Laminitis is a severely debilitating, life-threatening disorder affecting the attachment between the epidermal and dermal tissues of the equine digit resulting in rotation or sinking of the distal phalanx in the hoof capsule. The development of laminitis in horses has been associated with many different conditions in the horse including sepsis/systemic inflammatory response syndrome (SIRS) occurring with many gastrointestinal disorders, pneumonia, metritis and grain overload and with endocrine diseases such as equine metabolic syndrome (EMS) and pituitary pars intermedia dysfunction (PPID). Acute laminitis can also be seen in horses secondary to mechanical overload due to severe contralateral lameness.1-4 While laminitis in the older horse can result from any of these predisposing conditions, the more common causes relate to endocrine dysfunction, particularly with conditions of EMS and PPID.

With many diverse conditions associated with the development of laminitis, the pathogenesis must be complex and although researchers have attempted to discover one unifying theory that will explain how this devastating disease occurs in the horse it has been increasingly clear that the numerous proposed mechanisms are likely interconnected with each other.5 Improving our understanding of the pathophysiologic mechanisms involved in the development of laminitis has resulted in improved preventions; however, the ability to treat these horses once clinical signs have appeared remains challenging for the equine practitioner.

Objectives:
1. To discuss clinical assessment of laminitis cases
2. To review conditions of EMS and PPID in the horse and discuss how to manage the condition
3. To discuss treatment and management of acute laminitis
4. To discuss the management of chronic cases of laminitis

Clinical Assessment of Laminitis in the Horse

Clinical history of horses presenting with laminitis can be variable, depending on the initiating cause. Horses with acute laminitis usually have either had a recent illness, recent non-weight bearing lameness, or recent changes in pasture grazing; however in some cases an initiating cause may be difficult to determine. Horses with chronic laminitis can present with an acute exacerbation of their chronic condition.

Clinical signs of laminitis include increased digital pulses, increased temperature of the affected hooves, weight shifting, lameness, reluctance to lift feet, and positive response to hoof tester applied to the toe region of the foot. The characteristic saw horse stance of a laminotic horse is described as the horse having increased weight placed on the hind limbs, with these limbs placed up under the horse and the forelimbs placed in front of the chest as if appearing to decrease the weight off the more commonly affected front feet. The severity of the lameness can be quite variable, but a stiff, short strided gait is often noted and appears worse when the horse is asked to turn. In horses with hind limb laminitis, the gait and stance will be different than when the front feet are alone are affected with the horse having an exaggerated lift of the hind limb and rapid return to stance in order to relieve pain in the opposite hind limb. It is not uncommon for horses to be reluctant to move and may even spend long periods of time in sternal or lateral recumbency. A grading system based off the severity of pain associated with laminitis was developed by Obel in 1948 (see table).
Changes to hoof shape or structure may occur gradually or rapidly depending on severity of laminitic episode. Horses with acute laminitis, having little to no rotation will have normal appearing hoof. As the third phalanx (P3) rotates, **prolapsing or bulging of the solar surface** may occur as the distal tip of the P3 points down and the distance between P3 and the solar surface decreases. Horses with severe acute laminitis that involve displacement of P3 (also known as **sinking**) will often have **bulging of the solar corium and cavitation of the coronary band**. In cases where complete laminar failure has occurred oozing of serum or blood from the coronary band can occur just prior to sloughing of the hoof capsule. Horses with chronic laminitis can have variable shape to the hoof, but is characteristically known to have a **dished appearance to the dorsal hoof surface** and **increased heel height**. **Horizontal growth rings** on the dorsal surface may be present indicating variation in growth between the heel and toe regions. The white line on the solar surface may be wider than normal and bruising of the solar surface can also be present.

Radiographs are essential when assessing the horse with signs of laminitis. Early in the course of disease there may be minimal to no change; however, radiographs taken at this time can serve as baselines when evaluation progression of disease. **Lateral (LM) and horizontal dorsal palmar (or plantar; DP) projections** are considered essential and the 60°dorsoproximal to palmar distal radiographs can have benefits in assessing the solar margin in chronic cases. Technique is very important when taking radiographs for laminitis. Regardless if only one foot is being evaluated, both feet must be placed on blocks of equal height.6 The x-ray beam for the LM view must perpendicular to the dorso-palmar plane of the foot and parallel alignment to the heel bulbs can be used to make sure there is no obliquity. The beam should also be centered a point between the toe and heels approximately 1.5-2 cm from the weight bearing surface.6 This should create superimposition of the medial and lateral wings of P3 and allow for accurate assessment of hoof balance, sole depth, dorsal hoof wall angle and palmar angles. Metallic or contrast agents for dorsal hoof wall markers are important to use in order to accurately determine the location of the coronary band and dorsal hoof wall. Markers that can control for variation in magnification can also be useful when performing measurements, particularly when comparing serial radiographs. The beam for horizontal DP radiographs should be centered in the sagittal plane approximately 1.5-2 cm proximal from the weight bearing surface.6 This view will allow for assessment of medial and lateral balance of the foot. Measurements are frequently made to serially assess laminitic patients and to help guide trimming recommendations. These include the following:

1) **Palmar angle (PA) of P3** (demonstrated by “A”) – typically should be 3-5 degrees in the normal horse; however variation is frequently noted. Horses with 0-negative angles will have increase stress from pull of the DDFT and it recommended by some veterinarians to increase the PA to 20 degrees to mechanically relieve the tension stress of the DDFT in at risk horses (as prevention for development of laminitis).
2) **Horn-lamellar zone width (HL zone)** (demonstrated by “B”) – should be equal distance proximal and distal. Typical measurements are 15-19 mm, but can vary from horse to horse.

