OSTEOMYELITIS ETIOLOGY AND PATHOGENESIS

Inflammation of bone (osteitis) or bone and bone marrow (osteomyelitis) is uncommon in large animals except when infection is introduced by traumatic injury or by the hematogenous route. Bacteria can reach bone by any of three routes:

• Hematogenously

• By extension from an adjacent focus of infection

• By direct inoculation through trauma or surgery. Focal metaphyseal osteomyelitis can occur following open fractures in the horse.

Specific diseases that may be accompanied by osteomyelitis include actinomycosis of cattle.

Nonspecific, hematogenous infection with other bacteria occurs sporadically and is often associated with omphalitis, abscesses from tail-biting in pigs, or infection of castration or docking wounds in lambs.

Foals and calves under 1 month of age and growing cattle 6 to 12 months of age may be affected by osteomyelitis in one or more bones. The majority of foals with suppurative polyarthritis have a polyosteomyelitis of the bones adjacent to the affected joints.

The infections occur commonly in the metaphysis, physis, and epiphysis, which are sites of bony growth and thus susceptible to blood-borne infections. The metaphyseal blood vessels loop toward the physis and ramify into sinusoids that spread throughout the metaphyseal region.

Lesions occur on both sides of the physis in both the metaphysis and the epiphysis. Multiple lesions are common.

Bone infection was classified into four types according to the site of infection:

1- Type 1 is metaphyseal and/or epiphyseal osteomyelitis close to the growth plate.
2- Type 2 is primary subchondral osteomyelitis, mostly accompanied by septic arthritis
3- Type 3 is infectious osteoarthritis with subchondral osteomyelitis, implying that infection in the subchondral bone originates from the infection.
4- Type 4 includes bone infections that cannot be categorized in the other groups.

Hematogenous osteomyelitis in cattle can be of two types:

• **Physeal type**, in which an infection generally of metaphyseal bone originates at or near the growth plate, usually affecting the distal metacarpus, metatarsus, radius, or tibia The physeal infections are usually caused by T. pyogenes and occur most commonly in cattle over 6 months of age.

• **Epiphyseal type**, in which an infection originates near the junction of the subchondral bone and the immature epiphyseal joint cartilage, most often affecting the distal femoral condyle epiphysis, the patellar, and the distal radiusEpiphyseal osteomyelitis is usually a result of infection with Salmonella spp. and is most common in calves under 12 weeks of age.

Osseous Sequestration in Cattle

Osseous sequestration is a common orthopedic abnormality in cattle and horses. In most cases, the lesions develop in the bones of the distal portion of the limbs. Sequestration is associated with trauma that results in localized cortical ischemia and bacterial invasion secondary to loss of adjacent periosteal and soft tissue integrity and viability.

Osteomyelitis Secondary to Trauma

In horses, osteomyelitis is a frequent sequela to wounds of the metacarpal and metatarsal bones and the calcaneus. These bones have limited soft tissue covering, which may predispose them to osteomyelitis following traumatic injury.

Inflammation of Bone Marrow

Acute inflammation of the bone marrow commonly accompanies bacterial sepsis,

CLINICAL FINDINGS

The common clinical findings of osteomyelitis include the following:

• Lameness

• Generalized soft tissue swelling and inflammation

• Pain on palpation of the affected area

• Chronic persistent drainage

• Secondary muscle atrophy of the affected limb Erosion of bone occurs, and pus discharges into surrounding tissues, causing cellulitis.

-The affected bone is often swollen and may fracture easily because of weakening of its structure. When the bones of the jaw are involved, the teeth are often shed, and this, together with pain and the distortion of the jaw, interferes with prehension and mastication.

-Involvement of vertebral bodies may lead paralysis.

-Lameness and local swelling are the major manifestations of involvement of the limb bones.

-The lesions are typically destructive of bone and cause severe pain and lameness. A painful, discrete soft tissue swelling over the ends of the long bones is often the first indication.

-Initially there is a stumbling gait, which then becomes stiff and restricted and with a reluctance to bend the neck.

DIAGNOSIS XXXXXX

Radiographs are an essential part of the diagnosis. Radiographic changes include the following:

• Necrotic sequestrum initially

• New bone formation

• Loss of bone density Radiographic lesions are characteristically centered at the growth and extend into both metaphysis and epiphysis.

Culture of the inflammatory exudate and necrotic sequestra removed surgically is necessary to determine the species of bacteria and their antimicrobial susceptibility.

Anaerobic bacteria are frequently associated with osteomyelitis and should be considered when submitting samples for culture.

NECROPSY FINDINGS XXXXXX

At necropsy the osteomyelitis may not be obvious unless the bones are opened longitudinally and the cut surfaces of the metaphysis and epiphysis are examined

DIFFERENTIAL DIAGNOSIS

A differential diagnosis for a destructive lesion in the end of a long bone of a foal or calf would include the following: a healing fracture, traumatic periostitis or

osteitis, bone tumor, nutritional osteodystrophy and infection of the bone as a result of external trauma, fracture, extension from adjacent infection or hematogenous spread.

TREATMENT

Despite advances in antimicrobial therapy and refined diagnostic techniques, the clinical management of osteomyelitis is difficult. Medical therapy alone is rarely completely successful because of the poor vascularity of the affected solid bone, the inaccessibility of the infection, and the potential for development of a biofilm slime layer by bacteria. In cases of long-term infection or those with extensive bone necrosis, surgery is generally recommended to remove sequestra, devitalized tissue, and sinus tracts that are harboring large numbers of bacteria.

In septic physitis, the implantation of homologous cancellous bone grafts following debridement of necrotic bone, the application of a walking cast for 4 to 5 weeks, and antimicrobial therapy for 2 weeks is usually a successful approach. Absolute asepsis is a fundamental requirement for successful application of a bone graft; after debridement of the necrotic bone, the cavity is flushed with saline and aqueous ampicillin or a combination of penicillin G potassium and ceftiofur. Antimicrobials are an integral part of the treatment, and selection of the most appropriate drug should be based on identification and susceptibility testing of the organism. Initial treatment may be based on the most common isolates, and a combination of penicillin G and gentamicin or amikacin provides an excellent initial treatment in horses until culture and susceptibility results are available. Aminoglycosides such as gentamicin or amikacin do not provide an ideal initial treatment option in food-producing animals because of the extensive slaughter

withdrawals associated with their use. Most anaerobic bacteria associated with osteomyelitis are sensitive to penicillin and the cephalosporins, Regional perfusion of the distal limb may be helpful as part of the initial treatment by providing higher antimicrobial concentrations at the site of infection.

