Vet 403 Musculoskeletal Block Learning Objectives / Questions

Lecture 1: Block Introduction

Lecture 2: Topographic Anatomy of Limbs + Intro to Dissection; *Dr. Gutierrez* *Not on exam

Muscle + Nerve + Vessels = functional anatomical unit

Lecture 3: General Osteology; *Dr. Clare Yellowley*

1. Understand the gross characteristics and function of long, short and flat bones.

The function of bone is to protect organs, house bone marrow, support locomotion and mineral reservoir.
Long bones are longer in one direction than they are in the other (femur)
Short bones are roughly the same size in all directions (carpal bones)
Flat bones are thin in one dimension and larger in the other two (skull, scapula)
Irregular bones vairy in shape and do not easily fall into any one category (vertebrae)

2. Define long bone regions

Long bones are longer in one direction than in the other and they are expanded at the ends. Each long bone is made up of an epiphysis, physis (growth plate), metaphysis, and diaphysis.

3. Describe the terminology used to describe boney features

Apophysis is a term used to describe a larger boney process. This process is an attachment site for muscle, is non-articular, and does not transmit weight.

4. Show and tell – bone bumps, pits, dips, lines, holes and more.....

Trochlea of the femur: articular surface for the patella
Head of the femur: articular surface for the acetabulum
Patella: Sesamoid bone
Faces/Surfaces and fossas are for muscle attachment
Tubercle, tuberosity, tuber, trochanter: Special bone formations for attachment of muscle fibers, tendons, and ligaments
*Trochanters are only present in the femur
Trochleas, condyles, and cochlea: Special formations associated with a joint. They have smooth areas
*Cochlea is present in the Tibia
Special foramina: Supracondylar foramen in cats (brachial artery and median nerve pass through)

Lecture 4: Bone Structure; *Dr. Clare Yellowley*
LO

1. Describe the morphology and location of trabecular and cortical bone

Trabecular (cancellous or spongey) bone: Lamellar bone with high porosity, it makes up the inner parts of short bones and the ends of long bones. Its function is mineral homeostasis and support

Compact (cortical) bone: Lamellar bone, makes up the shafts of long bones and the shells of most bones. Its function is mainly biomechanical support and protection. *have haversian systems / osteons

2. Compare the features and function of lamellar and woven bone

Woven bone: formed quickly, collagen fibers and osteocytes distributed randomly, usually temporary
Lamellar bone: Formed slowly, highly organized, stronger

3. Understand the composition and organization of the bone matrix.

Organic matrix (90% type 1 collagen) makes up roughly 20-40% of bone
Mineral (hydroxyapatite) makes up 50-70% of bone
Water makes up 5-10%
Lipids make up <3%

4. Understand the morphology and function of the periosteum and endosteum

Periosteum: Sheet of fibrous tissue that surrounds the outside of a bone
Endosteum: Lines the center of bone

5. Describe the blood supply of bone

Vascular foramen associated with epiphyseal vessels
Nutrient foramen
Nutrient artery supplies the inner 2/3 of the cortex
Periosteal vessels supply the outer 1/3 of the cortex
Vessel systems communicate

Qs

1. How can you tell the diaphysis from the epiphysis?

The diaphysis is the long part of the bone in the middle where as the epiphysis is above the physis (growth place) which is on the ends of the long bone.

2. What are the major differences between cortical and trabecular bone and where are they found?

Cortical bone is found along the shafts of long bones where as trabecular bone is found in the inner parts of short bones and the ends of long bones. Cortical bone is dens and less metabolically active where as trabecular bone is less dense with a spongey network that has a higher turnover rate and larger remodeling area.

3. What's in the medullary cavity? Is it the same in a younger animal as in an adult?

The medullary cavity is the hollow area of bone that contains bone marrow. In a young animal the bone marrow is more red indicating it is more haematopoietically active. Red marrow can be found in the vertebrae, ribs, sternum, skull, scapulae, pelvis, epiphysis, and metaphysis of adult long bones. In adults, the bone marrow is more yellow and contains many adipocytes. This marrow is less haematopoietically active but it can be converted to red if there is hemorrhage. Yellow bone marrow primarily makes up the diaphysis of long bones.

4. What is different about lamellar bone in cortical and trabecular bone?

Lamellar bone is organized into Haversian systems in compact bone (cortical bone).
Lamellar bone is organized into struts and plates in trabecular bone so you just see small layers of bone. *The haversian systems are too big for trabecular bone.

5. Can I describe the characteristics and location of a periosteum versus an endosteum?

Periosteum is the sheath outside your bones that supplies them with nutrients
Endosteum is a thin layer that is lined with osteoblasts and precursors to osteoblasts that lines the center of your bones.

6. What is woven bone and when /where would I find it?

Woven bone is bone that is formed quickly and made up of collagen fibers and randomly distributed osteocytes. This bone is usually temporary and would be found at the site of an injury during the healing process or during new bone development.

Lecture 5: Bone Cell Biology; *Dr. Clare Yellowley*

LO

1. Identify different bone cells based on their morphological characteristics, location and function.

Osteoblasts are secretory cells that have a large nucleus, enlarged golgi, and extensive rough endoplasmic reticulum
Osteocytes have a “spikey” morphology in cell structure. They are usually found in the matrix of bone
Osteoclasts are primarily mononuclear and are found in developing or bone that is being repaired

2. Understand the differentiation route of these cells from mesenchymal or hematopoietic precursors.

Osteoblast differentiation: Osteoblasts and osteocytes originate from the mesenchymal stem cell lineage and turning on Runx2 (CBfa1) makes the multiprogenetor stem cells travel down the osteogenic pathway. They then rapidly proliferate to form many osteoprogenitors that mature into osteoblasts which then have the ability to turn into osteocytes.

Osteoclast differentiation: Osteoclasts originate from the hematopoietic stem cell lineage. Hematopoietic precursor cells with RANK need to interact with osteoblasts which present RANKL on their surface. This leads to the formation of a mononuclear osteoclast that has the ability to fuse to other mononuclear osteoclasts and can become a multinucleated osteoclast.

