

DISEASES OF SKELETAL MUSCLE VETERINARY PATHOLOGY

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2015/16

REFERENCES

Pathology of Domestic Animals 4 and 5th editions. Jubb KVF, Kennedy PC and Palmer N. Volume 1
Thomson's Special Veterinary Pathology. 3rd edition. McGavin MD, Carlton WW and Zachary JF

I. INTRODUCTION

Skeletal muscle includes muscles of posture, movement and respiration. Each muscle is composed of fascicles. Each fascicle is composed of multiple myofibres. There are two basic types of skeletal myofibre (Table 1).

Table 1. Skeletal myofibre types

Feature	Type I	Type II
Type of muscle	Postural	Exercise
Rate of contraction	Slow	Fast
Level of oxidative enzymes	+++ (high oxidative activity) Use lots of O ₂	+ (high glycolytic activity) Uses little O ₂
Myoglobin level	+++	+
Gross colour	Red	White
Function	Postural	Exercise

II. RESPONSE OF MUSCLE TO INJURY

Muscle has a limited array of ways in which to respond to injury. The main ones are:

- a) Degeneration / Necrosis
- b) Atrophy
- b) Regeneration
- d) Hypertrophy

In contrast, the factors which can induce these changes are innumerable (trauma, toxins, infectious agents, nutritional deficiencies, ischaemia, hereditary diseases).

Thus, it follows that specific diagnosis is often NOT POSSIBLE BASED ON MORPHOLOGICAL OR HISTOLOGICAL FEATURES ALONE.
Other additional tests, clinical information and history are usually vital

a) Degeneration / Necrosis

- These two words are virtually synonymous in muscle pathology
- Necrosis is often segmental; necrosis of an entire myofibre is uncommon (causes include crush injury or widespread ischaemia resulting from pressure on a large artery)
- Muscle cell contents may leak into the blood if the cell membrane is damaged; creatine kinase (CK) is an enzyme which leaks following injury and is commonly used to measure the extent of muscle damage

b) Regeneration

Skeletal muscle myofibres have substantial regenerative ability. Success depends on:

- An intact sarcolemmal tube (to act as a support and guide)
- Availability of satellite stem cells (to act as progenitor cells for new sarcoplasm production)
- Macrophages to clear up cell debris
- If these conditions not met (e.g. severe thermal damage) fibrosis will occur

c) Atrophy

Decreased myofibre diameter or decreased whole muscle diameter

- Causes:
- i) Disuse (e.g. fracture, failure to use limb, recumbency)
 - ii) Denervation: Any interference or damage to its nerve supply results in muscle atrophy
Can be rapid - over 50% of muscle mass may be lost in a few weeks e.g. roarer horses with laryngeal hemiplegia
 - iii) Malnutrition, cachexia, senility: Muscle protein is metabolised to provide nutrients

d) Hypertrophy

Increased myofibre or whole muscle diameter. Cause is an increased work load on myofibres:

- i) Increased physiological work
- ii) Compensatory

III. MUSCLE DISEASES: MYOSITIS (Inflammation of muscle):

a) INFECTIOUS

- i) Bacteria: Gain entry via direct penetration, blood stream or extension (Table 2)
- ii) Viruses (rare in UK)
- iii) Parasites
 - Nematodes: *Trichinella*, *Ancylostoma* and Ascarid larvae
 - Cestodes: *Taenia solium* (cysticercosis in swine and humans)
T. ovis (cysticercosis in sheep)
 - Protozoa: *Toxoplasma gondii*
Neospora caninum
Sarcocystis

Table 2. Important bacterial diseases of muscle

Bacteria	Spec.	Disease or manifestation
<i>Trueperella pyogenes</i>	B, P	Abscesses
<i>Streptococcus equi</i>	E	Abscesses
<i>Corynebacterium pseudotuberculosis</i>	O, C, E	Abscesses
<i>Clostridium chauvoei</i>	O, B	Black leg (spores gain entry to GI tract → blood → muscle → lie latent → under right conditions – usually anaerobic following injury – they germinate and bacilli grow)
<i>C. septicum</i> , <i>C. novyi</i> <i>C. perfringens</i> , <i>C. sordelli</i>	O, B, E, P	Gas gangrene (bacteria gain entry as spores via penetrating wounds)
<i>Actinobacillus lignieresii</i>	B	Wooden tongue

NB: B (Cattle), P (Pigs), E (Horses), O (Sheep), C (Goats)

b) IMMUNE-MEDIATED

i) Canine masticatory muscle myositis (MMM)

- Autoantibodies selectively attack muscles of mastication (type IIM fibres)
- Manifests in the masseter and temporalis muscles; bilateral but not necessarily symmetrical
- Acute stage = eosinophilic myositis; chronic stage = atrophic myositis

ii) Polymyositis

- Can affect masticatory muscles but dogs **DO NOT HAVE antibodies to type IIM fibres**
- Generalised inflammatory myopathy: inflammation, muscle necrosis and regeneration
- May need to sample multiple sites to make the diagnosis