TAIL-TIP NECROSIS IN BEEF CATTLE

Tail-tip necrosis occurs in cattle housed in confinement on slatted floors. The disease has occurred in steers, heifers, and bulls being fed for beef production, and less frequently in dairy cattle.

The lesion is most commonly caused by a traumatic injury of the tail caused by tramping of the tail by other animals. Focal damage is more severe when the tail tip is tramped on slatted floors. Tail-tip necrosis is rare in dairy cattle confined in free stalls because most cows lie down in free stalls and their tails are thereby relatively protected from being tramped. The presence of the hard fecal mass increases the likelihood of damage to the tail tip, particularly when animals are confined. The lesion begins at the tip of tail followed by varying degrees of extension proximally. Initially, the tip of the tail is swollen, followed by inflammation and infection with Trueperella pyogenes.

Histopathologic changes are compatible with cutaneous ischemia as a pathogenic mechanism. Extension of the infection can result in metastases to other parts of the body, resulting in abscesses and osteomyelitis. Affected cattle do not grow normally, and deaths from pyemia may occur. The morbidity is about 5%. Approximately 10% of affected animals may be condemned for osteomyelitis and abscessation.

Risk Factors XXXXXXX

Risk factors include slatted concrete floors, close confinement, warm seasons, and a body weight above 200 kg. Most cases occur from May to September when the temperature is above 18° C (64 F). This may be associated with increased contamination as a result of increased humidity and temperature under confinement conditions. In slatted-floor barns, abnormal locomotor patterns occur in 20% to 25% of the times when animals get up and lie down.

When animals get up abnormally, they first rise from the front, then consequently assume a dog-like sitting posture. To obtain momentum to rise in the rear, they then start to sway back and forth. The tail may become pinched between the hock of the rocking animal and the floor, resulting in blunt trauma to the tip of the tail

TREATMENT XXXXXXXX

Treatment consists of early amputation combined with intensive antimicrobial therapy. Early detection is important.

During warm months, cattle confined on slatted floors and weighing more than 200 kg should be closely inspected at least 2 or 3 times weekly.

This includes palpation of all tail tips because early lesions are difficult to see.

LAMINITIS OF HORSES

Laminitis refers to a spectrum of processes and clinical signs related to breakdown of the connection **between of the basement membrane of the secondary dermal lamellae and the basal cells of the secondary epidermal lamellae**, with subsequent disruption of the anatomic relationship between the hoof and the distal phalanx. Understanding of the condition is dependent on a specialized vocabulary and jargon, including the following:

• Hoof—the layers of integument of the foot from the secondary epidermal lamella distally (outward, toward the hoof surface). The keratinized portion of the hoof is the hoof capsule.

• Distal phalanx—the most distal of the bones in the limb of the horse (synonyms of pedal bone, P3, or third phalanx)

• Lamellae (colloquially, “laminae”)— primary and secondary lamellae originate from the inside of the hoof and from the surface of the distal phalanx. Primary lamellae give rise to secondary lamellae.

The basal cells of the primary and secondary epidermal lamellae attach the hoof to the basement membrane of the primary and secondary lamellae of the distal phalanx through numerous anchoring points, the hemidesmosomes Hemidesmosomes are composed of multiple anchoring filaments that connect to laminin-5, a unique glycoprotein that attaches to type IV collagen in the lamina densa of the basement membrane. Type VII collagen connects the lamina densa to the distal phalanx. laminin-5 in the basement membrane is connected through the

hemidesmosomes by integrin (which crosses the cell wall) and plectin to the cytoskeleton of the basal cell. Protein BP-180 is associated with the hemidesmosomes and might be involved in anchoring. Basal cells are connected to one another by desmosomes (containing cadherins, a group of compounds responsible for cell–cell adhesion).

• Parietal integument (incorrectly, "lamellar integument")—that part of the space between the hoof capsule and distal phalanx occupied by the lamellae, parts of the dermis, and all subcutaneous tissue.

• Laminitis—the conventional definition is that of a clinical syndrome of foot pain, usually in an acute setting, in horses resulting from separation of the dermal and epidermal lamellae. Laminitis implies an inflammatory component or etiopathogenesis, which does not appear to always be present in all phases of the disease.

• Prodromal laminitis (developmental laminitis)—that phase between initiation of the disease process in the foot and appearance of clinical signs.

• **Acute laminitis**—that phase between first development of signs of foot pain and displacement of the distal phalanx (often 72 hours but variable and displacement does not occur in all cases).

• **Chronic laminitis**—phase of the disease after displacement has occurred. It can be further divided into **early chronic laminitis**, chronic active laminitis, and **chronic stable laminitis**.

• Acute founder—clinical signs of laminitis (strong digital pulses, toe relieving stance, and frequent weight shifting) plus signs of disruption of the normal gross

anatomy of the foot evident as supracoronary depressions or radiographic evidence of rotation or distal displacement of the distal phalanx within the hoof ("sinking").
• Chronic founder—clinical signs of concave dorsal hoof wall, abnormally wide dorsal white lines, and divergent growth rings in the hoof wall. Sometimes referred to as "chronic laminitis," this syndrome is not characterized by continued disruption of the lamellae but rather represents the sequelae to laminitis or acute founder. If there is ongoing disruption of the epidermal-dermal connection, then this would be laminitis or acute founder.

• Prolapse of the sole—a consequence of distal displacement of the distal phalanx resulting in loss of concavity of the sole.

• Penetration of the sole—progression of prolapse of the sole to the point where the dermis or pedal bone protrudes through the sole.

