destroyed.
- The teeth in the affected portion of the jaw become loosened, lost, or buried in granulation tissue.

Actinomycosis

- On cut surface, the affected mandible has a "**honeycomb**" appearance with reactive bone surrounding pockets of inflammatory tissue.
- Fragments of necrotic trabecular bone accumulate in purulent exudate as **"bone sand.«**
- The pus is also likely to contain many 1-2-mm diameter, soft, light yellow granules referred to as **"sulfur granules."**
- These consist of an internal mass of tangled, gram-positive filaments mixed with some bacillary and coccoid forms, and a periphery consisting of closely packed, club-shaped, gram-negative bodies.

Viral Infections of Bones

- **Classical swine fever**
- **Canine distemper virus**
- **Canine adenovirus type I** infection in pups may be accompanied by grossly visible metaphyseal hemorrhages at costochondral junctions due to virus-induced injury to endothelial cells, some of which contain characteristic intranuclear inclusion bodies.

Viral Infections of Bones

- **Feline herpes virus** causes necrosis in the turbinate bones of germfree cats following intranasal inoculation, and produces necrosis in the metaphyses and periosteum of growing bone when administered intravenously.

- **Feline leukemia virus,** Medullary sclerosis may occur in cats infected with *Feline leukemia virus.*

- **Bovine viral diarrhea**

TUMORS AND TUMOR-LIKE LESIONS OF BONES

- *Primary tumors of bones are common in dogs and to a lesser extent in cats,* but occur infrequently or rarely in other domestic animals.
- In dogs, most tumors of bones are malignant.
- They may arise from any of the mesenchymal tissues present in bones, including precursors of bone, cartilage, fibrous tissue, adipose tissue, and vascular tissue, but *tumors of bone and cartilage-forming cell lines are the most common.*
- The clinical history and radiographic appearance are often crucial to an accurate diagnosis of a bone lesion and the pathologist should not rely on microscopic features alone.

TUMORS OF BONES

- **Bone-forming tumors:** *Osteoma, ossifying fibroma, and fibrous dysplasia,*
- *Osteosarcoma* ➔
- Poorly differentiated osteosarcoma
- Osteoblastic osteosarcomas
- Chondroblastic osteosarcomas
- Fibroblastic osteosarcomas
- Telangiectatic osteosarcoma
- Giant cell osteosarcomas

TUMORS OF BONES

- **Cartilage-forming tumors:**
- *Chondroma, Osteochondroma, Multilobular tumor of bone* and *Chondrosarcoma.*
- **Fibrous tumors of bones:** fibromas, fibrosarcoma ➔In dogs,
- Central fibrosarcomas
- Periosteal fibrosarcomas
- Maxillary fibrosarcoma
- ***Vascular tumors of bones:*** hemangioma, hemangiosarcoma

TUMORS OF BONES

- **Other primary tumors of bones:**
- Giant cell tumor of bone,
- Liposarcoma
- Plasma cell myeloma,
- Malignant lymphoma.
- **Secondary tumors of bones:**
- *Carcinomas metastasize to the skeleton of dogs much more commonly than sarcomas and the most common tissues of origin are the mammary gland, thyroid, prostate, ovary, and lung.*
- *The ribs, vertebrae, and proximal long bones are the favored locations for skeletal metastases in dogs.*

DISEASES OF JOINTS

DEVELOPMENTAL DISEASES OF JOINTS

- **Osteochondrosis:** Osteochondrosis is a common and important disease of pigs, horses, and large breeds of dog.
- The etiology and pathogenesis of osteochondrosis are poorly understood.
- The etiology is multifactorial, but most likely involves the effect of trauma or biomechanical factors on cartilage that has been weakened by nutritional or hormonal imbalances, vascular disruption, or genetic factors.
- Trauma almost certainly plays an important role, as supported by the increased prevalence of articular lesions at sites of greatest

DEVELOPMENTAL DISEASES OF JOINTS

- **Subluxation** is the term referring to a partial separation of the joint.
- The most commonly subluxated joints in dogs include the hip and elbow, although any joint can be affected.
- "Trauma, such as an automobile accident, is the most common cause of sudden or acute joint subluxations in veterinary practice.

DEVELOPMENTAL DISEASES OF JOINTS

- **Atlanto-occipital subluxation:**
- In dogs, goats, cattle, and horses.
- It is inherited in some Arabian foals.
- Affected foals may be dead or tetraparetic at birth, or develop progressive ataxia within a few months.
- **Temporomandibular subluxation:**
- It is reported in Basset Hounds and Irish Setters.
- Clinically; The jaw joint is locked and the mouth is open.