IV. MUSCLE DISEASES: CONGENITAL/HEREDITARY

a) Defects in muscular form

1. Congenital diaphragmatic defects
2. Myofibrillar hypoplasia in piglets (splayleg): Cause unknown but can spontaneously resolve.
3. Hyperplasia of muscle fibres (calves, lambs): “Double muscling” due to ↑ number of myofibres in affected muscle (thighs, rump, loin); predisposes to dystocia.

b) Muscular dystrophies

- Inherited group of degenerative muscular diseases causing progressive muscle weakness and wasting
- Usually due to a genetic fault leading to a muscular protein deficiency
 - e.g. Duchenne MD in humans due to dystrophin deficiency
- Dystrophin gene mutations reported in the Golden Retriever, Rottweiler, Irish terrier, amongst others

V. MUSCLE DISEASES: TOXIC, ENDOCRINE AND NUTRITIONAL MYOPATHIES

Toxic

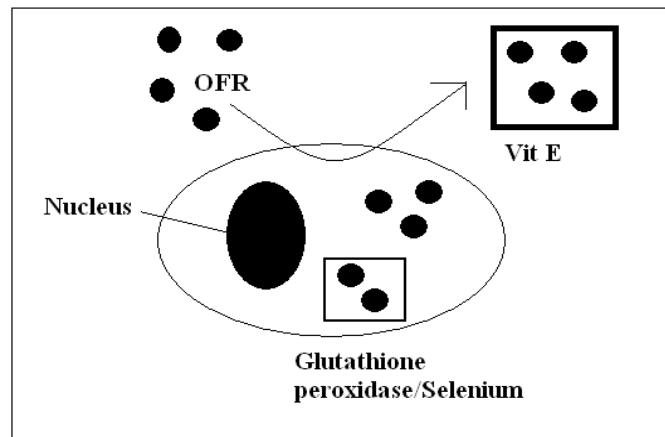
- Plants
- Drugs
 - Monensin is a coccidiostat toxic to horses, donkeys, zebras, cattle, sheep, dogs and birds
 - Causes muscle necrosis in heart and skeletal muscle; can cause rapid onset recumbency and potentially death; usually due to mixing errors in feed.
- Chemicals (e.g. iron injections can cause local myonecrosis)
- Mycotoxins

Nutritional myopathy (white muscle disease)

- Very important economic disease of sheep, cattle and pigs
- Cause: Deficiency of selenium, vitamin E or both
- Gross lesions are bilaterally symmetrical in hard working muscles (vary with species)

- Pigs also have lesions in their heart and liver
- Pathogenesis (Fig 1): Oxygen free radicals (OFR) can damage cell membranes but vitamin E usually mops them up and glutathione peroxidase (selenium is part of this enzyme complex) can neutralise their effects. If Vit E or Se are deficient, the balance shifts to membrane damage, calcium entry and mitochondrial damage → cell swells and dies

Fig 1. Pathogenesis of nutritional myopathy:



Exertional myopathies

- Caused by intensive and exhaustive activity of major muscle masses
 - Azoturia (Monday morning disease)
 - Exercise following a prolonged period of rest; unable to move, sweating, tremors
 - Myoglobin leaks from muscle cells → leaks into urine → urine is dark red/brown (myoglobinuria) → damages renal tubules
 - Tying-up is similar to azoturia but much milder; linked to polysaccharide storage myopathy in many breeds
- Other forms include capture myopathy and porcine stress syndrome

VI. MUSCLE DISEASES: NEUROMUSCULAR JUNCTION PROBLEMS

1. Myasthenia gravis (MG)

i). Acquired

- Autoimmune disease – antibodies directed against acetyl choline receptors (Fig 2b)

ii) Congenital

- Inherited deficiency in acetyl choline receptors (rare)
- No antibodies against acetyl choline receptors in serum (Fig 2c)

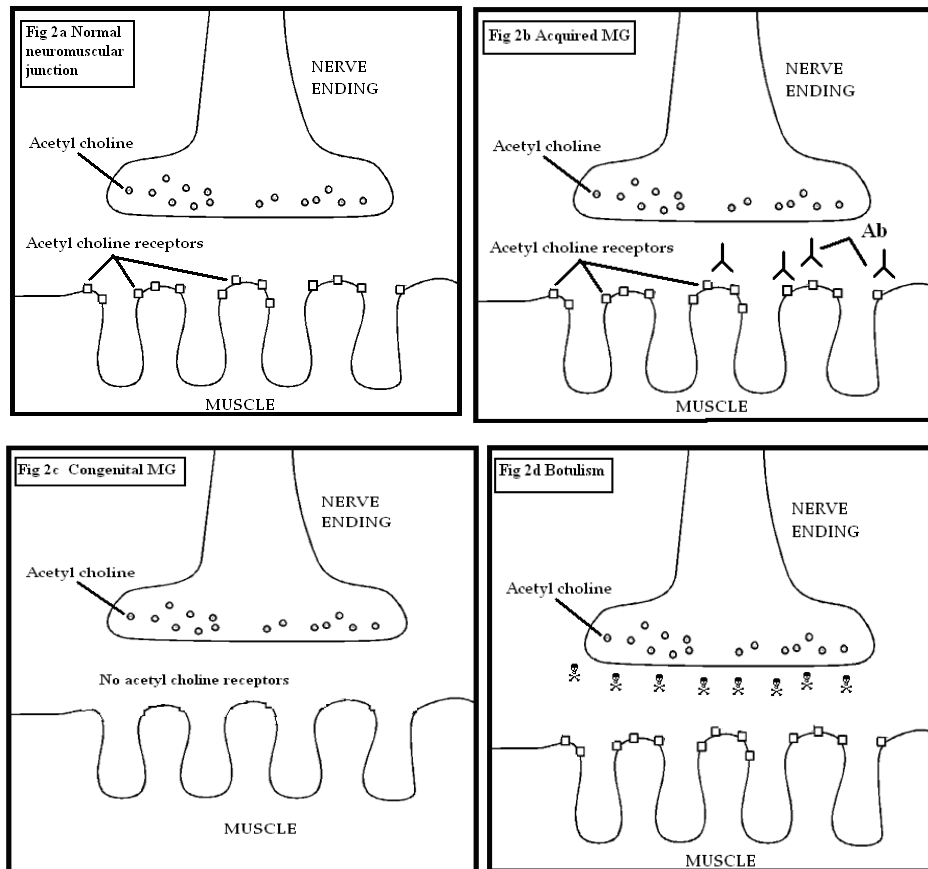
Both forms manifest as weakness which worsens on exercise