3) **EP-CB distance** (demonstrated by “C”) – Used to determine displacement of P3 (sinker). Typical measurement is between 10-16 mm. Best evaluated on serial radiographs when determining if the horse has “sunk”. Consistent marking of the coronary band is important when measuring serially.

4) **Sole depth** (demonstrated by “D”) - Can be measured at toe or wing. Toe to ground is the most important measurement. Ideal measurement of solar depth is 15-20 mm. If the hoof has significant concavity then this must be taken in consideration when interpreting measurements. Decrease in solar depth can occur with rotation and sinking of P3. In the absence of rotation decrease in sole depth on serial radiographs would be highly suggestive of sinking. Additionally horses that continue to have shallow sole depths (i.e. have minimal sole growth) are likely to have continual pain particularly at the solar margin.

5) **Capsular Rotation** – Positioning is key when determining rotation and if oblique could increase measurement. Determination of degrees of rotation may have some benefit, particularly in the acute case. Cases with >11 degrees of rotation are considered moderate to severe and may have decrease in prognosis (however, this can be variable and should not be used alone in determining overall prognosis). Chronic cases often develop a lamellar wedge which can result in a large degree of rotation. Degrees of rotation can be measured by taking the angle of the dorsal hoof wall (δ) to the ground minus the dorsal aspect of P3 (ε) to the ground (δ – ε).

Other changes seen radiographically in chronic cases include remodeling or resorption of the distal tip of P3 and increased concavity of the dorsal hoof wall. **Venography**, which involves application of a distal limb tourniquet, injection of an iodinated contrast agent into the palmar/plantar digital vein, and acquisition of lateral and horizontal DP radiograph of P3, has also been used more recently in both acute and chronic cases to determine if adequate blood flow is present throughout the foot. Lack of contrast in certain areas of the foot can be suggestive of disease severity and serial venograms may be used to assess progression of disease and response to treatment.

Materials needed for performing venograms include the following:

1) Sedation (detomidine)
2) mepivacaine
3) 21 gauge butterfly catheter
4) 2 – 12 cc syringes
5) Contrast agent (Isovue-300; iopamidol)
6) Tourniquet
7) Elasticon
8) Hemostat

The procedure is performed as follows: Horse is sedated and an abaxial or low 4-pt block is performed. Horse’s feet are placed on radiographic blocks. A tourniquet is applied at the level of the fetlock. A 21 gauge butterfly catheter is placed in the palmar digital vein. 10 cc of contrast agent is administered steadily into the vein. An additional 10 cc of contrast is administered while the leg is unloaded by gently rocking the foot back and forth (just need carpus to flex slightly). The catheter is occluded with a hemostat and
taped to the fetlock joint with the butterfly catheter left in place (not removed from the vein). Lateral, horizontal DP and 60°DP views are taken with the limb loaded. These views are repeated with the limb non-loaded. An additional late weight bearing lateral view is taken before removing tourniquet. Occlusion of the vein with gauze and white tape before tourniquet removal will help prevent hematoma formation at the site. A bandage may be applied.

Proper technique is important for success. Problems can occur when the tourniquet is not appropriately applied (too loose will result in inadequate filling) and if the horse does not partially unload the limb (required to get adequate filling of lamellar tissues). If performed appropriately horses with abrupt loss of contrast at the terminal arch, circumflex area and lamellar vessels have a poor prognosis for recovery.

Equine Metabolic Disease and PPID

Endocrinopathic conditions associated with either obesity, insulin dysregulation (EMS), pituitary dysfunction (PPID), or glucocorticoid administration, has been increasingly found to have a significant role in the cause of laminitis. Equine Pituitary Pars Intermedia Dysfunction (PPID), also known as equine Cushings, is a well-known endocrine disorder in the horse. It is estimated that 15-30% of aged horses demonstrate signs (hair coat abnormalities) of PPID. One study, using plasma adrenocorticotropic (ACTH) or α-melanocyte-stimulating hormone (α-MSH) concentrations as a diagnostic test, 20% of aged horses were determined to be positive for PPID. Age is the largest risk factor for the development of PPID with recognition of clinical signs typically occurring between 18-20 years of age. However, younger horses can present with clinical signs as early as 8-10 years of age. Pony and Morgan horses appear to be over-represented in clinical case reports.

PPID, once thought to be a benign neoplasia, is now considered to be a neurodegenerative disorder. Hyperplasia of the pars intermedia by either a single adenoma or multiple small adenomas occurs with loss of dopaminergic inhibitory input to the melanotropes. The cause of pars intermedia degeneration is unknown, but loss of dopamine inhibition results in proliferation of melanotropes and increased production of POMC. POMC is further processed into adrenocorticotropic (ACTH) and melanocyte-stimulating hormone, in addition to other hormones, lipotropins and small peptides. Lack of dopaminergic inhibition also further increases ACTH production in melanotropes, through decreasing production of the ACTH cleavage enzyme.

Clinical signs of PPID include hirsutism, muscle atrophy, laminitis, polyuria/polydipsia, hyperhidrosis, abnormal fat distribution, insulin dysregulation, reproductive infertility, and neurological signs (ataxia, seizure, blindness). Not all horses with PPID will develop laminitis, but it is thought that horses with PPID that also have dysregulation of insulin will have a significantly increased risk to develop laminitis.