Qs

1. Do these cells interact in any way?

Osteoclasts and osteoblasts require each other to work. Osteoblasts secrete factors that are needed for osteoclast development.

2. Where are these cells located histologically?

Osteoblast and the osteoclasts are seen in repairing and developing bone. Mature bone has osteocytes but not as many osteoblasts and osteoclasts.

3. Can you describe how an osteoclast degrades bone matrix?

An inactive osteoclast (not attached to bone) contains acidified vesicles with H+-ATPase on their membrane, microtubules, and a varied distribution of a_vB_3 integrin on the plasma membrane.
After attachment to the bone a_vB_3 integrins concentrate on podosomes, sites contacting the bone matrix. The H+-ATPase are inserted in the ruffling and plasma membrane by vesicle exocytosis. Bone degradation starts when the a_vB_3 integrin-F-actin-osteopontin complex organizes the sealing zone resulting in the isolation of the resorption space from the extracellular space. Protons generated by CAII are actively transported through the H+-ATPases present in the ruffled membrane and an acidic environment mobilizes bone minerals. Cathepsin K is secreted by exocytosis and degrades the bone organic matrix.

4. Where would I expect to see these cells in an immature or mature specimen?

In a mature specimen, you are not going to see many of the big, multinucleated cells. Mature bone will have osteocytes but unless it is undergoing repair, it will not have many osteoclasts or osteoblasts. On the other hand, in an immature specimen you are more likely to see osteoclasts and osteoblasts as well as osteocytes since there is more development happening.

Lecture 6: Cartilage Biology; *Dr. Clare Yellowley*
LO

1. Understand the development, characteristics and function of chondrocytes

Cartilage is derived from mesenchymal stem cells. Sox9 induces MSC's to differentiate into chondroblasts which then produce extracellular matrix (primarily type II collagen and proteoglycans). Once sequestered among the extracellular matrix, chondroblasts become chondrocytes.

2. Learn the mechanisms by which cartilage growth occurs

Interstitial growth: Occurs throughout the interior of immature cartilage. Chondroblasts undergo mitosis. Each daughter cell produces a matrix. Expansion occurs in all directions.
Appositional growth: Occurs in the perichondrium. Mesenchymal stem cells divide and differentiate. Chondroblasts are involved and expansion occurs perpendicular to the perichondrium.

3. Understand the molecular and biophysical nature of the cartilage matrix

The extracellular matrix water contains gases, small proteins, metabolites, and a high concentration of cations. Some of the water can move freely in and out and it interacts with matrix molecules to contribute to the mechanical properties of the ECM such as making it more gelatinous. The cartilage matrix is made up of a collagen network. Water is attracted into the matrix because of the proteoglycans which makes it swell and stretch allowing it to become firm and support load. *Papin breaks down proteoglycans and results in a loss of turgidity and structural support

4. Distinguish the different types of cartilage and know their location in the body

Hyaline cartilage: Most abundant type of cartilage. Found in synovial joints on articular surfaces, and in the airways. Start with the general cartilaginous matrix. Think of this as your basic model and you build from there. *has a perichondrium except at articular surfaces
Elastic cartilage: Found in the ears, not many other places. Start with the general cartilaginous matrix (hyaline) and then add elastic fibers. *has a perichondrium
Fibrocartilage: Found where tendons insert into bones and in between vertebral bodies. Start with the general cartilaginous matrix (hyaline) then add collagen I fibers.

Qs

1. How does a perichondrium affect the capacity of cartilage to repair?

Cartilage with a perichondrium has more of a capacity to repair compared to cartilage without a perichondrium because the perichondrium provides nourishment through blood vessels and protection. Cartilage has a limited capacity to repair because there is often a lack of active blood flow / limited vascularity.
Hyaline cartilage (articular cartilage) does not have a blood supply, but they can secrete enzymes that break down some of the collagen and secrete new collagen. This is very minimal and is only beneficial around the cells so there is not a mass beneficial effect. That is why damaging cartilage is so detrimental.

2. How does cartilage bear load?

Cartilage bears load through the cartilage matrix which is made up of proteoglycans that draw water in causing the matrix to swell. This swelling makes the matrix turgid and able to support load.

3. Where do chondrocytes obtain nutrients from?

Ear Cartilage has a perichondrium so it gets its nutrients via diffusion
Articular surfaces do not have a vascular supply so it has a hard time with diffusion. It gets its nutrients through the joint space which is a fluid-filled cavity with lots of nutrients. The top layer of cells in the articular cartilage get their nutrients from diffusion through the joint cavities but the cells that are deeper get their nutrients through loading when we “squish” the tissue (facilitated diffusion through use and “sloshing of water).

Lecture 7: Comparative Osteology; *Dr. Claudio Gutierrez*

1. Identify major differences between the Bovine and Equine osteology of the Thoracic Limb.

Scapula: Bovine have an acromion whereas equine do not
Serrated face of the scapula: more of a “W” shape in equine

Humerus: No super trochlear foramen in large animals
Equine have an intermediate tubercle while bovine do not

Radius/Ulna: Bovine have a fused radius and ulna and the ulna travels all the way down with the lateral styloid process
Equine: Completely fused and the lateral styloid process belongs to the radius

Metacarpus: Bovine have two articular trochlea because they have two digits while equine only have one. Equine also have splint bones

2. Identify major differences between the Bovine and Equine osteology of the Pelvic Limb.

Femur: Equine have a third trochanter whereas bovine do not. They also have a supracondylar fossa which is the origin for the superficial digital flexor

Tibia/Fibula: More developed in the horse, the bovine tibia and fibula are fused. Equine do not have a malleolar bone. Tibia tuberosity in equine has a fossa called the tibial tuberosity groove, this is not in bovine.

Tarsus: Bovine have a malleolar bone and a distal trochlea while equine do not. Equine also have fused carpal bones 1 and 2.