2. Botulism

- Due to ingestion of *Clostridium botulinum* toxin which inhibits acetyl choline release (☞ denotes toxin below in Fig 2d)

- Diagnosis: demonstrate toxin in faeces, ingested material, serum

Fig 2 Different abnormalities of the neuromuscular junction



VII. NEOPLASIA

Rare in domestic animals

RHABDOMYOMA is primary benign while RHABDOMYOSARCOMA is primary malignant

Metastases can also occur to skeletal muscle (e.g. carcinoma, haemangiosarcoma)

PATHOLOGY OF BONES AND JOINTS

VETERINARY PATHOLOGY

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Pathologic Basis of Veterinary Disease 5th edition McGavin MD and Zachary JF

PATHOLOGY OF BONES

✂ INTRODUCTION

Bone is a hard, highly specialised connective tissue comprising interconnected cells embedded in a calcified, collagenous matrix. It is a living, dynamic, responsive tissue, growing and remodelling throughout life. The pathogenesis of many bone diseases is complex and may involve genetic defects, diet or infection (or even a combination of these on occasion).

I. NORMAL FUNCTION AND STRUCTURE

Functions: Support, protection, movement, stem cell storage, mineral bank

Structure: Bone is composed of cells and matrix

Cells: Osteoblasts, osteocytes and osteoclasts

Osteoblasts

- Mesenchymal cells of bone marrow stromal origin
- Form the bone matrix, which is known as osteoid

Osteocytes

- Osteoblasts that have become surrounded by mineralised bone matrix
- Occupy cavities called lacunae

Osteoclasts

- Multinucleated cells derived from haematopoietic stem cells
- Responsible for bone resorption

Matrix:

- The matrix is composed of type I collagen and mineral
- Mineral – accounts for 65% of bone and includes Ca, P, Mg, Mn, Zn, Cu, Na

Bone organisation:

Not all bones are organised in the same way. Organisation of bone is dictated by the pattern of collagen deposition:

1. IMMATURE (WOVEN) BONE

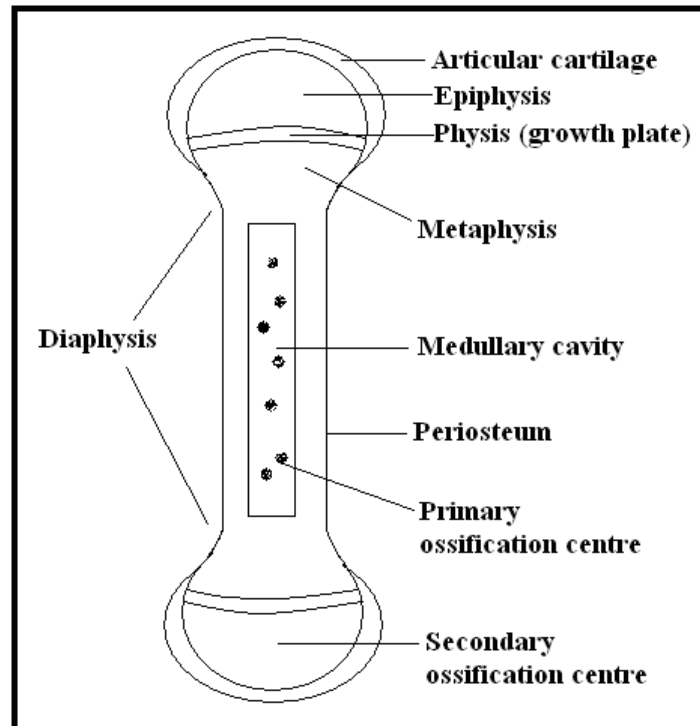
- Collagen is arranged in a “random weave”. **THIS IS ONLY NORMAL IN THE FOETUS**
- In adults randomly woven bone is a sign of a pathological condition (e.g. fracture, inflammation, neoplasia)

2. MATURE (LAMELLAR) BONE

- The collagen is arranged in orderly layers which are much stronger than woven bone
- Two main types:
 - a) Compact or cortical bone: forms the diaphyses of long bones and the shell of all other bones; contains osteons

- b) Cancellous (spongy or trabecular) bone occurs in vertebrae, flat bones and epiphyses of long bones; it contains no osteons

Fig 1. Long bone anatomy



Periosteum and blood supply

The periosteum is a sheath of connective tissue covering bone (except at the articular surfaces). The inner layer merges with the outer layer of bone and contains osteoblasts and stem cells. The blood supply to the mature bone enters via the periosteum. Damage to the periosteum triggers a hyperplastic reaction of the inner layer.