Equine metabolic disease is both an endocrine and metabolic disorder. Components of EMS include: increased adiposity, insulin resistance (IR) and hyperinsulinemia. Additionally, horses and ponies with EMS are predisposed to pasture associated laminitis. Both genetic and environmental factors are suspected to be involved in the etiology. Age onset is variable from 5-15 years old. Horses with insulin
dysregulation/EMS usually have a phenotype that includes increased fat deposits along the neck/nuchal ligament and rump areas.

The exact pathophysiology on how laminitis occurs with insulin resistance is unknown. Laminitis models for IR or insulin dysregulation include induction of hyperinsulinemia with normal glucose concentrations. This model reliability results in laminar damage and laminitis. Proposed mechanisms that may contribute to laminar failure include impaired glucose uptake of the laminar epithelial cells, insulin effects on vascular dysfunction, and obesity related inflammation.

Testing for PPID and EMS in horses:

Testing for PPID and EMS is not always straightforward and no gold standard tests exist. There are numerous types of test and variations in testing protocols for both PPID and EMS, and preferred testing type depends on clinician preference.

Test that can be used to diagnose PPID include:
- Dexamethasone suppression test
- Endogenous plasma ACTH or α-MSH concentrations
- TRH stimulation test
- Combined dexamethasone suppression and TRH stimulation test
- Domperidone response test
- Serum insulin concentration

Of these test the most common used includes measurement of endogenous ACTH concentrations and TRH stimulation test. Due to the perceived potential for glucocorticoids to cause laminitis, I am reluctant to use dexamethasone suppression test in horses at risk at developing laminitis or in horses that have had laminitis; therefore, I do not use this test in clinical cases.

Determination of endogenous ACTH concentrations is relatively easy, requiring a single blood draw. However there are some disadvantages to this diagnostic test including: sample handling issues and seasonal effects on test results. Endogenous ACTH concentrations can also be insensitive in horses with early onset of PPID. Evaluation of paired samples (taken 5 minutes apart) demonstrated no benefit in PPID diagnosis when compared to a single sample. ACTH in the horse is more stable than in humans or dogs, but samples should be carefully handled. Samples can be collected in glass but should be processed within 8 hours of collection. Samples collected plastic EDTA containing tubes can be stored upright for up to 12 hours before separation without resulting in a decrease in ACTH concentrations. After plasma has been separated it should be frozen until shipped to the diagnostic laboratory. Seasonal effects on endogenous ACTH concentrations have been well documented and ACTH is known to increase in autumn.
months (August-October). Therefore testing is recommended to be performed from late November through mid-June. If testing must be performed in the fall then cutoff values for ACTH concentration levels should be increased. Normal reference range will depend on laboratory’s method of testing and time of year (see Table 1 below). Stress, including pain and illness, can increase endogenous ACTH concentrations in horses and should be taken into consideration during interpretation of results if present.

**Thyrotropin-releasing hormone (TRH) stimulation** is a dynamic test that is considered to be safe and relatively quick to perform. *Administration of 1 mg of TRH intravenously will result in a 30-50% increase in serum cortisol concentrations within 30 minutes in horses with PPID.* Pre-TRH and 30 minute post-TRH administration serum samples are all that is necessary for collection. This test can result in false positive results however, and is believed to occur in 1 out of 3 test performed. Additionally pharmaceutical grade TRH is expensive and may be difficult to obtain. Compounding sources for TRH have made it easier for the veterinarian to use this test in practice.

**Fasting serum insulin concentration** is not a specific test for PPID; however, as many horses with PPID demonstrate insulin dysregulation and serum insulin concentrations have been shown to be predicative for the development of laminitis, it is recommended that serum insulin concentrations be monitored in patients with PPID. Horses should be fasted overnight for at least 8 hours prior to blood sampling. False positives and negatives can occur. Stress (including pain) and disease can increase insulin concentrations; therefore, evaluation of fasting serum insulin concentrations in sick or painful horses can be difficult. Normal concentrations will depend on laboratory and method of determination used.

Testing for EMS includes:
- **Fasting serum insulin concentration**
- **Oral sugar test (karo light corn syrup)**
- Infeed oral glucose challenge test
- Intravenous glucose tolerance test (IVGTT)

**Fasting serum insulin concentration** is considered a screening test for EMS. In addition to measuring insulin concentrations, it is also recommend to measure glucose concentrations as persisting hyperglycemia can also be a concern. However, glucose samples should be processed quickly as utilization by blood cells within the tube can decrease values quickly. Horses should be feed only one flake of hay the night before (no later than 10 o’clock) and are not fed in the AM until the test is completed. False positives and negatives can occur. Stress (including pain) and disease can increase insulin concentrations; therefore, evaluation of fasting serum insulin concentrations in sick or painful horses can be difficult. Normal concentrations will depend on laboratory and method of determination used, but horses with concentrations greater than 20 MU/L are considered to be hyperinsulinaemic. Glucose concentrations should be within the normal reference range.