Lecture 8: Embryology of the Musculoskeletal System; *Dr. Crystal Rogers*

1. Understand the concepts of hereditary and congenital anomalies.

Understanding embryogenesis and aging allows us to describe links between structure and function.
Congenital skeletal malformations include phocomelia, amelia, congenital hip dysplasia, polydactyly, and bicephalus dicephalus.

2. Define the relationship of germ layers to future organ and tissue development.

Endoderm: Gut, most internal organs
Ectoderm: Skin, CNS, PNS
Mesoderm: Muscle, bone, blood, kidney etc.
*The mesoderm is formed during gastrulation and is composed of multiple parts;
Central mesoderm: Chordamesoderm/axial mesoderm -> notochord
Required for patterning and structure and is the origin of Sonic Hedgehog signal (Shh)
Adjacent to center: Paraxial mesoderm ->presomatic mesoderm ->somites or head mesoderm
Skeletal muscle in limb and abdomen, dermis, vertebrae and ribs
Distal from somites: Intermediate mesoderm ->
Urogenital system kidneys, gonads, and ducts
Most distal: Lateral plate mesoderm
Heart, blood vessels, blood cells, pelvic skeleton, limb skeleton

3. Describe the differentiation of somites into segmental dermatome, myotome, and sclerotome. Q: What tissues do these become in the musculoskeletal system?

Dorsal somite: Dermomyotome -> dermatome and myotome
Dermatome is a region of the integument system that forms the dermis
Myotome is a group of muscles that a single spinal nerve innervates

Ventral somites respond to Sonic Hedgehog signaling and undergo an epithelial to mesenchymal transition to become sclerotome and then segmented cartilage.

4. Describe the role of the major signaling proteins in vertebrate limb formation.

Sonic Hedgehog protein is necessary for bone and cartilage formation from somite. It is secreted from the notochord and CNS floorplate. It induces ventral somite transition from epithelial to mesenchymal transition and the sclerotome forms and migrates to surround neural tube and notochord.

Bone Morphogenic Protein is secreted by the CNS roof plate and patterns dermomyotome.

5. Explain the development of vertebrae, long bones, and limb lengthening associated with the apical ectodermal ridge (AER).

Limb tissues are derived from the ectoderm and mesoderm. Apical ectodermal ridge (AER) controls limb growth and the zone of polarizing activity (ZPA) controls anterior-posterior patterning via Shh and FGF signaling pathways.

6. Understand the general direction of development is cranial → caudal.

The general direction of development is cranial to caudal, proximal to distal, and limbs develop from ectoderm (nerves/skin) and mesoderm (muscle, bone, blood)

7. Understand how abnormalities might arise during development and how defects in this process may result in anomalies and embryonic/fetal death.

Genetic mutations in the ZPA and expanded Shh expression can lead to polydactyly in cats. Thalidomide exposure inhibits both patterning (Shh) and growth (FGF) resulting in shortened forelimbs.

Summary:
Paraxial mesoderm forms somites which give rise to the axial skeletal bone/cartilage, tendons, and skeletal muscle. They are patterned by Shh and BMP.
Ventral somite cells for the sclerotome (axial skeleton)
Dorsal somite forms individual sclerotome, dermatome, myotome
Lateral plate mesoderm gives rise to limb bones and body wall
Limbs are derived from the mesoderm and ectoderm. The ZPA secretes Shh which creates the anterior posterior axis in the limb. The ARE is necessary to maintain undifferentiated mesenchyme during proximal to distal growth.

Lecture 9 and 10: Bone Development and Osteogenesis *Dr. Clare Yellowley*

1. To understand the difference between endochondral and intramembranous bone formation.

Intramembranous ossification: Forms the cranial vault and some facial bones along with part of the mandible and clavicle. This process involves the direct transformation of mesenchymal cells into osteoblasts.

Endochondral ossification: Forms the axial skeleton excluding the cranial vault and some facial bones as well as the appendicular skeleton.

2. To understand in detail the stages of endochondral ossification.

Endochondral ossification (primary ossification center): Hyaline cartilage is the template of a long bone. Proliferation of chondrocytes followed by their hypertrophy at the midpoint of the shaft initiates the formation of the primary ossification center. Hypertrophic chondrocytes secrete VEGF to induce sprouting of blood vessels from the perichondrium. Then the calcification of the matrix and apoptosis of hypertrophic chondrocytes occur. The osteoprogenitor cells of the perichondrium form the periosteal collar and then blood vessels form the periosteal bud and branch in opposite directions.
(Secondary ossification center): Blood vessels and mesenchyme infiltrate the epiphysis and a secondary ossification center is established. A similar secondary ossification center appears in the opposite epiphysis.

3. To identify the different regions of the growth plate

A growth plate has a resting zone, proliferative zone, prehypertrophic maturation zone, hypertrophic zone, and calcification/vascular invasion.

Lecture 11 and 12: Imaging Osteology; *Dr. Ehren McLarty*

1. Become familiar with orientation of radiographic projections of the limbs

Lateral projections the patient should be running to the left
Cranial or dorsal should be to the left
Proximal is at the top and distal at the bottom

2. Be able to name radiographic projections

Radiographic projections are named based upon the path taken by the x-ray beam through the patient.

3. Apply your knowledge of why it is necessary to use radiographic markers

Markers allow us to orient ourselves with the patient and know what limb we are looking at. The marker should always go on the lateral aspect of the patient.

4. Recognize anatomic features on musculoskeletal radiographs

Study anatomy and become familiar with “normals”

5. Know the factors that affect radiographic opacity

Opacity: Gas, Fat (soft tissue), Water, Mineral (Bone), Metal

6. Know radiographic appearance of musculoskeletal tissues

Study anatomy and become familiar with “normals”

7. Start to develop a systematic approach to reading radiographs

Don't just focus on the area of interest, examine the image as a whole so that nothing critical gets missed. Internal organs should also be examined, not just the bones!