ETIOLOGY

The proximate cause of laminitis is acute degeneration of the connections between the basal cells of the primary and secondary epidermal lamellae and the basement membrane of the primary and secondary dermal lamellae. Loss of these connections can lead to microscopic and macroscopic disruption of the normal architecture of the foot and development of clinical signs of foot pain. The factors inciting or leading to breakdown of the epidermal-dermal connections within the hoof are uncertain and the subject of much active investigation.

Laminitis is recognized in a number of settings, which could have differing inciting causes:

• Endocrinopathic laminitis—laminitis associated with hormonal influences favoring hyperinsulinemia and often associated with insulin resistance as part of equine metabolic syndrome (EMS) or pasture associated

laminitis—horses with septic illness characterized by signs of a systemic inflammatory response (fever, tachycardia, depression), such as horses with enterocolitis, pneumonia and/or pleuritis, and postpartum septic metritis, or after ingestion of large quantities of soluble carbohydrate, are at increased risk of laminitis.

• Weight-bearing laminitis—horses that chronically bear more weight on one limb.

• Concussive laminitis—associated with prolonged or unaccustomed exercise on a hard surface.

• Toxic laminitis—exposure to shavings of black walnut (Juglans nigra) causes laminitis.

• Sustained (lasting 48 hours) digital hyperthermia does not cause laminitis.

EPIDEMIOLOGY XXXXXXXXX

The epidemiology of laminitis is poorly documented.

•Age—good evidence that increasing age is a risk factor for laminitis

• Sex (gender)—inconsistent evidence; most studies did not find an association

• Breed—inconsistent evidence; most studies did not find an association

• Height—no evidence of an association

• Bodyweight—inconsistent evidence

• General obesity—no evidence

• Cresty neck—weak evidence

• Health variables—no evidence

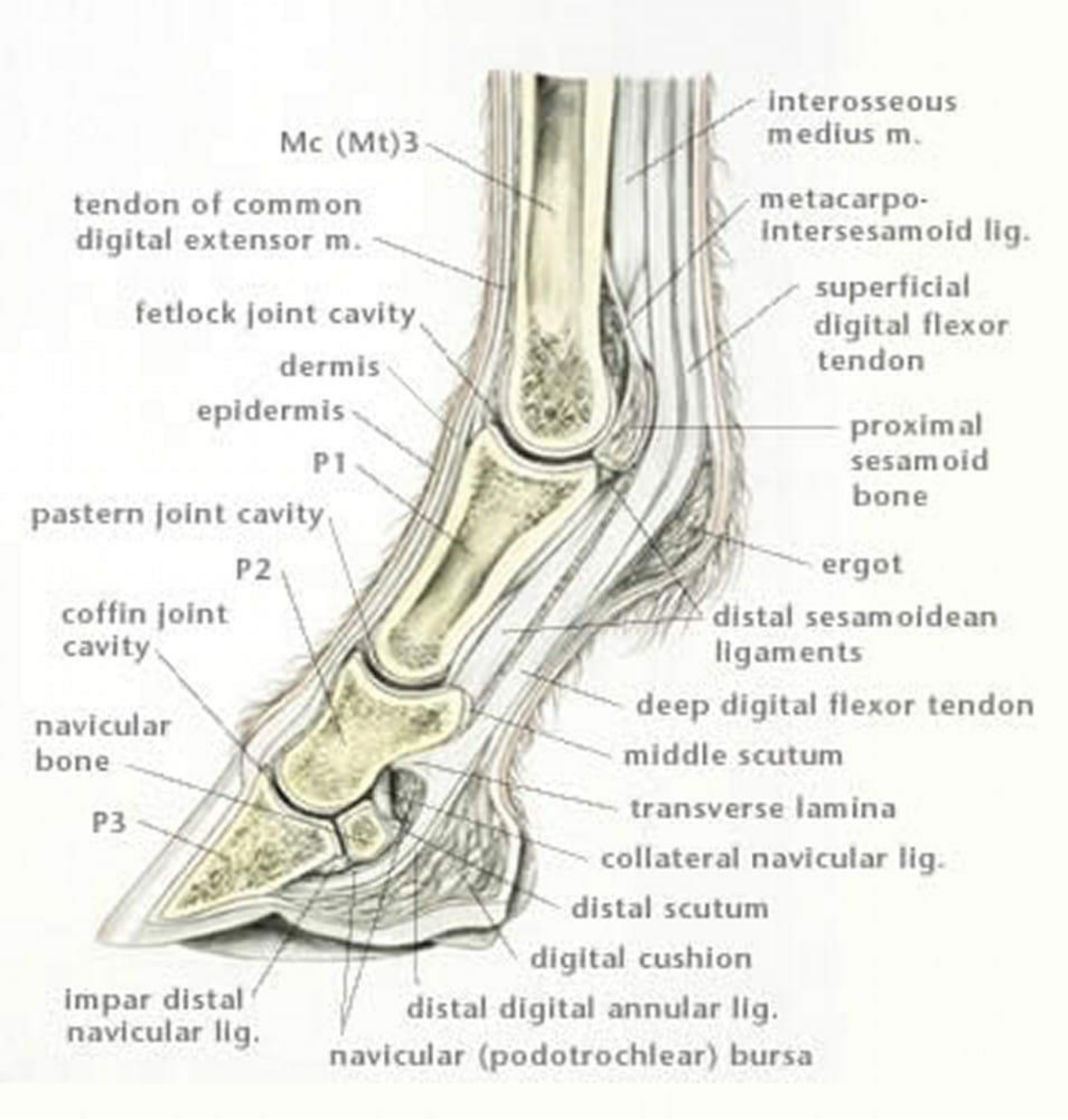
• Exercise—weak evidence that reduced exercise level is a risk factor

• Endotoxemia—weak evidence, noting that experimental endotoxemia does not cause laminitis

• Pituitary pars intermedia dysfunction— no evidence

• Seasonality—inconsistent evidence

• Weather—weak evidence



PATHOGENESIS مهم

The pathogenesis of laminitis is complex and in **most cases involves systemic disease that is at least partially expressed in the foot as a part of a systemic disease and not only a localized disease**

Systemic inflammatory responses, including infiltration of neutrophils, are noted and these findings suggest that systemic inflammation and degradation of proteins common to a wide range of tissues, and including the basement membrane, are common to many epithelial tissues during equine laminitis,

The local pathogenic process common to all forms of laminitis is disruption of the connective tissue (involving laminin-5 and collagen types IV and VII) providing connections between the lamellar basal cells and the basement membrane of the third phalanx.