**Oral sugar test (OST)** is frequently used as a dynamic test to improve the veterinarian’s ability to diagnose EMS cases when fasting serum insulin results are not conclusive. This test has been evaluated experimentally and can easily be performed in the field. **Corn syrup (karo light syrup)** is administered orally at a dosage of 0.15 ml/kg of body weight (approximately 75mls for a 500 kg horse) and a blood sample is collected 60-90 minutes post administration. Samples can be collected in a heparin (green top) or serum (red top) tube, kept cool after collection, and should be processed within 8 hours. Insulin concentrations should be less than 60 μg/mL and glucose should be less than 115 mg/ml. This is also thought to be safe to perform in horses with laminitis. An in-feed oral glucose challenge test (OGT) can be performed as an alternative. Dextrose powder is mixed into hay (nonglycemic feed) at 1 g/kg of body weight. Blood samples are collected 2 hours post feeding and insulin concentrations should be less than 85 μg/mL.
Table 1. Normal reference range:

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Normal reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endogenous ACTH</td>
<td>ACTH &lt;35 pg/ml (Nov-July)</td>
</tr>
<tr>
<td></td>
<td>ACTH &lt;50 pg/ml (Aug-Oct)</td>
</tr>
<tr>
<td>TRH Stimulation Test</td>
<td>&lt;30-50% increase in serum cortisol 30 min post TRH administration</td>
</tr>
<tr>
<td></td>
<td>ACTH &lt;35 pg/ml</td>
</tr>
<tr>
<td>Fasting serum insulin</td>
<td>&lt;20 mU/L</td>
</tr>
<tr>
<td>Oral sugar test</td>
<td>Glucose &lt;115 mg/mL</td>
</tr>
<tr>
<td></td>
<td>Insulin &lt;60 μg/mL</td>
</tr>
<tr>
<td>In-feed oral glucose challenge</td>
<td>Insulin &lt;85 μg/mL</td>
</tr>
</tbody>
</table>

Management of the EMS/pasture associated laminitic horse:

Principle management of the EMS horse involves 2 things 1) induction of weight loss and 2) improve insulin regulation through dietary management. A recent study by Morgan et al\textsuperscript{16} clinically evaluated an individualized dietary/exercise program for weight loss and improved insulin sensitivity in 19 cases. They were able to significantly decrease body weight, body condition score, basal insulin concentrations and glucose/insulin concentrations after an IV glucose tolerance test through dietary and exercise management alone. Veterinary education to clients in regards to weighing of horses and body condition scoring was considered important as well as the strict dietary/exercise plans individualized for each horse and follow-up veterinary evaluations.\textsuperscript{16}

Recommend weight reduction diets include elimination of grain and pasture and gradual decrease in hay feeding (Table 2). An example of hay allotment for weight loss is demonstrated in the table below. Initial feeding for the first 1-2 weeks is at 1.5% of the horse’s current body weight. At the 2\textsuperscript{nd} week hay feeding at 1.5% of the horse’s ideal body weight per day is recommend. At 6 weeks if further weight loss is needed then the recommended hay feed is dropped to 1% of the horse’s ideal body weight, which is the minimum amount of hay recommend per day.\textsuperscript{17}

**TABLE 2.** Recommend hay intake to induce weight loss.

<table>
<thead>
<tr>
<th>WEEKS</th>
<th>% of BW</th>
<th>BW (lbs)</th>
<th>Lbs of hay</th>
<th># of flakes hay*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>1.5%</td>
<td>1,200 lbs Current BW</td>
<td>18 lbs</td>
<td>6 flakes/day</td>
</tr>
<tr>
<td>2-6</td>
<td>1.5%</td>
<td>1,000 lbs Ideal BW</td>
<td>15 lbs</td>
<td>5 flakes/day</td>
</tr>
<tr>
<td>&gt;6</td>
<td>1.0%</td>
<td>1,000 lbs Ideal BW</td>
<td>10 lbs</td>
<td>3 flakes/day</td>
</tr>
</tbody>
</table>

*1 flake of hay = 3 lbs

Hay analysis is also recommended for these horses. Of the components measured (Table 3) the amount of non-structural carbohydrates (NSC) is considered most important. NSC of 10\% (dry matter basis) or less is recommended for insulin resistant horses, particularly with those that have high resting insulin values or that have been historically difficult to manage in regards to their insulin sensitivity.\textsuperscript{17} Hay with low NSC will also be less digestible and therefore assist with weight loss. In addition to hay analysis, an accurate and thorough evaluation of the horse’s overall diet is necessary. This should include type, frequency, quality and quantity of any grain, supplements, and pasture the horse is feed. Setting goals for weight loss and assessment on a bi-weekly to monthly basis of body weight, body condition score and mean neck circumference is recommend to adjust nutritional plan as needed. It is also recommend that horses do not go for long periods without eating as this can result in dramatic...
shifts in insulin concentrations; therefore meals should be spread out over a 24-hour period. Hay nets with small openings or grazing muzzles can be used to help prolong feeding time when limited intake is required for weight loss. Treats, such as carrots and apples, should be minimized if not eliminated as they contain large amounts of sugars and starch. Grains (oats, barley, and corn) and sweet feeds are not recommended as they are rich in starches and sugars with NSC content in some grains approaching 30-40%.

Table 3. Hay analysis

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Starch</strong></td>
<td>Polysaccharide</td>
</tr>
<tr>
<td><strong>ESC</strong></td>
<td>Ethanol-soluble carbohydrates including primarily simple sugars (mono- and di-saccharides)</td>
</tr>
<tr>
<td><strong>WSC</strong></td>
<td>Water soluble carbohydrates includes mono- and di-saccharides (ESC) and some polysaccharides (mostly Fructans)</td>
</tr>
<tr>
<td><strong>NSC</strong></td>
<td>Non-structural carbohydrates which are calculated by taking the sum of the WSC and the starch</td>
</tr>
</tbody>
</table>

* from [www.equi-analytical.com](http://www.equi-analytical.com)

Increasing the horse’s exercise will promote weight loss through increased energy expenditures. However, this can be very difficult to achieve in the laminitic horse, and is contraindicated in horses undergoing an acute episode/flare. If exercise is possible up to 30 minutes of trotting and/or cantering 4-7 times a day is recommend. An alternative for horses with chronic laminitis and mild clinical lameness is pasture turnout with a pasture mate that will encourage movement without being too excessive in exercise (i.e. no young horse that will chase the affected horse around!).

