

## Insulin Resistance, Equine Metabolic Syndrome, Cushing's and Cushingoid

To see what IR, or EMS looks like: [go here](#)

Equines that have laminitis are frequently found to be insulin resistant or hyperinsulinemic. ([Field abstract](#)) Glucose may be normal, but insulin levels are high. I agree with some researchers that IR as a stand alone condition may not be a pathology, but a genetic predisposition as part of natural selection to enable an equine to make most of the poor quality forage common to the environment in which it evolved. This may be more about inappropriate diet than disease.

New research has shown that insulin causes laminitis directly, although the mechanism is not understood. [Asplin abstract](#) This new study should make you and your vet realize just how important diet is to horses with laminitis.

Insulin resistance and high blood glucose levels create inflammation and vasospasm in vascular tissue, which is likely involved in laminitis associated with impaired glucose metabolism. ([Johnson abstract](#)) ([Eades pdf link](#)) Many have found that by minimizing the NSC in the diet, as part of a holistic management program including exercise, addressing mineral deficiencies, and proper hoof care, their insulin resistant horses can be kept free of clinical symptoms. Any horse that has been diagnosed as insulin resistant should be monitored for development of Cushing's disease. Baseline ACTH is the preferred method, as it does not carry the risk of causing laminitis which happens occasionally with the Dexamethasone Suppression Test. I use Cornell, which has a test for ACTH/insulin for \$33. Special handling is required. See Favorite Links page for link to the Cornell Veterinary Diagnostic lab website.

The preferred drug for treatment of Cushing's is pergolide ([Donaldson abstract](#)), AKA pergolide mesylate (brand name Permax) previously used for treatment of Parkinson's disease in humans. Many veterinary compounding pharmacies now carry very cost effective formulations of this drug, although question your pharmacy on it's quality control testing procedures for concentration and stability. As testing for IR and Cushing's might be too inconvenient and expensive for some owners, some veterinarians are treating refractory laminitis with pergolide without testing, assuming a positive response to the drug as a positive diagnosis. No studies have been done on the affects of pergolide on healthy horses. Please note that researchers now agree that not all Cushing's horses have the long, non-shedding coat. Depending on what portion of the pituitary is diseased, different hormonal systems may be involved. Not all horses with insulin resistance have Cushing's, ([Reeves abstract](#)) and not all Cushing's horses are insulin resistant, although there is high risk for it to develop eventually as more of the pituitary becomes affected over time. Confounding this further is the fact that there are no absolutely infallible tests for Cushing's, and it's often difficult to tell if you have just an IR horse, or one with early stage Cushing's that doesn't show up yet in the tests. In a study at Michigan State, horses responded well to pergolide even in the absence of a positive Cushing's test. ([PDF link](#)) I was convinced my older mare was just IR for the first few years, but her test results have slowly changed over the years to where I'm pretty convinced she has Cushing's, or something that is very similar. Researchers are having difficulty defining what this 'non- traditional Cushing's syndrome' is exactly. The practice of science and magic require that to have power over something we must know it's true name. The invention of new acronyms to describe this condition seems fashionable, and shows that veterinary science cannot agree about the true nature of this disease. I'll add one to the growing list. My horses have PREL. Pergolide Responsive Endocrinopathic Laminitis. My older mare remained sound on 1 mg/day of pergolide for a couple years, needed 1.5 mg/day at age 19, and after a mid-winter relapse at age 20, only responded after dosage was increased to 4 mg/day. Once stabilized, she has done well the last couple years on 2 mg/day.

Pergolide interferes with insulin production, and may therefore lower insulin levels, regardless if it is caused by a pituitary dysfunction, or just a diet that includes excess carbs. ([Arneric abstract](#)) However, I fear that pergolide is often being prescribed without first fixing the diet, which must include minimizing NSC in forage. Too often we find it easier to take a pill to alleviate symptoms, instead of addressing the CAUSE for those symptoms. It's analogous to taking pills to control cholesterol, but still eating at McDonalds every day. Due to expense and unknown consequence of long term use, it is probably best to minimize the dose needed to keep the affected horse free from laminitis. On the other hand, I can find no real data to suggest that pergolide use should be avoided when indicated. When it works, it works very well to end laminitis and make the horse feel a lot better.

Dopamine acts as a signaling agent in the pituitary, turning metabolic pathways on or off as needed. Dr. Phillip Johnson has put forth a theory that long term uncontrolled insulin resistance creates excess oxidative stress which in turn may cause a loss of dopaminergic innervation of the pituitary. In very simplistic terms, high levels of sugar and starch overloads the metabolism that was never designed to deal with it, and the consequences are a damaged pituitary. This would create a situation where pergolide, a dopamine agonist (which means "activator") might reactivate the pathways that had shut down due to loss of dopamine signaling. Dr. Johnson calls this condition Equine Metabolic Syndrome. This is a very controversial theory, and very hard to prove. An article that discusses increased markers for oxidative stress in Cushing's horses is found at

<http://www.ivis.org/proceedings/AAEP/2003/mcfarlane/ivis.pdf> The relationship between insulin resistance and Equine Cushing's disease and EMS is extremely complicated and hopefully more research will help us sort it out.

This suggests that horses with insulin resistance might benefit from higher amounts of anti-oxidant vitamins and minerals, although this research has not been conducted yet. This may be a difficult concept to prove, but in the meantime, I shall continue to make sure my insulin resistant (PREL?) ponies have adequate levels of anti-oxidants in their diet. I have not and don't expect to see any improvement from their use, but I can only hope it might slow the progress of their condition.

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