Bone development

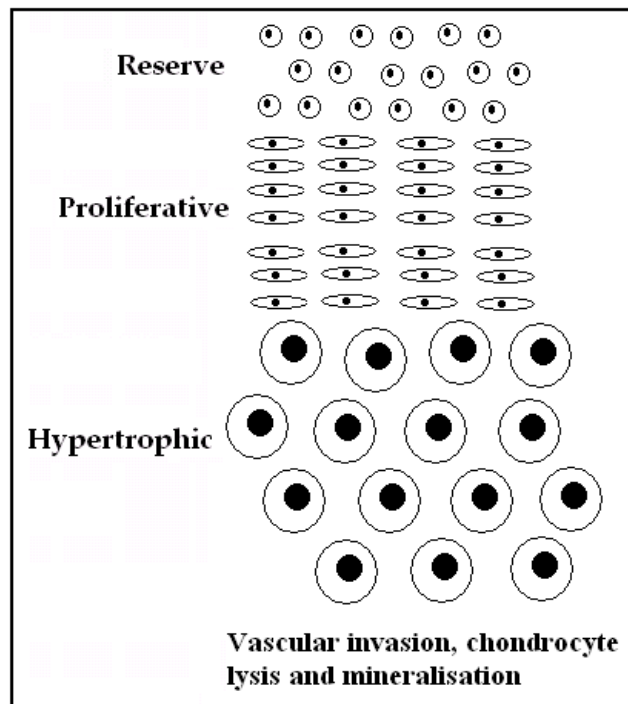
There are two main types of bone development:

- Endochondral ossification
 - Long bones mainly
 - Cartilage model of the bone to be formed is vascularised and replaced by bone
- Intramembranous ossification
 - Flat bones mainly (e.g. skull)
 - Mesenchymal cells differentiate into osteoblasts. There is no cartilage precursor template.

Physis

- The physis (growth plate) is essentially a remnant of the cartilage model located at the junction of diaphysis & epiphysis. This is an **important site** since many congenital or nutritional bone diseases in the growing animal manifest here.
- In neonates and growing animals, the growth plate is “open”, i.e. chondrocyte proliferation balances cell maturation and death (Fig 2). The growth plate “closes” and ossifies at maturity.

Fig 2. Growth plate cartilage is divided into zones



Bone resorption

Mediated by two hormones

- Parathyroid hormone (PTH) produced by *chief cells* in the parathyroid glands in response to *decreased* serum calcium
- Calcitonin produced by *C-cells* in the thyroid glands in response to *increased* serum calcium (Ca^{++})

Low Ca^{++} → induces PTH secretion → osteoclasts increase in number → they attach to bone and resorb mineralised matrix → Ca^{++} ↑

CALCITONIN HAS THE OPPOSITE EFFECT - IT **INHIBITS** OSTEOCLASTS

Bone dynamics

Bone growth and maintenance of normal structure are directly related to mechanical forces which generate bioelectrical potentials (piezoelectricity). These potentials strengthen bone while inactivity reduces them, leading to bone loss. In neonates, bone growth predominates and modelling is important. In adults, formation of bone is balanced by resorption; this is known as remodelling. It continues in a subtle but active way throughout life under the influence of hormones and mechanical pressure. Bone resorption may exceed formation in pathological states (hormonal, trauma, nutritional) or in old age and disuse.

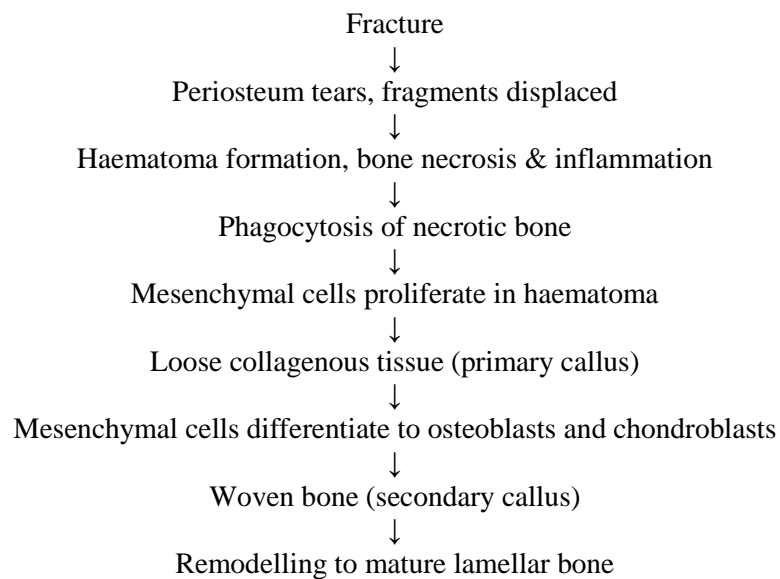
II. PATHOLOGY OF BONE

- | | |
|----------------------------|--------------------------------|
| a) Fractures | (d) Neoplastic bone diseases |
| b) Metabolic bone diseases | (e) Hyperostotic bone diseases |
| c) Inflammation | f) Developmental bone diseases |