DEVELOPMENTAL DISEASES OF JOINTS

- **Subluxation of the corpus:**
- is reported as a sex-linked recessive trait in a colony of dogs in which hemophilia.
- Signs of carpal subluxation first appear when the animals begin to walk.
- Most carpal subluxations and luxations are secondary to trauma.
- **Patellar luxation and subluxation:**
- are common in dogs, less so in horses, and rare in other species.
- It is more common in females and thought to be hereditary.

Hip dysplasia (acetabular dysplasia)

- *Hip dysplasia is the most common skeletal disease of large and giant breeds of dogs,* but may occur in all dog breeds and is occasionally reported in cats, cattle, and horses.

- The *disease is characterized by a lack of conformity between the femoral head and acetabulum resulting in subluxation and, invariably, degenerative joint disease.*

Hip dysplasia (acetabular dysplasia)

❖ Two forms are distinguished;

- Congenital type is the hereditary dominant feature. The joint depends on the capsule-ligament slackness.
- The delayed type develops later and is associated with acetabular dysplasia.

❑ There are two theories in their development:

✓ It develops due to insufficient pelvic muscle mass.

✓ It develops due to osteochondrosis.

Hip dysplasia

- Radiographic evidence of hip dysplasia in affected pups is usually not apparent until about 6 months of age.
- Radiographic diagnosis of hip dysplasia is based on the presence of subluxation of the joint or evidence of degenerative joint disease, or both.
- The gross lesions of canine hip dysplasia vary with the stage of the disease.
- The lesions are most prominent in weightbearing areas of the femoral head and the dorsal rim of the acetabulum.
- Hip dysplasia in cattle is best known in Herefords but also

DEGENERATIVE DISEASES OF JOINTS

- It can be either monoarticular or polyarticular and may be classified as either primary or secondary.
- **Primary** degenerative joint disease refers to those cases where there is no apparent predisposing cause and generally occurs in older animals.
- **Secondary** degenerative joint disease is associated with an underlying abnormality in the joint or its supporting structures, predisposing to premature degeneration of the cartilage.
- Any condition that causes direct damage to the articular cartilage, creates instability, or results in abnormal directional forces can predispose to degenerative joint disease.

DEGENERATIVE DISEASES OF JOINTS

- In general, two main factors are effective in the development of degenerative arthropathy:

1. Mature articular cartilage is not sufficient to repair itself

2. Constant mechanical pressures

- The most important and severe degenerative changes occur in large joints in the extremities, which are important in the movement and in the heavy load.

Traumatic Injuries

- Traumatic injury is handled in two headings:
- The first one is sudden and severe (acute) and the second is chronic injuries.
- Acute cases are the cause of degenerative arthropathy.
- Synovial tissue and capsule is stretched, lasered and rotated in acute injuries of sprains (distortion, incomplete, dislocation and dislocation).
- The ligament can be separated from the bone.

Spondylosis
(Spondylosis Deformans, Ankylosing Spondylosis)

- Spondylosis is a common degenerative disease of the vertebral column characterized by the formation of osteophytes at the ventral and lateral margins of vertebral bodies adjacent to intervertebral spaces.
- The pathogenesis of spondylosis is believed to involve an initial degenerative change in the ventral annulus fibrosus, probably secondary to trauma.
- Spondylosis occurs most frequently in bulls, pigs, and dogs.

INFLAMMATORY DISEASES OF JOINTS

- Inflammatory diseases of joints are generally referred to as either arthritis or synovitis
- **Synovitis refers to inflammation of a synovial membrane, whereas arthritis implies** *of other joint components in addition to the synovial membrane.*
- **Inflammation of tendon sheaths often accompanies inflammation of an adjacent synovial joint and is referred to as tenosynovitis (synonyms: tendosynovitis or tendovaginitis).**

INFLAMMATORY DISEASES OF JOINTS

- Arthritis may be either infectious or noninfectious, depending on the etiology.
- Infectious arthritis occurs most frequently in farmed livestock and horses, especially in young animals where it is a common sequel to neonatal bacteremia.
- Most cases of noninfectious arthritis occur in dogs or cats and are immune-mediated. Further classification is based on the duration of the lesion, the nature of the exudate, and the host response.