Additional therapy to help improve weight loss in horses that may not be able to exercise or where exercise and diet control is not enough is the use of exogenous thyroid hormone supplement. *Levothyroxine sodium* (Thyro L™) has been reported to result in weight loss and increased insulin sensitivity in healthy horses. Recommended treatment dosage to accelerate weight loss is 0.1 mg/kg of body weight q24h (48mg/horse/day which equals 4 teaspoons of Thyro L). If weight loss is not achieved then you can increase the dose to 72 mg/horse/day. Higher dosages can have effects on the heart and are typically avoided if possible. Typically treatment is removed once the horse achieves the desired body condition; however some veterinarians will continue to treat horses at lower dosages. Weaning off the thyroid supplement is necessary and usually achieved by decreasing the dose by half for a period of 2 weeks followed by additional decrease to 12 mg/day where it then can be discontinued.

Other dietary/supplements that have been proposed to have the potential to improve insulin sensitivity include: chromium, magnesium and omega 3-fatty acids. These supplements have demonstrated varying degrees of benefits to insulin sensitivity in man. *Chromium* has been evaluated in both normal and obese laminitic horses experimentally and has not been found to alter insulin concentrations in either study. *Magnesium* has also been evaluated in obese laminitic horses but was not able to significantly decrease resting insulin concentrations. Another oral supplement made by Equithrive® called Metabarol™ has been discussed as a supplement with potential benefits to horses with EMS. The active ingredient is resverasyn which is microencapsulated resveratrol. *Resveratrol* is a stilbenoid compound believed to have antioxidant and anti-inflammatory actions. In one study of 15
horses, Metabarol, significantly decreased resting leptin concentrations and insulin concentrations after an oral sugar test (OST).21

In EMS horses that do not exhibit the typical obese phenotype or those where weight loss has been achieved but continue to have insulin dysfunction increasing the amount of hay or adding low-NSC pelleted feed into the horses diet can help to increase caloric intake. Metformin can also be used in the lean horse that remains hyperinsulenic. The exact mechanism of action of metformin is unknown, but it will result in decreases in insulin and glucose concentrations in the horse22 which suspected to occur through improve glucose utilization. Metformin was also able to reduce the glycemic and insulinemic responses in horses with experimentally induced insulin resistance to an oral dextrose challenge.23 The current recommended dosage is 30 mg/kg PO q12h.

Pituitary pars intermedia dysfunction (PPID) is frequently present in older horses with EMS. The insulin resistance that occurs with PPID can further exacerbate hyperinsulinemia by slowing insulin clearance. Treatment with pergolide is recommended. The dose of pergolide is 2-4 µg/kg PO q24h with current recommended treatment of Prascend® starting at 1 mg tablet / adult horse (est 450-500kg; Table 4). Dosages should be titrated to individual response and administered at the lowest effective dose. If no improvement in clinical signs are noted and/or if ACTH concentrations do not significantly decrease (ideally <35 pg/ml) then you may increase up to 2 mg tablet PO/day (some horses may need up to 3 mg/day but increased occurrence of side effects may be noted and include decrease appetite, diarrhea, colic and lethargy). If horses treated with maximal dosage of Pergolide (3-5 mg/day) are not responding then combination therapy with Cyproheptadine can be used.10 Cyproheptadine is added at 0.25 mg/kg PO q12h.10 Cyproheptadine is a serotonin antagonist but its mechanism of action in the treatment of PPID is unknown.

<table>
<thead>
<tr>
<th>Table 4. Prascend® Dosing Table</th>
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<tbody>
<tr>
<td><strong>Dosage</strong></td>
</tr>
<tr>
<td><strong>Body weight</strong></td>
</tr>
<tr>
<td>136 - 340 kg (300 - 749 lb)</td>
</tr>
<tr>
<td>341 - 568 kg (750 - 1,249 lb)</td>
</tr>
<tr>
<td>569 - 795 kg (1,250 - 1,749 lb)</td>
</tr>
<tr>
<td>796 - 1,022 kg (1,750 - 2,249 lb)</td>
</tr>
</tbody>
</table>

Pasture/grazing management is also essential in EMS horses. While complete removal from pasture may be indicated for weight loss or in the difficult to control hyperinsulinemic horse, some grazing may be tolerated by others. The overall goal is to limit the amount of non-structural carbohydrates the horse consumes. Recommendation for pasture grazing includes:

1) Limit grazing during the spring and early summer months. This is rapid growth time and has the highest productions of fructans during this time. This can also occur any time of the year when increase rain occurs after a drought period.
2) Do not allow horses to graze midday. Early morning and late evening is best. Highest sun allows for greatest photosynthesis resulting in increased production of NSC/fructans. Grazing in shady areas will also decrease photosynthesis and thereby NSC.

3) Do not allow grazing on “flowing grass”, those that are actively producing seed heads as they can be quite high in fructans. Mature seed head or dry grass is more likely to have low NSC/fructan levels.

4) Avoid overgrazing pastures. Short grass will have more access to light and therefore increase in NSC.

5) Grazing is better on native grasses vs. improved varieties as they have been selected for increased growth and therefore have higher NSC contents.