Lecture 13: Bone Adaptation and Remodeling; *Dr. Clare Yellowley*

LO

1. To understand the 6 stages of bone remodeling.

Resting: nothing is occurring, cells are quiescent
Activation: Cells retraction, mineral resorption
Resorption: Osteoclasts erode a parcel of bone
Reversal: coupling
Formation: Osteoblasts replace bone (osteoid forms)
Mineralization: Tissues is beginning to become mineralized

*Cutting cones are observed in compact bone remodeling and follow a similar pattern of formation, reversal, and resorption

2. To be able to identify the various architectural characteristics of the bone matrix and appreciate how they have formed.

Understand histology; secondary osteons have cement lines and appear darker whereas primary osteons do not

3. To understand the nature of the mechanostat, Wolff's Law and bone adaptation

Wolf's Law: Form follows function meaning that bone adapts to the loads under which it is placed. Increased load = increased bone mass just like decreased load = decreased bone mass. Bones have mechanosensitive bone cells which can sense strain and when there is increased strain, there will be bone deposition and when there is decreased strain, there will be bone loss.

Qs

1. What is the difference between modeling and remodeling?

Modeling is when osteoblasts and osteoclasts are not working together on the same part of bone. This results in a change in shape (widening)
Remodeling is when the osteoblasts and osteoclasts are working at the same place in the bone and is the ongoing replacement of old bone tissue by new bone tissue typically due to a crack.

2. Remodeling in compact bone results in the formation of what characteristic feature?

Haversian systems

3. Are cement lines found in trabecular bone?

Yes, when remodeling is occurring

4. If microcracks are not removed by remodeling what could happen?

The bone could be more predisposed to fracture

5. A new weightlifting hobby is anabolic or catabolic for the skeleton?
Anabolic, the increased strain would cause the cells to lay down more bone

6. Would you go to mars?
No, I like my bone mass

Lecture 14: Functional Myology Locomotor Structure and Function; *Dr. Jessica Morgan*

1. Learn the components and their respective functions in the musculoskeletal system
Bone levers are attached at joints whose motion is constrained by ligaments and induced by muscle contraction and conveyed to bone levers by tendons.

2. Deduce muscle function by position of muscle relative to joint center of motion
Collateral ligaments facilitate movement in the sagittal plane but limit movement out of the sagittal plane. Muscle mass is concentrated at the proximal aspect of the limb which minimizes energy required for limb motion.
In order for a muscle to effect an action the muscle must cross a joint, the action depends on the surface of the joint that is crossed, and the action may be modified depending on limb restriction (weightbearing).

3. Know the key functions of muscles and how muscle architecture affects functions
Muscles have an origin and an insertion. The origin is the most fixed location and is usually the most proximal site in the limbs. The insertion is the movable location relative to the fixed site. In the limb, this is usually the most distal site. Flexor surfaces are the smaller angle during stance and the extensor surfaces are the larger angle during stance. This has one exception, the metacarpophalangeal and digital joints have the flexor on the palmar/plantar surface and the extensors on the dorsal surface.

4. Understand how musculoskeletal structures in the ‘stay apparatus’ minimize energy expenditure during stance and locomotion
The front limb stay apparatus is made up of the biceps brachii, triceps brachii, laterus fibrosis, collateral ligaments, ECR fascia, palmar carpal I, flexor T and check I, palmar carpal I, and suspensory apparatus. These work together to allow the animal to remain standing with little to no muscular effort.
The hindlimb stay apparatus is made up of the quadriceps, stifle fixation, reciprocal apparatus to fix tarsus, and suspensor apparatus to support the fetlock.

Lecture 15: Introduction to Skeletal Mechanics; *Dr. Jessica Morgan*

1. Know the types of forces experienced by the musculoskeletal system
Internal forces: muscle contractions, interactions with joints, tendons and ligaments
External forces: Gravity, Friction, Wind etc.
Types of forces: Compression, tension, shearing, bending, torsion

2. Understand how bone geometry optimizes load bearing and transfer of loads

Loads must cross cartilage in joints. Form follows function (Wolff's law). The head of long bones is usually the primary compression group, the diaphysis is the secondary compression group and the greater tuberosity is the primary tension group.

3. Learn how excessive forces lead to different types of fractures

Tension leads to transverse fractures
Compression leads to oblique fractures
Torsion leads to spiral fractures
Bending is tension and compression which leads to transvers and oblique fractures

4. Understand how the body utilizes levers for locomotion

Input force: the force generated by muscle contraction acting on the effort arm of a lever
Output force: The force generated by muscle contraction after modification by a lever and acting on the load arm of a lever
Fulcrum: Joint about which the forces act
Load: an external force acting on the skeleton
*Positioning of the fulcrum determines the output force and displacement
If the effort arm force is greater than the load arm, there will be a large output force, small displacement, and slow effect movement
If the effort arm force is less than the load arm there will be a small output force, large displacement, and rapid effect movement

5. Learn adaptations of bones that facilitate movement

Hollow bones proved greater strength : weight than solid bone
Bone adapts to loading conditions
Tubercles, trochanters, and tuberosities create lever arms
Sesamoid bones change force direction and increase leverage

Lecture 16: Bone Response to Trauma; *Dr. Brian Murphy*

1. What are the different forces acting on bone?

Bending, torsion, shearing, tension, and compression

2. What is the difference between primary and secondary bone healing?

Primary bone healing requires stable fracture fragments, anatomic reduction, adequate / good nutrition, adequate blood supply and a sterile fracture environment. Bone remodeling units directly bridge the fracture with bone tissue (no callus). Usually done with surgical intervention and internal fixation.
Secondary bone healing usually involves minimal movement at the fracture site, poor/suboptimal anatomic reduction or less than perfect healing conditions. All fractures that heal in nature are through secondary bone healing. (callus is involved)

3. Describe the process of fracture healing.

Hematoma, inflammation, callus (fibrous, cartilage, bone) remodeling/modeling.