FRACTURES

- Traumatic: Normal bone broken by excessive force
- Pathologic: Abnormal bone broken by minimal or no trauma

Fracture repair



Factors which slow healing

- a) Malnutrition
- b) Inadequate blood supply (leads to hypoxia)
 - i. Leads to excess cartilage in callus
 - ii. Healing can still occur since this can turn to bone
- c) Excess movement
 - i) Leads to excess fibrous tissue in callus
 - ii) This forms a false joint and can't heal properly
- d) Presence of necrotic bone (may form a sequestrum)
- e) Bacterial infection

METABOLIC BONE DISEASE

Metabolic bone disease arises when **systemic disease manifests itself in the skeleton**, particularly systemic disease of endocrine, nutritional or toxic origin.

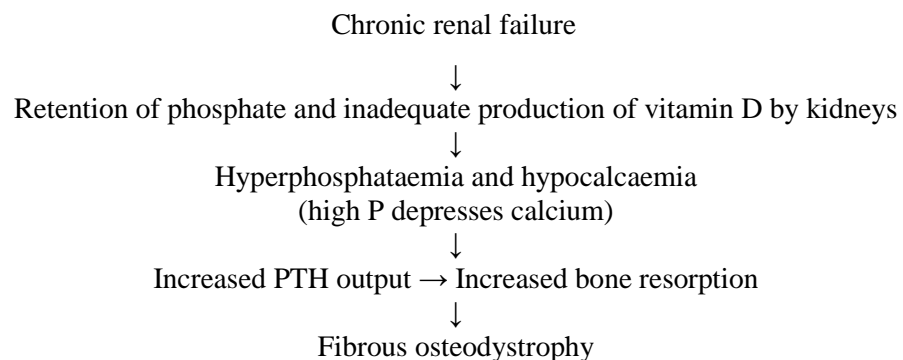
Four main ones:

1. Fibrous osteodystrophy
2. Osteoporosis
3. Rickets
4. Osteomalacia

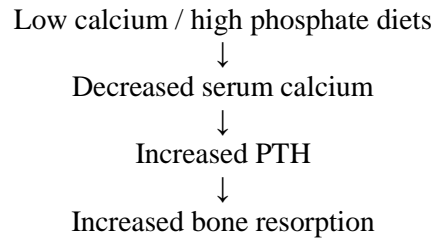
1. Fibrous osteodystrophy

- Metabolic bone disease in which *bone is resorbed and replaced by fibrous, “rubbery” connective tissue*
- Due to persistently elevated PTH
- Causes of ↑PTH (hyperparathyroidism)
 - PRIMARY (rare)
 - This is increased production of PTH **not related to calcium or phosphorus levels, i.e. autonomous**
 - Due to parathyroid neoplasia or bilateral idiopathic parathyroid hyperplasia
 - Results in *hypercalcaemia*
 - SECONDARY (much more common)
 - Renal
 - Nutritional
 - PTH secretion triggered by ↓ plasma calcium
 - PARANEOPLASTIC
 - Parathyroid hormone-related protein produced by certain neoplasms

Pathogenesis of Renal Hyperparathyroidism



Pathogenesis of Nutritional Hyperparathyroidism



Nutritional form:

- More common in young, fast-growing animals (with exception of horses)
- **Poor diet**
 - Calcium deficiency
 - Excess phosphorus
 - Vitamin D deficiency
- Regardless of pathogenesis, the result is increased osteoclastic resorption of bone and deposition of fibro-osteoid matrix that fails to mineralise. Flat bones of the skull swell, including maxillary and nasal bones. Long bones become soft with thin cortices which fracture easily
- Also called fibrous osteodystrophy, “rubber jaw” or “bran disease”

2. Osteoporosis

- This is a **lesion**, not a distinct disease entity
- It means a reduction in bone quantity, not quality
- Bone resorption exceeds formation → pathological loss of bone
- The bone which remains is normally mineralised
- Causes
 - Starvation, nutritional deficiency (calcium)
 - Senility
 - Physical inactivity (disuse)
 - Thus, can be localised or generalised

3. Rickets

Rickets is a classic metabolic bone of humans and animals. It is a disease of the young, fast growing skeleton.

- **Pathogenesis: Failure of mineralisation of physal and epiphyseal cartilage during endochondral ossification and of newly formed osteoid**
- Mostly due to diets low in Vitamin D or, less commonly, phosphorus

- Vitamin D is so important in this disease because it maintains normal plasma levels of calcium and phosphorus through acting on the intestines, bones and kidneys
- **Growth plates are thickened** as the zone of proliferation does not mineralise and mature; blood vessels and chondroclasts cannot invade so the cartilage is not removed
- **Metaphyses are flared** because bone and cartilage cannot be removed; osteoclasts cannot bind to poorly mineralised bone – further accentuated by weight bearing
- **Enlarged costochondral junctions** – “rachitic rosary”

4. Osteomalacia

Similar to rickets except it is a disease of the adult skeleton. It results in failure of newly formed osteoid to mineralise.