6) Grazing muzzles can be used to limit overall intake in aggressive eaters otherwise limited time and gradual introduction is recommend to limit the amount of NSC consumed.

7) If managed well laminitis should not be a problem, however, move horses off pasture at the first sign of lameness and keep them off pasture for at least 3-4 weeks if not for the remainder of the season.

Management of Acute and Chronic Laminitis (in addition to EMS and PPID management techniques)

As the overall pathogenesis of laminitis remains to be elucidated, so does the magic silver bullet that will stop the development of this devastating disease. Preventative therapies currently in use by veterinarians include treatment of the primary disease, anti-endotoxic therapies, anti-inflammatories, anti-oxidants, cyrotherapy, analgesics, vasodilators, anti-thrombotics, and mechanical support. Although early intervention is essential in preventing or limiting laminar damage, even the most aggressive protocol is sometimes not enough or is initiated too late to prevent significant laminar damage and subsequent failure. Many horses have primary conditions, such as EMS or PPID, that keep them at risk of having recurring episodes. These horses require both systemic management of their primary condition (EMS and PPID - described above) and mechanical management of the foot.

Anti-inflammatories: Inflammation is known to be present in the lamina from horses with both experimental and naturally occurring laminitis; therefore it is only logical that anti-inflammatories are used in the treatment and prevention of laminitis. NSAIDs by far are the most common therapies used in the treatment and prevention of laminitis. In an epidemiological study of laminitis by Slater et al., it was reported that 68% of cases were treated with phenylbutazone and 19% of cases with flunixin meglumine. Typical doses for phenylbutazone range between 2.2 mg/kg and 4.4 mg/kg administered once or twice a day and doses for flunixin meglumine ranging from 0.25 mg/kg IV q8h to 1.1 mg/kg IV q12h. Both of these NSAIDs are COX-1 and COX-2 inhibitors and therefore have the possibilities of resulting in side effects often associated with COX-1 inhibition, including gastrointestinal ulceration and renal papillary necrosis, particularly when higher doses are utilized. Recent development of an equine COX-2 specific NSAID firocoxib would suggest that its use would have increased benefits over the traditional NSAIDs by having decreased gastrointestinal side effects while still being able to limit the up-regulation of COX-2 in the lamina reported with laminitis. However, with the negative cardiovascular effects associated with the use of COX-2 specific inhibitors in humans there is some question of their use in horses early in the developmental stages of laminitis. It is unknown what affects firocoxib has on the balance of thromboxane-A2 and prostacyclin at the level of the laminar vessels, but a shift in the balance could possibly result in pro-coagulatative state. Despite that numerous veterinarians use firocoxib in both acute and chronic cases of laminitis for both its anti-inflammatory and pain relieving effects. Reported dosages 0.1 mg/kg PO q24h or 0.09 mg/kg IV q24h. It is recommend by Merial to providing a loading dose that is 3x the recommended amount (0.27 mg/kg IV) to shorten the period of time needed to reach therapeutic concentration.

The use of antioxidants in horses with laminitis, such DMSO has been used by some veterinarians for many years. DMSO has been used as an anti-inflammatory and free radical scavenger at 100 mg/kg of BW IV q12h diluted to a 10% solution. One retrospective study found that DMSO was used in 27% of laminitic cases, despite that no controlled studies have been reported to show definitive benefits of this therapy. The lack of benefit may due that little evidence of oxidant stress has been found during the developmental phases of laminitis.
**Cryotherapy:** Digital hypothermia, also known as cryotherapy, has been used to ameliorate experimentally induced laminitis when applied during the developmental period. Continuous cryotherapy has been found experimentally to significantly reduce the up-regulation of degrading enzyme MMP-2 and reduce the expression of proinflammatory chemokines and cytokines in the early stages of laminitis after oligofructose administration. Suggested protocol for cryotherapy of the equine digit requires maintenance of hoof temperatures of around 5°C via submergence in an ice-water boot until the resolution of the primary disease. I use cryotherapy in acute cases of laminitis and chronic cases that are having an acute episode. Initial studies involved the use of modified wader-style boot that includes immersion of the limb from the upper metacarpus down to the digit allowing for direct cooling of the hoof as well as cooling of the blood prior to entering the foot. Other methods of cooling the foot have been evaluated for temperature maintenance but have not been evaluated for their effectiveness in preventing laminitis. Clinically I have use an empty 5 liter fluid bag, placed on the foot and then filled with ice and taped around the pastern and have found this to be a relatively simple method which has been found to achieve hoof temperatures close to that of previous reports; however, it does not cool the blood in the metacarpal region and does require replenishment of ice at relatively frequent intervals. Soft ride now also makes ice boots with soft inserts that allow for the foot and distal limb to be bathed in ice and allows for relatively easy ice replacement.

**Pain management:** Pain control is an essential component in managing laminitis and in the prevention of the development of support limb laminitis secondary to non-weight bearing lameness. Previous discussion of the use NSAID medications is also important for pain management in these cases. **Phenylbutazone**, by far is the most common of the NSAIDs used but both **flunixin meglumine** and **firocoxib** have benefits as well. **Gabapentin**, a GABA analogue, has been used as a treatment for neuropathic pain in humans and horses. Initially reported to have success in a horse with post-anesthetic femoral neuropathy at a dosage of 2.5 mg/kg PO q12h, later studies have found this drug to be poorly bioavailable and dosages of up to 20 mg/kg IV or PO were found to have no detrimental effects in the horse. Although it is difficult to determine how successful this medication is for the management of laminitic pain, I will combine this drug with NSAIDs and dose it at 20 mg/kg q8h.