As a consequence of the loss of these connections, the weight of the horse is no longer transmitted through the numerous lamellae to the hoof wall but is instead transmitted toward the sole of the foot.

Loss of the connection between the third phalanx and hoof allows the third phalanx to rotate within the hoof capsule,

Serum accumulates in the space created by degeneration of the laminae and displacement of the third phalanx, and there is breakdown of the white line.

Laminitis induced by administration of black walnut is characterized by early (1.5 hours) marked infiltration of neutrophils and expression of **neutrophil adhesion molecules in lamellar endothelial cells and cytokines** favoring extravasation of neutrophils into lamellae. There are similar changes during carbohydrate overload laminitis but with a somewhat delayed time frame with some extravasation of leukocytes, which are predominantly **monocytes and macrophages** (compare with neutrophils in black walnut laminitis), during the prodromal phase but maximal accumulation in lamellar tissues at the onset of clinical signs. This suggests that endothelial activation, leukocyte emigration, and proinflammatory cytokine

expression. The concentrations of insulin required to induce laminitis in insulin sensitive horses are very high (>1000 µU/ mL.

Increased cellular proliferation in the secondary epidermal lamellae, infiltration of the dermis with small numbers of leukocytes, and basement membrane (BM) damage occurred later at 24 and 48 hours. Narrowing of the secondary epidermal lamellae was progressive over the 6- to 48-hour period.

There were signs of apoptosis of basal cells. Cellular lesions preceded leukocyte infiltration and BM lesions, indicating that the latter changes may be secondary or downstream events in hyperinsulinemic laminitis to initial insults to basal cells.

Increases vascular reactivity and response to various vasoconstrictors and has, in the absence of direct experimental evidence in horses or ponies, been speculated to contribute to excessive vasoconstriction in the dermis of susceptible horses. Other theories for the etiopathogenesis of laminitis include the following:

• **Ischemia** of the laminae with subsequent dysfunction or death of basal cells or degeneration of the basement membrane—proposed causes of ischemia include vasoconstriction, development of arteriovenous shunts, interstitial edema, and presence of microthrombi in digital vessels. Ischemia as a result of microthrombus formation is no longer considered a potential cause of laminitis. However, there is evidence from experimental laminitis, both black walnut and carbohydrate models, that there are changes to the microvasculature of the dermis, possibly secondary to changes in circulating concentrations of vasoactive amines or contractile activity of vessels in the hoof. Alternatively, increases in capillary filtration pressure, resulting from venoconstriction, might cause edema and increased interstitial pressure with subsequent ischemia of the laminae.

• **Enzymatic digestion of connective tissues of the lamella** by matrix metalloproteins (MMPs) induced by circulating factors including products of Streptococcus bovis infection has been proposed as a cause of the **loss of integrity of the basal cell–basement membrane junction.**

• There is no evidence that laminitis is an autoimmune disease. The disease occurs in three distinct phases:

(1) a developmental stage in which lesions are detectable in the sensitive laminae but during which there are no clinical signs,

(2) the acute phase from the development of the first clinical signs through to rapid resolution or to rotation or ventral displacement of the third phalanx, and

(3) the chronic stage evidenced by rotation of the third phalanx with or without ventral displacement and characterized by variable but persistent pain.

CLINICAL FINDINGS

The disease presents as both an acute disease and as a chronic disease. The severity of the acute disease varies considerably from very mild with rapid (5 to 7 days) recovery, to severe with progression to the chronic, refractory stage. Severity of lameness attributable to laminitis can be graded according to a scale proposed by Obel in 1948:

Grade 0—normal

Grade 1—horse alternately and intermittently lifts its feet; lameness is not evident at a walk but the gait is short and stilted at a trot.

Grade 2—there is a stilted gait at the walk, but the horse moves willingly; a foot may be lifted by a handler without the horse resisting.

Grade 3—the horse moves reluctantly and resists attempts by a handler to lift a foot.

Grade 4—the horse refuses to move and does so only if forced.

These studies demonstrate that the Obel grading system is useful for clinical description of laminitis and therefore assessment of the response to therapy.

The acute disease develops rapidly; apparently normal horses can founder within hours. Signs of the disease are entirely attributable to **pain in the feet**. **All hooves can be affected**, but more **commonly the forefeet are affected** and the hindfeet are spared.✓

The disease is rarely unilateral except in cases in which the disease develops because of severe lameness in the contralateral limb or repeated **pawing**. Mild, or early, disease is apparent as a **resistance to movement and repetitive and frequent shifting of weight from one foot to the other.**

There is a characteristic **shuffling gait**. More severe disease is apparent as **refusal to move or to lift a hoof**. At this stage the horse has an anxious expression that can be accompanied by **muscle fasciculation, sweating, a marked increase in heart rate to as high as 75/min, and rapid and shallow respiration.**

There is a characteristic posture with all four feet being placed forward of their normal position, the **head held low, and the back arched**. There is usually a great deal of **difficulty in getting the animal to move**, and when it does so the gait is **shuffling and stumbling**, and the animal evidences **great pain** when the foot is put to the ground.

The act of lying down is accomplished only with difficulty, often after a number of preliminary attempts. There is also **difficulty in getting the animals to rise,** and **some horses may be recumbent for long periods**.

It is not unusual for horses to lie flat on their sides. In occasional cases, the separation of the wall from the laminae is acute, and the hoof is shed. There may **be exudation** of serum at the coronet, and this is considered a sign of impending **sloughing of the hoof and a poor prognosis**.

Clinical signs in laminitis include pain on palpation around the coronet and a marked withdrawal response when hoof testers are applied to the hoof.