Other metabolic bone disorders

Hormone-related

Hormones which directly affect bone growth and resorption, other than PTH and calcitonin, are:

**Insulin, growth hormone (somatotropin), glucocorticoids,
oestrogens, androgens and thyroid hormones**

Other vitamin-related conditions

i) Vitamin A:

- Essential for normal bone growth in foetuses and neonates
- Hypovitaminosis A due to dietary deficiency in dam can be teratogenic in pigs and large cats
- More common situation is deficiency in neonates (puppies, kittens, calves, piglets) on vitamin-deficient diets. Vitamin A stimulates osteoclasts so deficiency causes *failure of osteoclastic remodelling* resulting in bone overgrowth and nerve compression (esp. optic nerves).

ii) Hypervitaminosis A:

- Classically occurs in cats fed liver for prolonged periods; vertebrae fuse with each other due to bone proliferation (ankylosing exostoses of the vertebral column) especially in the neck
- Pathogenesis is not clear
- Hypervitaminosis A can also be teratogenic (cleft plate)

iii) Hypervitaminosis D:

- May be of dietary or iatrogenic origin and is usually chronic
- Key features are hypercalcaemia with metastatic calcification of soft tissues

INFLAMMATION OF BONE

Osteitis: Inflammation of bone
Periostitis: Inflammation of periosteum
Osteomyelitis: Inflammation of medullary cavity
Osteopathy: Any disease of bone (non specific)

- Causes of inflammation
 - Bacteria most commonly
 - Viruses, fungi and protozoa less commonly
- Routes of infection
 - “Inoculated” at time of fracture
 - Extension from other infected sites (sinuses, middle ear, joints)
 - Haematogenous (mostly young farm animals)
- Gross lesions
 - Suppurative exudate (in bacterial infection), necrosis, bone proliferation, pathological fractures
 - Dead bone portions may be separated from blood supply, forming bone sequestra
- Consequences
 - Extension to adjacent bone
 - Haematogenous spread to other bones and soft tissue
 - Pathologic fractures
 - Sinus tracts to exterior

Metaphyseal osteopathy

- Young, fast growing dogs of large or giant breeds
- Distal radius and ulna most severely affected; bilaterally symmetrical
- Swelling in metaphyses of long bones corresponding with neutrophilic infiltrate
- Most resolve spontaneously but can progress to periosteal bone proliferation
- May wax and wane
- Idiopathic (infectious aetiology, probably bacterial, most likely)

NEOPLASTIC BONE DISEASES

Neoplasms of bone and cartilage. Fill in the blanks:

	Benign	Malignant
Bone		
Cartilage		

Osteoma

- Uncommon, smoothly contoured, slow-growing tumour
- Horses and cattle
- Sites: Flat bones (skull, scapula)
- Disfigurement, obstruct nasal passages
- Recur if not completely removed

Chondroma

- Benign neoplasm of cartilage
- Rare in animals
- Slow growing and expansile with smooth border

Osteosarcoma (OSA)

- Any malignant neoplasm of mesenchymal origin **in which the cells produce osteoid**
- Generally very uncommon except in dogs and cats
- In dogs osteosarcoma accounts for ~85% of primary bone tumours
- **Giant breeds of dog are at massively increased risk**
- Median age of onset: 8-10 years
- Strong site preference in dogs:
 - Appendicular skeleton 3 or 4 times more frequently involved than axial
 - Proximal humerus, distal radius, proximal tibia and distal femur
- Survival time is a little better for axial than appendicular OSA in dogs
- Prognosis is poor due to early metastasis
 - Pulmonary metastases
 - Bone metastases

Chondrosarcoma

- Any malignant neoplasm in which mesenchymal cells produce chondroid matrix
- Most common in dog and occurs in flat bones more frequently than others
- Slower growth rate, longer clinical course and later to metastasize than OSA
- Metastatic rate is around 20%

REMEMBER

Non-neoplastic bone proliferation can occur under many different circumstances

- ❖ Fracture repair
- ❖ Chronic osteomyelitis
- ❖ Superimposed on a neoplasm
- ❖ Hypertrophic osteodystrophy (see below)
- ❖ Hypertrophic pulmonary osteopathy (see below)
- ❖ Craniomandibular osteopathy (see below)

HYPEROSTOTIC BONE DISEASES (Hyperostosis = Excessive thickening of a bone)

Hypertrophic pulmonary osteopathy (HPO)

- Periosteal proliferation of bone on diaphyses and metaphyses of distal limbs
- Progressive and bilateral
- Most cases have an **intrathoracic neoplasm** or chronic inflammatory focus
- **But** has also been associated with non-thoracic lesions – e.g. botryoid rhabdomyosarcoma in the canine urinary bladder and ovarian tumours in horses

Types of intra-thoracic lesions associated with HPO (fill in the box)

1.
2.
3.
4.
5.