INFLAMMATORY DISEASES OF JOINTS

According to the type of exudate;

- **Fibrinous arthritis**
- **Purulent (suppurative) arthritis**
- **Fibrinopurulent arthritis**

According to the etiologic agent;

Infectious arthritis

- ***Bacterial arthritis***
- Erysipelas
- Streptococcal septicemia and polyarthritis
- Coliform polyarthritis
- Staphytococcal arthritis
- *Haemophilus* and *Histophilus* septicemia and arthritis
- Borretiosis
- Rickettsial polyarthritis
- Chlamydial polyarthritis
- Mycoplasmal arthritis
- ***Viral arthritis***
- ***Fungal arthritis***
- ***Protozoal arthritis***

Noninfectious (immune-mediated) arthritis

❖ ***Erosive arthritis***

- Rheumatoid arthritis
- Polyarthritis of Greyhounds
- Feline chronic progressive polyarthritis

❖ ***Nonerosive arthritis***

- Idiopathic polyarthritis
- Drug-induced polyarthritis

Fibrinous Arthritis

- This is typical of many acute inflammatory diseases of synovial joints, particularly those caused by bacterial infections.
- The presence of fibrin within synovial fluid indicates increased permeability of blood vessels in the synovial membrane, as fibrinogen and other large molecules are normally excluded.
- Fibrin clots may be floating free within the joint fluid, attached to the synovial membrane or lodged within recesses of the joint.

Fibrinous Arthritis

- In some cases, *sheets of yellow fibrin* partially or completely cover the synovial membrane, which is often edematous and hyperemic or may be studded with petechiae
- *Synovial villi,* which are barely noticeable in normal joints, may become prominent macroscopically due to the edema and hyperemia.
- The synovial fluid is increased in volume and is usually slightly *turbid and mucinous.*
- When the inflammatory reaction is severe, there may be *gross edema of the periarticular tissues.*

Fibrinous Arthritis

- At this early stage, microscopic changes in the synovial membrane consist of edema and vascular engorgement, with few inflammatory cells.
- *Serous fluid or serofibrinous exudate* often infiltrates the fibrous layer of the articular capsule and the adjacent periarticular tissue.

Fibrinous Arthritis

- In arthritis of longer duration, edema of synovial tissues is less apparent but the joint capsule and synovial membrane are thickened due *to proliferation of stromal cells and synoviocytes,* the latter often becoming several layers thick.
- *Sheets of fibrin containing variable numbers of neutrophils and fibroblasts may be attached to the surface.*
- Villi continue to enlarge as a result of the cellular proliferation and may become extensively branched, with increasing numbers of lymphocytes and plasma cells, but few neutrophils.

Fibrinous Arthritis

- Early resolution of the infection in animals with fibrinous arthritis is common, especially in smaller joints.
- The synovial lining is repaired by proliferation of synoviocytes.
- Articular cartilage generally remains intact in fibrinous arthritis, except in areas where it is covered by pannus.
- Pannus formation in joints with restricted movement may result in adhesions between apposed articular surfaces, leading to ankylosis.

Purulent (suppurative) arthritis

- This is characterized by the presence of *significant numbers of neutrophils in the synovial fluid, synovial membrane, and sometimes in adjacent structures.*
- When caused by bacterial infection, the neutrophils are usually abundant and may show *degenerative changes* in cytologic preparations of joint fluid.
- This is often referred to as **septic arthritis.**
- Neutrophilic inflammation is a feature of arthritis caused by *Mycoplasma* spp., *Borrelia burgdorferi,* and certain viruses, but in these infections the neutrophils in synovial fluid are *nondegenerate.*

Purulent (suppurative) arthritis

- Noninfectious, immune-mediated arthritis is also characterized by the presence of nondegenerate neutrophils in synovial fluid and differentiation from infectious arthritis is often difficult.
- Septic arthritis is often monoarticular and is potentially a much more destructive process than fibrinous arthritis.
- The synovial fluid is initially thin and cloudy but may resemble flank pus after a few days.

Purulent (suppurative) arthritis

- *Destruction of articular cartilage* is much more likely to occur in septic arthritis than in fibrinous arthritis.
- *Lysosomal enzymes,* particularly collagenase, released from degenerating neutrophils probably play an important role in the cartilage destruction.
- Flegmon is formed by the spread of the purulent arthritis to the surrounding tissues
- The circumference of the joint extends greatly and the fistula may form in the skin.

Purulent (suppurative) arthritis

- *Complete resolution of septic arthritis is possible* if the infection is eliminated spontaneously or by antibiotic therapy before erosion of cartilage occurs, but if the inflammatory process persists, the joint and adjacent structures will be severely altered.