4. What are the different types of physeal fractures?

Salter Harris Fractures: “Slipped, above, lower, through, rammed”

SH I: Complete separation of the physis (growth plate), also referred to as a “slipped epiphysis”

SH II: The fracture plane travels through a portion of the growth plate and then diverges through the metaphysis. This is the most common physeal fracture of dogs, cats, horses, and humans!

SH III: The physeal fracture extends from the physis and then diverts through the epiphyseal bone, involving the joint surface (articular cartilage). *Worse prognosis since a joint surface is involved

SH IV: The fracture line extends from the metaphyseal bone, through the physis and through the epiphyseal bone and articular cartilage. *Even worse prognosis than SH III since the growth plate is crossed and the joint surface is involved!

SH V: Compression fracture of the physis that can lead to premature closure of the growth plate

5. What are the pathogenic mech of angular limb deformities?

Physeal fractures that lead to cessation of growth in a single member of a bone pair (radius/ulna) can result in varus or valgus deformation. These can occur even if only a portion of the growth plate was damaged. Developmental disorders of incomplete ossification of the cuboidal bones in the carpus/tarsus can result in limb angulation as well. They are common in species with rapid growth, especially foals and can be associated with OCD.

6. What are pathologic fractures? What are the possible causes?

Pathologic fractures are fractures in which some type of pre-existing bone pathology predisposes the bone to fracture. Possible causes include metabolic bone disease, neoplasia, infection/inflammation, stress fracture, and skeletal dysplasia.

Lecture 17: Imagine Features of Trauma; *Dr. Katie Phillips*

1. Accurately describe fractures using appropriate terminology

When describing a fracture you need to describe the soft tissue damage (open/closed), the fragment design (displacement), and the anatomical location (what part of bone, what bone, what limb).

2. Identify pathologic fractures

These fractures occur in bone weakened by an underlying pathologic process

3. Recognize the radiographic features in the progression of bone healing

Primary bone healing with primarily have apposing fracture margins, almost no fracture gap, stable fixation, and no callus.
Secondary bone healing with have a hematoma, fibrous callus, and bridging bony callus

4. Recognize the major complications, and associated radiographic features, of bone healing

Uncomplicated fracture healing is nonaggressive. You may see mild resorption/rounding of the fx margins. The edges will be smooth with well-defined margins, there will be a variable, but

short, transition zone and it will improve over time.
Complicated healing can appear aggressive. This can indicate infection or motion at the fracture margin. Complicated fracture healing can result in premature closure of the physis leading to angular limb deformity, osteoarthritis, delayed union, malunion, or nonunion.

Lecture 18: Clinical Fracture Healing; *Dr. Po-Yen Chou* (Poba)

1. List the bio-mechanical requisites for the two different types of bone healing after fracture

Primary bone healing requisites: Blood supply, fracture gap <1mm, absolutely stable strain <2%
Secondary bone healing requisites: Blood supply, fx gap >1mm, relatively stable strain <10%

2. Describe absolute and relative stability (strain) and how it affects formation of different tissue type during bone healing

When strain is between 10 and 100% granulation occurs, when it is between 2 and 10% fibrocartilage forms and when it is less than 2% bone forms.

3. Discuss how the following factors may affect the decision making to achieve different types of bone healing (patient factors and fx configuration/location)

The overall debate should be which type of fracture healing can be achieved with less complication and a faster return to function.
Primary bone healing MUST be done when there is an articular fracture (simple and comminuted) or a simple diaphysis fx in large or older patients. It CAN be used with a simple diaphysis fx in young growing patients.
Secondary bone healing MUST be done with comminuted diaphysis fractures (more than 3 fragments). It CAN be done for simple non-articular fractures in young patients with good healing potential.

Lecture 19: Developmental and Degenerative Bone and Joint Pathologies; *Dr. Brian Murphy*

1. What is the pathogenesis of IVD disease? What are some possible clinical sequelae?

Some dogs have disproportionate dwarfism which makes them predisposed to IVD. Premature, accelerated degeneration and mineralization of the nucleus pulposus can be the root cause of this disease. Furthermore, herniation of the degenerate nucleus pulposus can lead to impingement of the spinal cord, spinal nerves, and neurologic dysfunction (pain and paresis).
The NP is composed of vacuolated nodochordal cells which are responsible for maintaining the proteoglycan-rich disc matrix. These proteoglycan result in increased fluid within the NP and their absence causes the NP to be more compressible.

2. What type of spinal dysplasia occurs in dogs? Horses?

In dogs, spinal dysplasia occurs in breeds like Boxers and are characterized by wedge or trapezoidal-shape vertebrae known as hemivertebrae. These dogs may have abnormal curvature of the spine, scoliosis, lordosis (deep curvature of the lower spine) and or kyphosis (deep curvature of the upper spine). Spinal dysplasia in dogs may or may not result in spinal cord impingement, pain and neurologic manifestations.
In horses, spinal dysplasia can result in stenosis (narrowing) of the cervical vertebral canal. This may manifest as static (regardless of position) or dynamic (position dependent). This can result

in proprioceptive deficits to the legs. These lesions need to be clinically distinguished from malformation of the cervical facets as a result of osteochondrosis. Osteochondrosis results in the facets becoming broad and irregular (like pancakes) and results in “Equine Wobbler Disease”.

3. What is the pathogenesis of osteopetrosis? In which animals does it occur?
   Which bones are involved?

Osteopetrosis is the result of a failure of osteoclasts to resorb bone (they don’t turn the primary spongiosa into secondary spongiosa). This causes the primary spongiosa to persist and fill up the metaphyseal and diaphyseal marrow cavity. The diaphysis is often wider than normal and the gross lesions can look like an hour glass. The distinction between cortex and medullary bone are often lost. Intramembranous ossification remains normal. This disease occurs primarily in cattle (Angus, Hereford, Simmental, and Belgian Blue) but has also been see in sheep and on the rare occasion, horses. Dogs and cats seldom get this disease and it is currently referred to as Patellar fracture and Dental Anomaly Syndrome (PADS) also known as “Knees and Teeth syndrome”. This disease is thought to involve a variety of genetic abnormalities with a few of the acquired cases resulting from an infection with canine distemper virus, feline leukemia virus, or bovine viral diarrhea virus. The viral infection inhibits osteoclast function creating a phenocopy of the osteopetrosis lesion.