Craniomandibular osteopathy

- West Highland white terriers and Scottish terriers
- Puppies: Arises at 4-7 months of age
- Bilaterally symmetrical
- Periosteal proliferation of bone leading to irregular thickening of the mandibular rami and some skull bones, including tympanic bullae

DEVELOPMENTAL BONE DISEASES

Mistakes can occur when the skeleton is made. They may be:

- 1° abnormalities of bone, cartilage or mesenchyme
- Hereditary or environmental
- Localised or generalised

GENERALISED

1. *Proportionate dwarfism* (e.g. miniature breeds; due to growth factor deficit)

2. *Chondrodysplasia*

- Literally means “abnormal cartilage development”
- Occurs in cattle, dogs, sheep, pigs and cats
- Affects bones which form from a cartilage model (endochondral ossification) – long bones are shorter than normal
- Leads to disproportionate dwarfism (contrast with miniature breeds)

- Localised forms occur in some dogs as a breed associated characteristic (e.g. affecting skulls of Pekingese and Bulldogs or the limbs of Dachshunds and Bassett hounds)

3. *Osteopetrosis (Marble bone disease)*

- Failure of resorption by osteoclasts and, as a result, failure of remodelling of cancellous bone
- Bones become thickened and dense but brittle; associated with viral infections, e.g. FeLV, BVD

LOCALISED

1. *Cervical Vertebral Stenotic Myelopathy (Wobblers)*

- Equine disease
- Narrowing of the vertebral canal due to vertebral malalignment or maldevelopment
- Fast growing male TBs ranging from 8 months to 4 years
- HL ataxia due to cord compression

2. *Angular limb deformity*

- Lateral deviation of distal portion of limb (usually)
- Most common in foals; congenital or acquired
- Causes: Malpositioning *in utero*, excessive joint laxity, hypothyroidism, trauma, overnutrition, defective endochondral ossification

MISCELLANEOUS BONE LESIONS

i) *Ossifying pachymeningitis*: Plaques of bone form in the dura of the spinal cord, especially in older dogs; they mean nothing

ii) *Heterotopic bone*: Spicules of bone form in the lungs of older dogs; they mean nothing

iii) *Ossifying epulides*: Epulides (singular form is epulis) are neoplasms of periodontal fibroblast origin; they occur in oral cavity; Boxers predisposed; benign → complete removal → good prognosis

DISEASES OF JOINTS

I. NORMAL STRUCTURE AND FUNCTION

There are many different types of joint but synovial joints are the most clinically relevant

Anatomy of synovial joint

- Composed of two bone ends bound together by a fibrous capsule and ligaments
- Inner surface of capsule is lined by synovial cells and the joint space contains synovial fluid

Function

- Absorb force of impact
- Allow a variable degree of movement
- Articular cartilage
 - Minimises friction
 - Transmits force to underlying bone

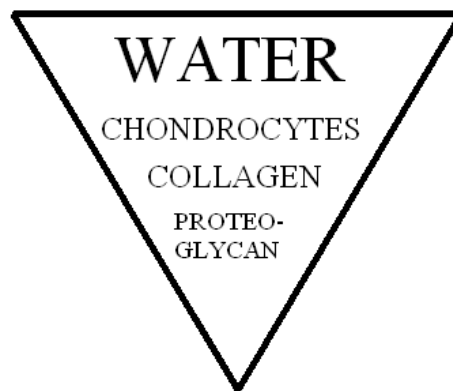
Causes of injury

- Trauma
- Instability
- Lubrication failure
- Infectious organisms
- Immune-mediated disease

II. PATHOLOGY OF JOINTS

Response to injury

- Articular cartilage has a limited response to injury and little repair capacity
- Cartilage is an avascular, reinforced gel composed of:



- Only proteoglycan is continually turned over, so it is the vulnerable component of cartilage (i.e. “the weakest link”)
- Proteoglycans hold water in the cartilage and this is important for turgidity and joint flushing

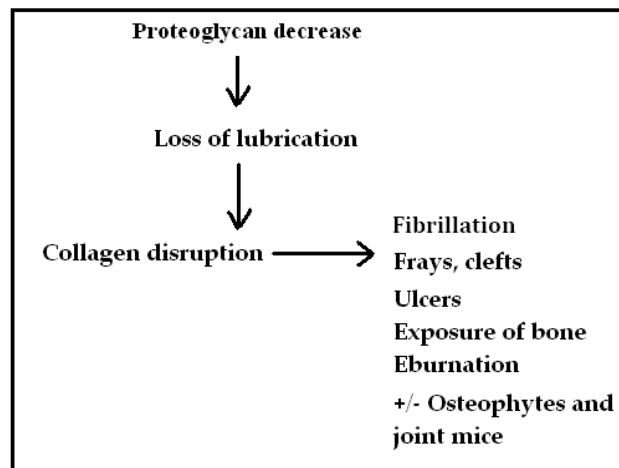
1. Degenerative joint disease (DJD), also known as osteoarthritis

- Destructive disease leading to loss of articular cartilage in one or multiple joints
- This term incorporates a variety of diseases with a common end stage
- It can be primary (idiopathic or age-related) or secondary
- Secondary DJD can be triggered by many conditions which lead to premature degeneration of the cartilage (Table 1). This may be caused by:
 - direct damage
 - joint instability
 - abnormal forces