The use of **lidocaine** as CRI, although difficult to monitor in non-hospitalized patients, anecdotally has helped manage pain in more severe laminitic cases. Other effects of lidocaine that were initially thought to have benefit in laminitis, such as decrease in neutrophil migration has been since disproven; however, administration of a loading dose (1.3 mg/kg administered over 5-15 minutes) followed by a CRI (0.05 mg/kg/minute) has been used for pain control. Since lidocaine is strongly protein bound, horses with low protein concentrations may need to have their dosages decreased as side effects such ataxia may be more profound at normal dosages. To further take advantage of a multimodal approach to pain management, I have combined the use of lidocaine with morphine and ketamine in a CRI and have found a positive response in several very painful patients. However, the use of this combination requires administration via a fluid pump and close monitoring and therefore not useful in on the farm settings.

Systemic administration of opioids has been used for the management of pain in the horse. **Butorophanol** although readily available to most veterinarians, is not as potent as other opioids and in my opinion is best reserved for visceral pain management. **Morphine** (0.05 – 0.1 mg/kg IM q24h) used systemically does provide analgesia to the horse however, side effects are not uncommonly seen with systemic use and include excitement, agitation, disorientation, ataxia, ileus, constipation and colic. The addition of acepromazine (0.04 mg/kg) or detomidine have been used to decrease the excitement/agitation side effects seen with opioid use. For horses having significant hindlimb pain epidural administration of pain medications has had significant benefits. Combination of morphine (0.2 mg/kg) and detomidine (30 μg/kg) q24h will give pain relief in many patients and help decrease the risk of systemic use of morphine. **Transdermal fentanyl** has been reported to decrease pain scores in patients but demonstrated
minimal improvement in lameness in horses with orthopedic pain\textsuperscript{44} and anecdotally has variable effects on pain relief in laminitic patients.

**Vascular therapies:** Vascular alterations such as the production of vasoconstrictor agents such as serotonin, thromboxane A2 and endothelin-1, and the presence of vasoconstriction (particularly venoconstriction) early in the developmental phases have been reported in horses with laminitis; therefore the incorporation of vasodilators into therapeutic regimes is not unreasonable. Vasodilators that have been used in the treatment of laminitis in the horse include **isoxsuprine**, **nitroglycerine**, **acepromazine**, and **pentoxifylline**. **Isoxsuprine** (0.6-4 mg/kg PO q12h) has reported α-adrenergic antagonist effects as well as β-adrenergic agonist effects that should result vasodilatation; however, oral administration has not been reported to produce any change in digital blood flow.\textsuperscript{30} **Nitroglycerine**, a nitric oxide donor, is known to be a potent venodilator yet the use of a transdermal patch demonstrated no change in digital blood flow and is currently not being used for the treatment/prevention of laminitis.\textsuperscript{45} **Acepromazine** (0.04 mg/kg IM q6h), a phenothiazine tranquilizer, cause peripheral vasodilation thorough its α-adrenergic blockade and is one of the only used vasodilators that have been shown to increase digital blood flow in the horse.\textsuperscript{30,46} However, the duration of increased blood flow is variable from horse to horse, and the use of acepromazine is contraindicated in the sepsis/SIRS patient due to its profound hypotensive effects. Currently, I do not use acepromazine in combination with cryotherapy as I feel the mechanisms contradict the use of both therapies at the same time. I will use acepromazine to help “take the edge” off a horse that is anxious in thoughts that it will help decrease the cortisol response.

**Pentoxifylline** (8.5-10 mg/kg PO q12h), a non-selective phosphodiesterase inhibitor and rheologic agent, is believed to help improve the flow of blood through capillaries by increasing the deformability of the red blood cell membrane; however, an increase in blood flow has not been demonstrated in the horse.\textsuperscript{30} Lower dosages than currently recommend were used in the initial studies and improved perfusion may not be demonstrated by altered digital blood flow. Additionally, pentoxifylline likely has benefits in the treatment/prevention of laminitis through other mechanisms, including anti-inflammatory (decreasing TNFα and IL-1β and neutrophil activation), anti-fibrotic, and via MMP inhibition.\textsuperscript{47} It has been demonstrated (Fugler and Eades, personal communication) to have clinical benefit in a CHO model of laminitis and inhibit MMPs during endotoxemia; therefore it is one therapy that I currently include in the prevention and early treatment of acute laminitis. This treatment can be used in acute and chronic cases of laminitis.

In addition to the vasoconstrictive events reported to occur in the developmental phases of laminitis, microthrombosis of the laminar capillaries and platelet aggregation also occurs and treatments aimed at these effects have been utilized by veterinarians.\textsuperscript{3,48,49} To help prevent formation of thrombi anticoagulants such as **aspirin** (10-20 mg/kg PO q48h) which inhibits platelet aggregation and **heparin** (40-80 IU/kg IV or SQ q8h) which down regulates the prothrombotic state have been used. Reports of their success of preventing laminitis in horses have been variable.\textsuperscript{33,34}