4. What animal gets craniomandibular osteopathy? What are the feature of the lesion?

Craniomandibular osteopathy is a proliferative bone disorder of dogs that results in new woven bone formation on the mandible and base of the skull, principally the occipital and temporal bones. The lesions are bilaterally symmetric and occur in young dogs ages 4-7 months. Westies are the poster-child for this disease. Histologically this disease is characterized by periosteal and endosteal woven bone undergoing intercurrent formation and resorption. Dogs may present with mouth pain during chewing or the inability to fully open their jaw.

5. What is metaphyseal osteopathy? What are the clinical and histological features?

Metaphyseal osteopathy is a disease that typically occurs in large or giant breed dogs around the ages of 3-8 months. The distal metaphyses of the radius and ulna are typically affected and the lesion is usually bilaterally symmetric. Animals usually present with pain, lameness, fever, anorexia, malaise, and metaphyseal heat/swelling. Histologically the metaphyseal lesions have numerous infractions (individualized clusters of bone trabeculae), necrosis, absence of osteoblasts, suppurative inflammation, and fibrin deposition. There is no evidence of microbial agents!

6. What are the types of osteochondrosis (OC)? Which animals get OC?
   What are the clinical and lesional manifestations?

Osteochondrosis is. Described as focal failure of endochondral ossification. It may be the result of focal failure of blood supply to the growing cartilage and physeal plate (vascular failure and ischemic chondronecrosis). Lesions can develop in the cartilage of either the physeal growth plate or the articular-epiphyseal complex. Mild lesions are referred to as osteochondrosis latens/manifesta. These may latter progress to clinical lesions. OC lesions in the articular cartilage that result in a partial to complete dissecting flap are typically referred to as osteochondrosis dissecans. These flaps can detach and mineralize

within the joint and are then called joint mice. Chronic OCD typically results in DJD (degenerative joint disease). In horses OC may present as subarticular cavitating lesions resulting in a subchondral pseudocyst.
Dogs: Humeral head, elbow stifle, hock (lat. ridge of talus)
Horses: Articular facets (cervical vertebrae) femoral condyle, femoral trochlea, hock, fetlock
Pigs: Distal femoral physis, hock (talus)

7. What are the features of ANFH? In which animals does it occur?

Aseptic necrosis of the femoral head (Legg-Calve-Perthe's disease) typically presents as a unilateral lesion caused by ischemic episodes to the capital epiphysis. In ANFH, the bone of the capital epiphysis is necrotic and the lacunae are empty (no osteocytes) and the intertrabecular space lacks viable adipose and hemopoietic elements. This eventually results in irregularities in the coxofemoral articulation, degeneration/necrosis of the articular cartilage culminating eventually in DJD. This disease typically presents in young 4-8 month old toy/miniature breed dogs without a hx of trauma. It may rarely occur in horses.

8. How is hip dysplasia different/how is it similar to DJD of the coxofemoral joint?

Hip dysplasia is a disorder of the coxofemoral joint and it typically manifests in young animals. Genetics, rate of growth, nutrition, and trauma can all play a role in this disease. Untreated hip dysplasia eventually results in degenerative joint disease. HD is not synonymous to DJD because there are many things that can lead to DJD such as ANFH and OCD. DJD is an overarching term used to describe an effect of multiple diseases.

Lecture 20: Imaging Features of Developmental Disorders; *Dr. Katie Phillips*

1. Recognize & describe the radiographic features and common anatomic sites of osteochondrosis

Osteochondrosis is the disruption of normal endochondral ossification which leads to defets in the subchondral bone. It may result in fragments moving freely in the joint space and that is called osteochondrosis dissecans. Radiographic features include subchondral bone defect, surrounding subchondral bone sclerosis, secondary lesions on opposing articular surfaces (kissing lesions) and secondary degenerative joint disease. Dogs commonly get this disease in the caudal humoral head, medial humoral condyles, femoral condyles, and trochlear ridges.

2. Describe & recognize the primary and secondary radiographic features of hip dysplasia

Primary features of hip dysplasia: Joint conformation (shape of acetabulum and femoral head), joint incongruity, joint stability (inferred from static images and distraction techniques). Normal hips should have 50% coverage by the dorsal acetabulum, parallel subchondral bone margins and a small distraction index.
Secondary features: Early-joint capsule enthesiophyte. Late-femoral head and neck remodeling and acetabular subchondral thickening and osteophyte production

3. Identify the specific orthopedic disorders included in the term "elbow dysplasia" and be familiar with radiographic features of each of these disorders

Elbow dysplasia is an aggregate of developmental disorders that may occur alone or in combination. These disorders include; fragmented medial coronoid process, ununited aconeal process, osteochondrosis of the humeral trochlea.

4. Recognize imaging features of panosteitis

Panosteitis has an unknown initiating cause and results in shifting leg lameness typically between the ages of 5 and 24 months. There is a breed predilection with GSD being commonly affected. This disease causes increased intramedullary opacity often originating near the nutrient vessel and there may also be a periosteal productive response present. The radiographic lesions may not correlate with clinical signs. This condition is not inflammatory – increased osteoblastic and fibroblastic activity.

5. Introduction to the imaging features of avascular necrosis and hypertrophic osteodystrophy

Aseptic necrosis of the femoral head results in ischemic events, bone necrosis, and attempted revascularization and remodeling.
Hypertrophic osteodystrophy results in reduced metaphyseal blood flow, failure of ossification, inflammation and necrosis. There are typically lucent lines parallel to the physis and a productive response in later stages of the disease. Periosteal reaction surrounding the metaphyses may be present in later stages as well.