The intensity of the pulse in the palmar digital artery, palpable over the abaxial aspects of the **proximal sesamoid**.

The hoof wall spreads and develops marked horizontal ridges, and the slope of the anterior surface of the wall becomes accentuated and concave.

The lameness might abate, but the animal becomes lame easily with exercise and can suffer repeated, mild attacks of laminitis.

Radiographic examination: The standard radiographic views that should be obtained to aid assessment of horses with laminitis are the lateromedial, horizontal dorsopalmar, and dorsal 45 degrees proximal palmarodistal oblique views.

Radiographs of more severe or advanced cases will demonstrate rotation of the distal phalanx within the hoof, evident as a tilting of the most distal aspect of the third phalanx toward the sole. The space created by rotation of the pedal bone can fill with gas or serum and be evident as a radiolucent line between the pedal bone and the dorsal hoof wall.

Displacement of the pedal bone toward the sole will be evident in approximately 25% of cases as a thickening of the dorsal hoof wall and reduction of the distance between the sole and solar aspect of the distal phalanx. Chronic or refractory cases can have osteopenia of the pedal bone with proliferation of bone at the toe.

Prognosis XXXXXXXXXXXX

The radiographic examination provides information of prognostic value, although because of differing radiographic techniques and interpretations the value of combining separate research studies to develop firm guidelines is difficult. Horses that return to their previous level of athletic function after a bout of laminitis have pedal bone rotation of less than 5.5 degrees, whereas horses that can no longer perform as athletes usually have more than 11.5 degrees of rotation, although there are exceptions to this rule and the prognosis should be developed through a holistic assessment of the horse (level of pain, number of feet involved, sole penetration). Therefore, these values should only be used as rough guidelines. The general rule is that the greater the degree of rotation or extent of displacement of the distal phalanx, the worse the prognosis for return to function and pain-free living. Objective radiographic variables include the distance between the proximal aspect of the hoof wall (marked on the radiographic image by a piece of wire or strip of metal stuck to the dorsal hoof wall) and the proximal limit of the extensor process of the distal phalanx (the “founder” distance), and the distance between the dorsal hoof wall and the dorsal cortex of the distal phalanx.

CLINICAL PATHOLOGY XXXXXXXXXXXX

There are no changes that are characteristic of the disease.

NECROPSY FINDINGS XXXXXXXXXXXXX

The disease is not usually fatal, but severely affected animals are often euthanized. In acute cases, there may be evidence of colitis, grain overload, or retained placenta and metritis in mares. No reliable gross findings are visible on the feet, but a midsagittal section of the hoof may reveal congestion, hemorrhage, and slight separation of the dorsal surface of P3 from the epidermal laminae of the inner surface of the horny hoof wall in severe cases. The separation of P3 becomes more obvious in subacute and chronic cases, leading to a ventral rotation of the phalanx. In some cases the degree of rotation of P3 results in perforation of the sole. Histologic examination is required only in acute cases, and confirmation of the diagnosis in such instances demands that the foot be cut into slab sections and fixed shortly after the death of the animal, before even moderate autolysis can ensue. Microscopically, the lesions are degeneration and necrosis of epithelial cells of the laminae, separation of epithelial cells from the basement membrane, and loss of the basement membrane.

TREATMENT

The adage “where facts are few experts are many” applies well to the treatment of laminitis. There are few welled signed studies of the treatment of naturally occurring laminitis, and thus the choice of treatment is based on personal experience, extrapolation from our imperfect understanding of the pathogenesis of the disease, the availability of certain drugs, and current fashion.

Indeed, the treatment of laminitis might one day be chronicled to demonstrate the power of “expert” opinion to determine treatments, many of which are now

recognized as useless. A fascinating example is that of the **application of nitroglycerin patches to the pasterns of horses with laminitis or at increased risk of laminitis.** A multitude of horses were treated in this way, some to the extent that they were rendered hypotensive, at considerable direct cost and opportunity cost, and all for naught.

Although not intended to discount the opinion of experts in the treatment of laminitis, it is a salutary tale demonstrating the strength of fashion and fad in promoting ineffective treatments of this important disease. In general, the treatments can be grouped into several classes, based on the intended intervention. These are as follows:

• Removal of the causative agent or treatment of the inciting disease

• Pain relief and minimization of inflammation

• Prevention of further damage to lamellae and rotation or distal displacement of the pedal bone

• Promotion of keratinization and hoof growth The efficacy of administration of analgesic, antiinflammatory, anticoagulant, and vasodilatory drugs and mechanical support of the hoof has never been demonstrated in appropriate clinical trials.

There is evidence that local cryotherapy (cooling of the distal limb) is effective **in reducing the clinical signs and severity of lesions of oligofructose-induced experimental laminitis, with limited although supportive clinical evidence. Acute laminitis is an emergency, and treatment should be started without delay because early and aggressive therapy might enhance the chances of recovery.**

Treatment of Inciting Process or Disease

The inciting disease should be treated aggressively and every attempt made to remove any causative agent. Horses with systemic inflammatory disease (colitis, metritis, etc.) should be treated aggressively to reduce the likelihood that they will develop laminitis. Treatment of colitis, metritis, pleuropneumonia, colic, and other diseases is dealt with under those topics. Horses with laminitis should be rested and housed in stalls that are well bedded with sand or soft shavings. Horses suspected of having PPID, insulin resistance, or EMS17 should have the diagnosis confirmed and appropriate therapy instituted. **Cryotherapy or Digital Cooling** There is experimental, and some clinical, evidence that chilling of the feet is effective in preventing development of laminitis and in attenuating the effects of established (acute) laminitis induced experimentally. Progression of experimental laminitis (CHO model) can be prevented by cooling (chilling) of the feet of horses during the prodromal and acute phases of the disease. **Cooling of the distal limbs of horses administered 10 g/kg body weight of oligofructose markedly reduced the clinical signs of laminitis and development of histologic lesions in the feet of treated horses. Cooling in the experimental model began at the time of administration of oligofructose and continued for 72 hours.** Horses treated by immersion of the limbs in cold water (0.5 to 2.0° C; 33–36 F) had only mild signs of lameness (grade I or less) at all times up until euthanasia at 72 hours. Furthermore, chilling of the limbs significantly reduced expression of a range of genes of proinflammatory proteins and increased expression of an antiinflammatory protein during both the prodromal and clinical phases of disease. Chilling of limbs after the onset of laminitis induced by oligofructose prevents lamellar structural failure and reduces the severity of damage to lamellae.80 Chilling (cryotherapy) of feet was initiated as soon as Obel grade II lameness was

detected (horses were examined every 4 hours) and continued until euthanasia 36 hours after onset of lameness. Horses were also administered **phenylbutazone (8 mg/kg IV—a high dose)** and **had continuous peripheral nerve block to alleviate foot pain.**