Table 1: Mechanisms of secondary DJD

MECHANISMS OF CARTILAGE DEGENERATION		
Increased joint laxity	Abnormal forces	Direct damage
Hip dysplasia	Osteochondrosis (opposing articular surfaces are incongruous)	Trauma
Ligament injury (e.g. cruciate rupture)	Malaligned limb fractures	Inflammation (e.g. septic or non septic arthritis)
	Angular limb deformities	
	Metabolic bone disease (causes collapsed subchondral bone)	

- The pathogenesis of DJD is complex and not completely understood
- Chondrocytes maintain balance between repair and breakdown of cartilage matrix
- The balance tips in favour of degradation, driven by matrix metalloproteinases that, under normal conditions, are suppressed by inhibitors
- Degradation leads to a reduction in proteoglycan

Fig 3. Pathogenesis of degenerative joint disease

2. Inflammation

Arthritis: Inflammation of intra-articular structures, incl. synovial membrane

Synovitis: Inflammation of the synovial membrane only

Arthropathy: An all-encompassing term referring to any joint disease, whether inflammatory or not

Arthritis

Arthritis can be classified based on (a) the cause, (b) the duration or (c) the nature of the exudate

CLASSIFICATION SYSTEM				
<i>Cause</i>		<i>Duration</i>		<i>Nature of exudate</i>
Infectious (bacterial, viral)		Acute		Serous
Immune mediated		Subacute		Fibrinous
Urate deposits		Chronic		Purulent
Sterile				Lymphoplasmacytic

Infectious arthritis

- Most common in food animals, especially young, usually bacterial
- Portals of entry include navel and GI tract → bacteraemia
- Bacteria reach joints haematogenously → polyarthritis
- Other portals of entry: Traumatic inoculation
Extension from bone or periarticular soft tissue

Non-infectious (immune-mediated) arthritis

This occurs mainly in dogs and cats and is the result of either persistent antigenic material in the synovium or deposition of Ag/Ab complexes in the synovium. These are derived from elsewhere in the body. Since the same mediators are produced in infectious and non-infectious forms of arthritis, the lesions appear similar. Immune-mediated arthritis is often a polyarthritis. Two forms are recognised:

1. Erosive

- Immune process is **joint centred**, i.e. the joint is the target
- Pannus formation (granulation tissue) → cartilage erosion
- Instability and luxation of multiple joints
- Rheumatoid arthritis in humans (similar type of disease can occur in dogs)

2. Non-erosive

- Joint NOT the primary target
- Immune complexes form elsewhere and settle in the joint
- Systemic lupus erythematosus (SLE)
 - Dogs
 - Anaemia, thrombocytopaenia, polymyositis, glomerulonephritis
- Chronic diseases such as pyometra, otitis externa can lead to immune complex deposition in joints

3. Abnormalities of growth and development

i) Arthrogryposis

- Persistent congenital flexure of a joint in conjunction with muscle contraction

- Causes:
 - Inactivity or paralysis *in utero*
 - Spinal dysraphism
 - Intrauterine viral infections (e.g. bluetongue virus, Schmallenberg virus)
 - Toxic plants (poison hemlock)

ii) Hip dysplasia

- **Common problem in dogs**
- Inherited disease in which joint laxity results in secondary degenerative joint disease (DJD)
- Joint laxity → subluxation → flattening of dorsal rim of acetabulum → modelling of the acetabulum and femoral head
- Contributing factors: Heredity, weight, over-exercise

Gross lesions of advanced hip dysplasia

Articular cartilage (femoral head & acetabulum)	Erosion and/or ulceration
Joint capsule / synovium	Capsule is stretched and thickened with cartilage and bone formation within; round ligament may be ruptured
Subchondral bone	Shallow, wide acetabulum Eburnation; osteophyte formation

iii) Osteochondrosis

- A disorder of growth cartilage occurring in growing animals (most species)
- **FAILURE OF ENCHONDRAL OSSIFICATION**
- Really a defect in cartilage growth (i.e. chondrodysplasia) but the term osteochondrosis has become embedded in the literature
- Growth cartilage is not mineralised so is focally or multifocally retained
- Manifestations include thickened articular cartilage/cartilage flaps (osteochondritis dissecans or OCD), retained cartilage cores, bone cysts, angular limb deformity and DJD
- Multifactorial: Trauma, genetic, rapid growth, ischaemia, nutritional all involved
- Basically idiopathic since everyone is still arguing about it, though more recent evidence supports **ischaemia**
- Common in humeral head of giant breeds (4-8 months of age), distal tibia (horses)
- Lesions bilateral in 70% of cases but lameness often unilateral

iv) Intervertebral disk disease

- Chondrodystrophic dogs: Predisposed to degenerative disk change from early age
The nucleus pulposus is replaced by chondroid tissue which mineralises and fragments; annulus fibrosus secondarily degenerates
- Non chondrodystrophic dogs: Degeneration begins in the annulus fibrosus
There is fibrosis of the nucleus, rather than chondroid degeneration
Middle-aged dogs affected and thoracolumbar area predisposed

In both forms, the disk can either **herniate** if the annulus is intact (more likely in non chondrodystrophics) or **rupture** through the annulus (more likely in chondrodystrophic breeds); extruded material is gritty, hemorrhagic or “cheesy”.