Lecture 21: Calcium Homeostasis; *Dr. Clare Yellowley*

1. Be able to describe what happens when
   • blood calcium levels rise Calcitonin is released causing blood ca levels to fall
   • blood calcium levels fall: PTH is secreted and cause the blood calcium concentration to rise

2. Understand the actions of PTH, Vitamin D and Calcitonin on bone, kidney and intestine.

PTH works on the kidney to conserve calcium through increased renal tubular reabsorption and increased phosphate excretion. It also stimulates 1z-hydroxylase which is an enzyme that activates vitamin D. PTH stimulates calcium release from the bone by inhibiting osteoprotogerin which allows for more osteoclast precursors that express RANK to bind to RANKL. This allows for the formation of mononuclear osteoclasts.
Vitamin D comes in two major forms, Vit. D2 and Vit. D3 which both need metabolic transformation in order to be activated. Vit. D is first activated by the liver via 25-hydroxylase and then the kidney which turns it into 1,25 dihydroxy-vit. D via 1a-hydroxylase. 1,25 dihydroxy-vit. D is the active form that acts on the intestine to increase calcium absorption. Vit. D also aids in bone mineralization through an indirect effect attributed to the maintenance of serum calcium levels.
Calcitonin prevents reabsorption of calcium and phosphate by the kidneys and it inhibits osteoclasts in the bone.

3. Know where PTH is produced and how secretion is regulated

PTH is secreted from Chief cells in the parathyroid gland when the CaSR "calciostat" detects low blood calcium and it works in co-ordination with calcitonin and vitamin D to regulate blood calcium and phosphate concentration. The extracellular calcium ion concentration is the key regulator of PTH secretion.

4. Understand the sources of Vitamin D, how and where it is activated and which hormone controls the process.

*Vitamin D comes in two major forms, Vit. D2 and Vit. D3 which both need metabolic transformation in order to be activated. Vit. D is first activated by the liver via 25-hydroxylase and then the kidney which turns it into 1,25 dihydroxy-vit. D via 1a-hydroxylase. 1,25 dihydroxy-vit. D is the active form that acts on the intestine to increase calcium absorption. PTH is the hormone that controls the process.

5. Know the source and role of calcitonin

Calcitonin is a 32aa peptide that is secreted by thyroidal C cells. It acts to inhibit osteoclast resorptive activity and secretion is regulated by blood calcium levels. Calcitonin is secreted as a response to small increases in plasma calcium and is switched off once plasma calcium is returned to the normal set point. Calcitonin is a physiological antagonist of PTH.

Lecture 22: Pathology of Metabolic Bone Disease; *Dr. Brian Murphy*

1. Be able to explain the basic aspects of calcium regulation, who are the 4 players? How are they interrelated? In which animals do these MBDs tend to occur?

The four players of calcium regulation are PTH, Vit. D, Calcitonin and FGF 23 from the phosphatonin system. Vitamin D and PTH work together to help increase Ca levels in the blood by increasing intestinal absorption of Ca and P, renal absorption of Ca, bone resorption of Ca, renal activation of vit. D3, and renal excretion of P. Calcitonin and FGF 23 work together to decrease serum Ca levels by inhibiting PTH, increasing renal excretion of P, and decreasing P and vit. D3. MBD typically occurs in young animals.

2. What are the common clinical and pathological features of metabolic bone disease (MBD)?

Clinical features of MBD are often soft bones, pathologic fractures (folding), pain, disuse, and deformities.

3. For osteoporosis, what are the diagnostic features, causes, pathogenic mechanisms?

Osteoporosis is characterized by a reduction in bone mass that leads to clinical disease. This disease can go undetected if the case is mild and spontaneous fx may be the first clinical sign. Advanced stages of this disease involve thickened bone cortices and increased porosity. Growth arrest lines may be present and indicate transient disease such as infection or anorexia. Some causes include; disuse atrophy, senile, starvation/GI parasitism (ruminants), pure calcium deficiency, chronic glucocorticoid exposure, post-menopausal (humans), genetic, and copper deficiency. Histologically, osteoporosis results in bones of normal quality however there is just less of it.

4. For fibrous osteodystrophy what are the subtypes? Pathogenic mechanisms? Lesional features? What is common between all these subtypes?

The subtypes of fibrous osteodystrophy include primary hyperparathyroidism, secondary hyperparathyroidism (renal and nutritional) and pseudohyperparathyroidism (humoral hypercalcemia of malignancy, HMM). All of these causes result in increased secretion of PTH directly or as a result of PTHrp secretion via tumor.
Primary hyperthyroidism is unregulated production of PTH via the parathyroid gland and is typically a result of parathyroid adenoma *dogs. PTH levels will be high, hypercalcemia, PU/PD and weakness.
Secondary hyperparathyroidism (renal): ID in young dogs and horses along with aged cats. Typically due to chronic renal tubular injury which causes reduced hydroxylation of vit. D, decreased tubular reabsorption of calcium and decreased excretion of phosphorous. NOT predictably associated with hypercalcemia! *Can result in rubber jaw due to renal injury
Secondary hyperparathyroidism (nutritional): Result of chronic dietary imbalance of P and Ca leading to reduced serum ca and increased PTH. NOT generally associated with hypercalcemia!
Pseudohyperparathyroidism (HHM): Paraneoplastic syndrome resulting in hypercalcemia via PTHrp. Typically found in dogs with lymphosarcoma and a process associated with bone lysis.
Histologic lesions: Increased osteoclast-mediated bone resorption, increased compensatory intertrabecular fibrous tissue deposition. *Big head in horses