Analgesics and Antiinflammatory Drugs

A mainstay of the treatment of both acute and chronic laminitis is the use of nonsteroidal antiinflammatory drugs (NSAIDs). **These are administered to provide pain relief, and there is no evidence that they delay progression of the disease. Phenylbutazone, at doses of 2.2 to 4.4 mg/kg IV or orally every 12 to 24 hours, is an effective analgesic in cases of mild to moderate laminitis. Higher doses (6.6 mg/kg every 12 to 24 hours) can be required in severe cases. However, the potential for phenylbutazone toxicosis, evident as colic, gastrointestinal ulceration, nephrosis, hypoproteinemia, leukopenia, and hyponatremia, is dose related, and high doses of phenylbutazone should only be used for at most several days and only in horses experiencing severe pain. Flunixin meglumine (1.1 mg/ kg, IM or IV every 8 to 12 hours) or ketoprofen (2.2 mg/kg, IM every 12 to 24 hours) are also effective analgesics.**

Their concurrent use with phenylbutazone can enhance pain relief but also increases the risk of NSAID toxicosis.

A number of other NSAIDs are available for use in horses (meloxicam, firocoxib) and might be useful for management of pain in some horses.

The use of aspirin is dealt with under "Anticoagulants." Narcotic analgesics such as butorphanol, morphine, and meperidine (pethidine) provide effective pain relief; α-2 agonists such as xylazine and detomidine provide only brief

respite from the pain. Horses with severe lameness (Obel grade III or IV) might benefit from administration of drug cocktails including tramadol and subanesthetic doses of **ketamine (0.6 mg/kg per hour IV)** ,

administration of analgesics is preferred over unstructured assessment of pain.

Local analgesia of the foot with agents such as lidocaine or bupivacaine provides marked pain relief. However, analgesia is usually only brief, depending on the agent used, and has the disadvantage of causing the horse to bear more weight on the affected limbs. Local analgesia can be useful in facilitating relocation of the horse, hoof trimming, corrective shoeing, or application of sole and frog support, but not as a routine treatment. Lidocaine, administered intravenously as a constant-rate infusion, has been advocated as an antiinflammatory drug for the treatment of laminitis. However, evidence from the black-walnut model of laminitis does not indicate efficacy in reducing markers of inflammation.84 Because of suspicion that corticosteroids induce or exacerbate laminitis, at this time their use is contraindicated in the treatment of laminitis.

Vasodilatory Drugs

Vasodilatory drugs are used on the premise that vasoconstriction is an important mechanism underlying the development or progression of acute laminitis. Several classes of drugs have been used, including α-adrenergic antagonists such as **phenoxybenzamine and phentolamine**, drugs with multiple mechanisms of action such as **acepromazine and isoxsuprine**, and **nitric oxide donors** such as glyceryl trinitrate (nitroglycerine) and larginine. None of the vasodilatory drugs should be used in horses with compromised cardiovascular function or dehydration. **Phenoxybenzamine and phentolamine** are not readily available and

have limited use. **Phenoxybenzamine causes sedation. Acepromazine is a potent vasodilator,** VetBooks.ir Diseases of Bones 1403 principally because of its α-adrenergic antagonist activity, that is currently used occasionally in the treatment of acute laminitis. Acepromazine increases blood flow to the digit, but its effect on nutritive flow to the lamellae is unknown, as is the case for all the vasodilators. **The effect of Acepromazine persists for approximately 90 minutes after IV administration. Acepromazine can be administered at dose rates ranging from 0.01 to 0.05 mg/kg, IM, every 6 to 12 hours.**

Sedation may be considerable at the higher doses and/or with more frequent administration and might be a desired effect in reducing movement (and hence potential for further damage to lamellae) and anxiety. **Isoxsuprine is a combined α-antagonist and β-agonist that increases blood flow to the leg but not to the foot in normal horses. It has been used at doses of 1 to 1.5 mg/kg orally every 12 hours. Pentoxifylline (4.4 mg/kg orally q8h),** which increases red blood cell deformability, does not increase digital blood flow in normal horses.

Application of nitroglycerine a nitric oxide donor, to the palmar digital arteries of affected horses has been reported to increase or not affect blood flow to the dorsal hoof wall. However, the effect of these substances on the course of the disease is unknown. In spontaneous cases of acute laminitis, nitroglycerine has been applied to the skin over both palmar digital arteries of affected feet at a dose of 15 to 30 mg per artery, once daily. However, because of lack of evidence of efficacy and the potential for systemic hypotension secondary to systemic absorption of the drug, its use is no longer recommended.

Anticoagulants Anticoagulant drugs are administered to prevent the development of microthrombi within the hoof. Current evidence does not support an important role for microthrombi in the development of laminitis.

However, activated platelets do accumulate in lamellar vessels and release vasoactive compounds. Aspirin is a very poor analgesic in horses but is used because it reduces platelet aggregation in normal horses by blocking formation of thromboxane A2. However, thromboxane may not be an important cause of platelet aggregation in horses.

Aspirin is administered at a dose of 10 mg/kg orally every 48 hours. The efficacy of aspirin in the treatment of laminitis has not been determined.