- Granulation tissue originating in the subchondral bone may grow out over the degenerate articular surface and predispose to ankylosis.

Infectious arthritis

- A variety of infectious agents, including *bacteria, viruses, and fungi,* are capable of infecting diarthrodial joints in humans and domestic animals.
- **Cattle**

- *Arconobocterium pyogenes*
- *Escherichio coli*
- *Histophilus somni*
- *Mycoplosmo bovis*
- *Salmonella* spp.
- *Streptococcus* spp.

Infectious arthritis

- **Swine**

- *Actinobacillus suis*
- *Arcanobacterium pyogenes*
- *Brucella suis*
- *Erysipelothrix rhusiopathiae*
- *Escherichia coli*
- *Haemophilus pomsuis*
- *Mycoplasma* spp.
- *Salmonella* spp.
- *Staphylococcus aureus, Staphylococcus hyicus* ssp. *hyicus*
- *Streptococcus* spp.

Infectious arthritis

Horses

- *Actinobocillus equuli*
- *Escherichio coti*
- *Klebsiella* spp.
- *Rhodococcus equi*
- *Salmonella* spp.
- *Streptococcus* (Group C)

Dogs

- *Blastomyces dermatitidis*
- *Borrelio burgdofferi*
- *Ehrlichia ewingii*
- *Escherichia coli*
- *Staphylococcus* spp.
- *Streptococcus* spp.

Infectious arthritis

- ***Sheep***
- Erysipelothrix rhusiopathiae
- Escherichio coli
- Histophilus somni
- Mycoplasmo spp.
- Staphylococcus spp.
- Streptococcus spp. (including types 1 & 2)
- **Goats**
- Mycoplasma spp.
- Retrovirus

Caprine Arthritis Encephalitis

- **Caprine arthritis encephalitis** (**CAE**) is a viral disease of goats caused by a lentivirus called **caprine arthritis encephalitis** virus.
- The main clinical finding is lameness and it is related to arthritis and carpal hygroma.
- There is also a decrease in weight loss and milk yield.
- The prevalence of flocks can reach 25-30% and even some flocks 100%.
- Single or double carpal hygroma is characteristic in the syndrome.

Caprine Arthritis Encephalitis

- The multisystem diseases caused by CAEV infection are: arthritis, pneumonia, mastitis, weight loss (all of which are more common in does and bucks), and encephalitis (more common in kids).
- Lesions in joints are characterized by thickening of the joint capsule and marked proliferation of synovial villi.
- In chronic cases, soft-tissue calcification involving joint capsules, tendon sheaths, and bursae is not uncommon.

Caprine Arthritis Encephalitis

- Severe cartilage destruction, rupture of ligaments and tendons, and periarticular osteophyte formation have also been described in advanced cases.

- Microscopic features of articular lesions include synovial cell hyperplasia, subsynovial mononuclear cell infiltration, villous hypertrophy, synovial edema, and synovial necrosis.

Caprine Arthritis Encephalitis

- Gross lesions associated with the neurologic form of CAE include asymmetric, brownish pink, swollen areas, most commonly in the cervical and lumbosacral spinal cord segments.

- Histopathologically, these lesions are characterized by multifocal, mononuclear cell inflammatory infiltrates and varying degrees of demyelination.

Immune-mediated Arthritis

1. Erosive form (primary-immunological disease in the joint)

2. Nonerosive form (secondary-immunological disease in elsewhere)

- **Erosive arthritis:**

- In the *erosive form,* the immunologic process is centered in the joint and stimulates pannus formation, which may result in erosion of the margins of articular cartilage, instability or luxation of joints, or fusion of low-motion joints.

- The erosive pattern of immune-mediated arthritis is a feature of *rheumatoid-like arthritis of dogs, polyarthritis of Greyhounds, and feline chronic progressive polyarthritis.*

- The most prominent findings are proliferative synovitis and fibrovascular pannus-induced tissue destruction.

Immune-mediated Arthritis

- ***Nonerosive arthritis***
- a) primary or idiopathic form
- b) systemic lupus erythematosus form
- c)variety of chronic diseases form (chronic parasites, bacteria, virus infections, hypersensitivity reactions to the drug, tumors etc.)
- It occurs most often in *dogs and cats.*

TUMORS of JOINTS

Benign tumors➔

- Synovial chondromatosis (osteochondromatosis)
- Benign giant cell tumors of tendons and tendon sheaths
- Synovial hemangiomas or vascular hamartomas

Malignant tumors➔

- Synovial sarcoma
- Histiocytic sarcoma