5. For rickets and osteomalacia, what are the causes, lesional features and in which animals do they occur?

Osteomalacia and rickets are caused by inadequate vit. D and/or phosphorous. Inadequate vit. D causes decreased Ca and P absorption from the intestines. The loss of these nutrients cause defective/inadequate mineralization of osteoid and cartilage. Histological features of osteomalacia include increased peripheral band of unmineralized osteoidal matrix along with active osteoclastic resorption typically confined to the cortical bone. H&E stain results in a pale pink bone. Growth plates may be absent and in advanced cases, pathologic fractures and deformities are common. The histologic lesions for Rickets are prominent where cartilage contributes significantly to skeletal growth (sites of endochondral ossification/physis). Thickened/dysplastic physis and trabecular bone with wide osteoid seams along with retained cartilage cores often present in the secondary spongiosa are common histological features. Folding fx may occur and the metaphyseal region of long bones may have intertrabecular fibrous tissue deposition. Rickets is often seen in young birds (herons, egrets, and hawks)

Lecture 23: Anatomy of the Brachial Plexus; *Dr. Claudio Gutierrez* *Not on written exam

1. Understand general aspects of the nerve + muscle + blood vessels anatomical unit.

A nerve, muscle and blood vessel form an anatomical unit and they work together to allow the body to function.

2. Understand general aspects of the topographic anatomy of the Brachial Plexus.

The Brachial Plexus: Ventral branches of spinal nerves c6 to T1 or T2. The radial nerve has a deep branch and a superficial branch. The superficial branch opens in 2 branches and these superficial branches travel close to the cephalic vein. The radial nerve is more specialized in

extensor innervation, the ulnar nerve supplies flexor muscles with the median nerve. The radial, ulnar, and median nerve also innervated the digital region of the limb.
In cats, the brachial artery and median nerve pass through the supracondylar foramen.

Lecture 24: Topographic anatomy of major blood vessels; *Dr. Claudio Gutierrez* *not on exam

1. Understand general aspects of arteries and veins anatomical names.

The subclavian artery becomes the axillary artery. The axillary artery travels to the thoracic limb to supply the musculature and becomes the brachial artery and later the median and radial artery.

2. Understand general aspects of topographic anatomy of blood vessels.

Important landmarks:
Subclavian to Axillary *when it loops around the first rib
Axillary to Brachial *when you find the cranial circumflex humeral artery (deltoid and humerus landmark)
Brachial to Median *when you find the common interosseous artery (dives between radius and ulna)

Discussions

DISC 1: Biometric Case Set; *Dr. Jessica Morgan*

Practice describing different limb issues and thinking about their biomechanical implications

DISC 2: Trauma Development and Pattern Recognition; *Dr. Katie Phillips*

Practice identifying and correctly naming/describing fractures

DISC 3: Calcium Metabolism; *Dr. Clare Yellowley*

1. Create a diagram or cartoon to explain what happens when blood calcium levels decrease.

Decreased blood calcium levels -> PTH secreted from Chief Cells in the parathyroid gland -> PTH acts directly on the kidney and bone via PTH receptors -> calcium is conserved via resorption in kidney and released from bone, there is also increased absorption of calcium from the gut (indirect via vit. D)

2. Draw a diagram to demonstrate how PTH stimulates osteoclast formation and activity?

PTH stimulates calcium release from the bone -> PTH inhibits osteoprotogerin which allows for more osteoclast precursors that express RANK to bind to RANKL -> this binding allows for the formation of mononuclear osteoclasts which can later fuse and become multi-nucleated.

3. What is Denosumab (prolia®)? Using your knowledge of bone biology explain what this compound does in bone.

Denosumab is a fully human monoclonal antibody that binds to RANKL. RANKL inhibition blocks osteoclast maturation, function, and survival thus reducing bone resorption. It is used to combat osteoporosis and works similarly to OPG.

4. What is Romosozumab (Evenity Amgen). Can you find how this might work in bone?

Romosozumab is a humanized monoclonal antibody that targets sclerostin. Sclerostin is a glycoprotein secreted by osteocytes and inhibits Wnt signaling (needed for bone formation) in osteoblast lineage cells. This leads to a decrease in bone formation by osteoblasts and increased bone resorption by osteoclasts. Romosozumab prevents Sclerostin -> Sclerostin cannot work its inhibitory effect -> promote Wnt signaling -> bone resorption is decreased.

DISC 4: Clinical Pathology of Ca: Phosphorous,; *Dr. Bill Vernau*

1. Understand how to apply the Ca / P physiology you have learned to the measurement and clinical interpretation of calcium and phosphorus concentrations in blood

Total calcium and phosphorous is measured with a RTT. Free ionized calcium is measured with a heparinized tube and whole blood is used. It should be run quickly for accurate results. Do NOT use EDTA or plasma, these processes result in calcium being chelated and you will have a calcium value of 0.
We measure total calcium due to the significant amount of calcium that is bound to albumin.
Decreased albumin concentrations commonly cause apparent hypocalcemia.
If a patient is hypocalcemic, look at the serum albumin concentration
If the patient has hyperphosphatemia look at BUN/creatinine and specific gravity; this is most likely due to decreased glomerular filtration.*Renal disease can be associated with increased or decreased calcium in the blood.
Evaluate Ca and P together and consider the magnitude of change and signalment

2. Learn some primary disease processes that cause increased and decreased blood calcium and phosphorus concentrations

Diseases that cause hypercalcemia:
Humoral hypercalcemia of malignancy
Hyperparathyroidism
Vitamin D toxicosis
Renal failure
Hypoadrenocorticism (Addison's disease)

Less common: Osteolytic lesions (multiple myeloma – plasma cell neoplasia)
Young, growing, large breed dogs
Granulomatous inflammation

Diseases that cause Hypocalcemia:
Hypoalbuminemia (most common cause in small animals)
Primary hypoparathyroidism
Renal disease / Failure

Vet 403 Musculoskeletal Block Learning Objectives / Questions

Acute pancreatitis
Milk fever (puerperal tetany, lactation)

Less common: Hypovitaminosis
Grass tetany
Exocrine pancreatic insufficiency
Nutritional secondary hyperparathyroidism