Heparin in sufficient doses prolongs blood clotting, provided that there is adequate antithrombin III in the patient's blood. Heparin has been reported to **prevent or to have no effect on the development of laminitis in horses with anterior enteritis or colic, respectively. Heparin can be administered at 40 to 80 IU/kg IV or subcutaneously (SC) every 8 to 12 hours for 3 to 5 days**. Anemia can develop during heparin administration but resolves rapidly when administration of the drug is stopped. **Administration of low-molecular-weight heparin is proposed as prophylaxis for laminitis in horses at high risk of the disease.** This one study cannot be considered to provide proof of efficacy.

Mechanical Support XXXXXXXXXXXXXXX

Mechanical support to provide pain relief, minimize further damage to lamellae, and in an attempt to prevent rotation or distal displacement of the pedal bone is an important part of the care of horses with acute laminitis.

Support of the frog and/or sole can be achieved using packing material such as dental acrylic or firm plastic or silicone that is molded to conform to the shape of the sole. Some clinicians prefer to use wedge pads to elevate the heel and reduce tension in the deep digital flexor tendon, with the aim of preventing rotation of the distal phalanx by reducing "break-over" forces.

Trimming of the toe could achieve the same effect. Housing the horse on sand or other soft bedding is frequently recommended. Corrective shoeing of horses with chronic laminitis is widely practiced, and there are proponents of a wide variety of shoe types (fullered egg-bar, heart-bar, glue-on shoes). Appropriate hoof care, which might include shoeing, is important in managing horses with chronic laminitis. Interestingly, there was not a difference among shoe types in efficacy for pain relief in horses with chronic laminitis. Promotion of Healing Methionine has been given to both acute and chronic laminitis cases on the known requirement for methionine in the chondroitin complex of collagen. There is some rationale for the treatment, but it seems more appropriate as a supportive than as a principal treatment. The oral dose rate is 10 g/day for 3 days followed by 5 g/day for 10 days. Antibiotics might be indicated to treat secondary infection of the degenerate lamellae. Rest is important in the convalescent phase. Horses with no rotation or sinking of the pedal bone should be rested after resolution of the clinical signs. Return to work should be gradual. Horses that develop rotation or sinking of the pedal bone should be monitored both by physical examination and radiographic examination. It will be many months before horses with even mild rotation can be returned to work. Horses with severe rotation or sinking will likely never resume active work, although they may become pasture sound.

TREATMENT

Summary of treatment of acute laminitis Depending on the cause, treatment of acute laminitis should include:

- **Chilling of the limb (cryotherapy) (R-1)**
- **Administration of nonsteroidal antiinflammatory drugs (R-1)**

- **Administration of vasodilators (acepromazine) (R-2)**
- **Support of the frog and/or sole (R-1)**
- **Application of nitroglycerin (R-4)**
- **Aggressive treatment of the inciting disease (R-1)**
- **Trimming the hoof, distal phalanx realignment, and corrective shoeing (R-1**

Chronic Laminitis XXXXXXXXXXXXXXXXXXX

The prognosis for return to normal of horses with chronic or refractory laminitis (laminitis of more than 1 week's duration) is poor (see previous discussion for the use of radiography to determine prognosis). **Treatment includes NSAIDs** for pain relief, corrective shoeing (egg-bar or heartbar shoes), trimming of the hoof (shortening the toe or complete removal of the dorsal hoof wall), and realignment of the distal phalanx.88 Rehabilitating rotational displacement usually involves shoeing changes that move the center of pressure of the foot caudally from its normal position under the toes, decrease tension on the deep digital flexor tendon to reduce rotational forces on the distal phalanx that act to increase the distance between the distal phalanx and dorsal hoof wall, provide axial support of load structures within the perimeter of the wall (sole, frog, bars), and ease break-over in all directions (medial, lateral, and dorsally) in an effort to reduce distraction forces on the lamellae during movement. Methods to move the center of pressure caudally and decrease tension on the deep digital flexor tendon using bar shoes and a heel elevation are recommended.75 Use of a wedge to counteract rotational forces might be beneficial. Tenotomy of the deep digital flexor can provide relief, but the

efficacy of this procedure in affecting long-term outcome has not been well demonstrated.

CONTROL XXXXXXXXXXXXXXXXXXXXX

The disease is not readily subject to control because of its sporadic nature, with the exception of management of diseases that increase risk of laminitis, such as PPID, insulin resistance, and EMS.

■ Diseases of the Musculoskeletal System management of these conditions is provided elsewhere. Moderate exercise by nonobese ponies previously affected with laminitis reduced serum amyloid A concentrations and haptoglobin concentrations and led to reductions in exercise-induced increases in postexercise serum insulin concentrations.89 These results suggest a beneficial role for relatively lowintensity exercise (10 minutes enforced walking followed by 5 minutes of trotting) on inflammation in ponies at risk of laminitis.

LAMINITIS IN RUMINANTS AND SWINE

ETIOLOGY

Laminitis is caused by acute degeneration of the sensitive primary and secondary lamellae of the hoof. The cause of this degeneration is unknown, although the

disease can be induced by administration of oligofructose (17 g/kg, orally) to dairy heifers.

The disease is less well characterized than that of horses, and several conditions are often classified as laminitis. Laminitis in dairy cattle occurs as part of a spectrum of foot diseases.There is a detailed description of the radiographic (CT) anatomy of the digit of cattle.

EPIDEMIOLOGY

Occurrence

In cattle the disease can occur as clusters in herds and on farms where a predisposition appears to be inherited or where access to large quantities of soluble carbohydrate are available, such as for high-producing dairy cows or feedlot cattle. On farms of high producing dairy cattle the prevalence may be as high as 78%. The prevalence of laminitis related hoof lesions in Norwegian dairy cattle is 18%,6 although the prevalence is lower in Switzerland. Among Swiss cattle, 5.4% had signs of subclinical laminitis, and 3.3% had signs of chronic laminitis. A recent study of 1352 dairy cows in Israel detected lameness in 387 (28.6%).8 Of these lame cows, 320 (82.7%) had 591 lesions that could be associated with subclinical laminitis. Risk Factors Cattle and Sheep Subclinical laminitis that predisposes to the development of other diseases of the hoof occurs in calves and first-calf heifers and is common in intensively fed feedlot cattle. Laminitis, conditioned by the inheritance of an autosomal-recessive gene, is recorded in Jersey heifers. There may be an association between the disease in feedlot ruminants and ruminal acidosis. Administration of oligofructose to dairy heifers induced ruminal acidosis, with clinical signs of laminitis (hoof pain and abnormal gait) occurring by 30 hours

after administration and being most severe at 3 to 5 days. Beef cattle being prepared for shows are often grossly overfed on high-grain rations and become affected with a chronic form of the disease that markedly affects their gait and may cause permanent foot deformity. The disease occurs in dairy cattle fed improper rations, especially first-calf heifers and cattle of herds attempting to increase milk production, and it is not uncommon for the disease to present as a herd problem. Among dairy cattle, the heifers are usually the most affected, and the disease usually develops soon after calving, with more than 50% of cases occurring in the period 30 days before and 30 days after calving.