**Management mechanical stress in the laminitic horse:**

Minimizing mechanical stresses is a very important factor in prevention and treatment of laminitis. Minimal to NO exercise/walking during the acute phase is strongly recommended.\textsuperscript{50} Any drastic changes and application of shoes should be avoided during the acute stages, and I typically wait 3-4 weeks before applying shoes to the horse’s feet. However, if the toe is exceptionally long it should be trimmed. Prevention of laminitis from a mechanical standpoint is aimed towards attempting to neutralize forces on the digit and include placing frog support and/or bedding the horse on deep soft footing (such as sand) to minimize compressive forces on the digital cushion and decrease the tensile forces of the DDFT. Recommendations for frog/sole/foot support in regards to what type of pad to use is variable and are dependent upon clinician
preference. Some suggest that the entire sole is packed or padded to allow for equal weight bearing throughout the foot and oppose mechanical forces down the leg. Others will recommend that at least the frog is cushioned/support. Some horses may not tolerate packing in the sole, particularly if rotation has already occurred. Placement of a cast or putting the horse in a sling to decrease weight bearing loads through the digit may also have beneficial effects. It is also recommended to consider placement of a heel wedge to decrease tensile forces of the DDFT.²

Placement of shoes after the acute phase of laminitis has subsided can be tricky. Each horse is different and some may not tolerate shoes or foot support that other horses may do quite well in. Placement of a heal wedge shoe or a Redden shoe that can be taped on may help decrease the pull of the DDFT and make the horse more comfortable. However, other horses may get worse with this shoe placement and may do better in sole support system that eases the breakover in all directions like the Wooden clog shoe. **Shoeing horses with chronic laminitis involves realignment of P3 in the hoof capsule.** This may involve trimming the foot to help derotate or rebalancing the medial or lateral sinker. Several principles should be adhered to when trimming or shoeing the laminitic foot and include:

1. **Realign the phalangeal axis by trimming**
2. **Preserve the thickness of the sole** (do not trim sole if less than 15 mm deep, just remove toe and heel)
3. **Recruit weight-bearing forces by the ground surface of the foot**
4. **Move the breakover in a palmar/plantar direction**
5. **Reduce the tension of the DDFT**

Shoe type will vary depending on veterinarian/farrier preference and some horses will do better in than others in the same shoe. Heart-bar shoes (with firm metal frog support) are a classic shoe that is used by some farriers/veterinarians. It is important that if this shoe is used that tip of the frog plate does not have any contact with the sole. Natural balance shoes that help ease breakover and used with frog support to increase the weight bearing forces towards the palmar/plantar aspect of the foot may also be used in some cases. Reverse shoes where the toe of the shoe is placed over the heels and the toe is left open, may be used by some farriers/veterinarians to remove loading of the dorsal lamina; however, an appropriate trim is necessary if these shoes are to be used (i.e. toe cannot be too long etc.). Rocker shoes are also helpful in chronic laminitic cases but require specific trimming for correct placement of these shoes. Rockers will move the breakover back toward the center of rotation of the foot. Additionally, when performing the trim for the rocker shoe you will decrease your palmar angle (PA) ideally to zero by trimming off the heel. The placement of the rocker shoe after the trim, therefore allows you to decrease your PA without increasing DDFT tension.
Through the biomechanical adjustments made with the trim and placement of this shoe, improved blood flow which encourages hoof growth has been anecdotally reported. It has been noted that horses wearing this type of shoe will often have significant solar growth over a 6-12 weeks period.

Horses should be radiographic at each shoeing change (which should be done every 6 weeks) to assess the foot and make the necessary corrections to realign P3 within the hoof capsule. Several shoeings are usually necessary in more advance cases before realignment may occur. Horses with chronic laminitis are also prone to the development of hoof abscess and should be treated appropriately when they occur to prevent problems in the supporting limb, which likely is already affected with laminitis.

In horses that continue to rotate or become refractory to all other therapy a deep digital flexor tenotomy can be performed to help remove the mechanical pull from the DDFT. This treatment; however, typically saved for more severe cases with significant rotation due to the negative effects of cutting the deep digital flexor tendon. Tenotomies are most successful in cases where there is no significant bone pathology in P3 and no sinking, but rotation only. Complications associated with the procedure include infection, dehiscence, contraction/fibrosis of the tenotomy site before correction of rotation possibly requiring repeat procedure in the pastern region, and subluxation of the DIP joint resulting in arthritis of that joint. Additionally horses that receive a DDF tenotomy require specialize shoeing (tenotomy shoe that has an extended heel that prevents the toe from flipping up during weight bearing) and are often not able to be used athletically (pasture soundness or light riding only) even if laminitic changes are reversed.

**Prognosis**

An accurate prognosis during acute laminitis often cannot be given. Laminitis is a life threatening disease and initial prognosis should always be guarded, regardless of severity when first noted. Laminar changes occur throughout the disease process and it may take several weeks before an accurate assessment of damage can be made. Owners should understand laminitis is a frustrating disease to treat. Horses will be at risk for relapse and the disease must constantly be managed, often by expensive shoeing. The amount of rotation of the distal phalanx has been found to be a fair prognostic indicator. In a retrospective study, those horses with less than 5.5 degrees of rotation returned to former athletic function, whereas those with greater than 11.5 degrees of rotation did not return to performance. However, another retrospective study did not support these findings but instead found that prognosis correlated to better to Obel grade. Distal displacement of coffin bone does carry a significantly increased poor prognosis. Despite these reports, if the owner will allow, I typically like to give the horse at least 3-4 weeks of acute therapy/management and depending on severity of radiographic and clinical changes several shoeings before determining the overall prognosis. It is essential that cases with EMS and PPID be closely managed and frequently assessed to prevent further exacerbation of laminitis from occurring. Cases of chronic laminitis with rotation and uncontrollable metabolic disease can be frustrating for both owner and veterinarian and challenging to treat.

**References**