There may be a relationship between being introduced to the herd, with the frequent harassment by dominant cows, when heavily pregnant, and when the surface of the yards is rough. Housing can be important, including standing in slurry or having to twist and turn in narrow passageways and races, and there is an association between the prevalence of the disease and rough concrete floors. Diet is an important risk factor for development of laminitis in heifers. Diets of wet, fermented grass silage are associated with a greater risk of laminitis than are diets rich in dry unfermented straw and a concentrate. Furthermore, transition from a lownet-energy diet to a high-net-energy diet immediately after calving increases the risk of subclinical mastitis in Holstein dairy cows. The disease is also reported to occur after metritis, retained placenta, mastitis, and mammary edema, but the incidence is not usually very high. Pigs Laminitis has been recorded in pigs, but the disease is difficult to diagnose in this species, and many cases secondary to other diseases (e.g., postparturient fever) can be missed. The disease is also recorded when pigs are fed very heavy concentrate diets. Importance Subclinical laminitis of dairy cattle predisposes to other hoof disease that decrease milk production.

PATHOGENESIS

The pathogenesis of laminitis in cattle, sheep, and pigs is unclear but likely has some similarity to that in horses (see “Laminitis in Horses”), with increased expression of genes coding inflammatory or proinflammatory products in corium of cattle with induced laminitis. The links between nutrition and lameness in cattle have been reviewed. Chronic laminitis leads to a low resistance of claw horn to mechanical insults in the dorsal wall, abaxial wall, and sole,13 which could explain why laminitis predisposes cattle to other foot lesions.

CLINICAL FINDINGS

Cattle and Sheep In cattle and sheep the clinical picture is similar to but less marked than that observed in the horse. In calves 4 to 6 months of age, and in heifers, an acute syndrome similar to that seen in the horse has been described. Affected animals lie down much of the time and are reluctant to rise. When they attempt to rise, they remain kneeling for long periods. Their standing posture is with all four feet bunched together with the back arched; they shift their weight from foot to foot frequently and walk with a shuffling, painful gait. The feet are painful when squeezed and later become flattened and enlarged and look as though slippers are being worn. There is severe ventral rotation of the third phalanx. In adult cows some cases have acute signs, whereas others show only local lesions. These include sole ulcers and patchy changes in the horn, including softening, waxy yellow discoloration, and red–brown patches suggestive of previous hemorrhage. The cow is chronically lame. Young bulls are very susceptible to laminitis and may develop abnormalities of gait and posture, such as a stilted gait and frequent knuckling of the fetlocks, which may mislead the diagnostician. Chronic laminitis in adult cows is characterized by a smaller anterior hoof wall-sole angle, down from 55 degrees to 35 degrees, a concave anterior wall, and the

appearance of horizontal grooves (growth arrest lines) around the entire claw. The sole is usually dropped a little, and bruising and sole ulcers may be present. Overgrowth of the sole of the lateral claw may reach the point of creating a false or double sole. The white line is greatly widened and disrupted, and stones and other debris may be impacted in it. Chronic, traumatic laminitis is most common in heifers when they are first introduced into the milking or dry herds. Housing them on concrete and exposing them to frequent confrontations with bossy cows lead to the development of sole hemorrhages and inflammation of the laminae. Radiographic signs in cattle include rarefaction of the pedal bone, particularly the toe, and the development of osteophytes at the heel and on the pyramidal process. Pigs In sows the clinical signs are similar and include arching of the back, bunching of the feet, awkwardness of movement, increased pulsation in the digital arteries, and pain when pressure is applied to the feet.

CLINICAL PATHOLOGY XXXXXXX

There are no changes that are characteristic of the disease.

NECROPSY FINDINGS

Histologic examination of claws from heifers killed 72 hours after overload showed changes consistent with acute laminitis, including stretched lamellae, wider basal cells with low chromatin density, and a thick, wavy, and blurry appearance of the basement membrane.

TREATMENT

Although similar principles to those used to determine treatment of laminitis in horses are likely to apply to cattle, treatment in cattle is usually limited to administration of NSAIDs (aspirin 20 mg/kg, orally every 12 hours, phenylbutazone 4.4 mg/kg orally every 48 hours, or flunixin meglumine 1.0 mg/kg

IV every 12 hours). The inciting cause (metritis, ruminal acidosis) should be treated aggressively.

CONTROL XXXXXXXXXXXX

Cattle and lambs that are brought into feedlots should be gradually introduced to grain feeds and a higher forage : grain ratio provided in the feed. Calves should not be fed intensively on grain until they are 14 months old because of the high frequency of internal hoof lesions at the earlier ages. Some protection against laminitis in dairy cattle in intensive units is gained by careful planning of housing cubicles to make them more comfortable and less damaging to the feet and by providing more straw in the cubicles. Exercise should be provided around calving time. Vaccination with a gram-negative bacterinendotoxoid combination vaccine has provided some protection against laminitis induced by grain overload. Dietary supplementation of biotin (20 mg per head per day) improves hoof health of primiparous dairy cows and may be beneficial in reducing the incidence or severity of lameness in a herd. This treatment might not improve objective indicators of hoof health, but it does improve production. Selection of traits for foot and leg conformation in Norwegian Red cattle is not associated with a reduced risk of disease of the claws.