INSULIN RESISTANCE

Part 1
with Dr Jennifer Stewart

Jenquine
BRINGING SCIENCE TO YOUR FEED BIN

Insulin resistance is linked to several diseases – including laminitis, hyperlipaemia, equine metabolic syndrome (EMS), Cushings (PPID = pituitary pars intermedia dysfunction), osteochondrosis, colic and grass founder in horses, and in humans, type II diabetes, obesity, cardiovascular disease, hypertension, polycystic ovaries & colorectal cancer.

EQUINE VETERINARIANS AUSTRALIA

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What does 'insulin resistance' mean?

To understand what is happening for horses with insulin resistance requires just a little bit of biology. Insulin is produced by the pancreas to regulate blood glucose levels. It does this by binding to muscle, liver and fat cells and allowing glucose to stream in so it can be used and stored for energy. When the glucose moves into muscle, liver and fat cells, blood glucose levels fall back down to normal – and when this happens, insulin levels also drop back to normal resting levels.

In insulin resistant (IR) horses muscle, liver and fat cells do not respond to insulin, glucose cannot enter the cells and blood glucose levels stay high – this stimulates the pancreas to release more and more insulin (up to 100 times more) in an attempt to reduce blood glucose. Eventually the pancreas becomes exhausted and can no longer produce insulin. Also, the cells that do not respond to insulin cannot take up glucose and become starved of energy. Muscles use around 80% of the glucose in the blood and if they cannot obtain enough glucose, the horse may show increased muscle tension, unwillingness to work, lethargy and muscle wastage.

High blood glucose leads to overload and increased amounts of body fat and this causes inflammation of the fat. Inflammation of fat produces some very nasty chemicals that have been shown to cause IR. In addition, the combination of high blood glucose + high blood insulin damages blood vessels throughout the body, disrupting cellular processes and resulting in tissue and organ damage and causing a variety of disease states. The role of insulin in the expansion and contraction of blood vessels is thought to underlie the link between IR and laminitis because the hoof blood vessels are extremely sensitive to blood supply and when damaged the bond between the hoof and the coffin bone weakens and degenerates — and the hoof separates from the coffin bone.

Why does IR occur?

Among the horse (and human!) population there are those commonly known as 'easykeepers' or 'good-doers'. They have lower nutritional requirements ie they are metabolically efficient and have what is known as a 'thrifty genotype'. This genetic makeup was a critical survival mechanism that increased appetite and haircoat thickness in autumn and ensured fat stores were built up before the onset of winter. Combined with this, the degree of IR varies between cells — muscles become IR before liver and fat cells, ensuring that blood glucose is diverted preferentially to fat for winter storage. At the end of winter body fat stores are depleted and IR reverses. Relying on grass and adapted to food-poor winters, horses with a thrifty

genotype are prone to obesity and IR when food is available throughout the year, and especially if the feed is energy-rich and the horse physically inactive.

The extent to which different breeds of horses have inherited thrifty genes is not known, but ponies, Morgans, domesticated Spanish mustangs, European Warmbloods and American Saddlebreds are more prone to both IR and laminitis. Temporary IR can occur due to infections, injury, starvation, pregnancy and puberty. In pregnancy, IR ensures glucose is not taken up by the mare's body but is redirected to nourish the growing foal; in young horses IR has been associated with osteochondrosis due to damage to blood vessels in joint cartilage. The risk factors, short and long term consequences and symptoms of IR are thus highly diverse and vary between individual horses.

IR and Body Fat

Obesity is a growing problem for domesticated companion horses with a recent study finding that 19% are obese (BCS 8 or 9) and 32% overweight (BCS 6.5–7.5). Obesity has been associated with IR, causes worsening of IR, and both obesity and IR increase the risk of laminitis. And, obesity causes chronic inflammation, which plays a major role in the development of IR because fat (no longer regarded as a simple repository for stored energy) produces nasty chemicals that cause inflammation throughout the body.

The composition and inflammatory state of fat varies depending on where it is located in the body. In humans, patterns of regional fat accumulation have particularly damaging health consequences – specifically abdominal fat which has been linked to changes in blood glucose levels and is a risk factor for IR, diabetes and other diseases. Increased fat deposits along the neck crest in horses and ponies (nuchal crest adiposity) has likewise been associated with altered metabolism. Fat crests are an adaptive mechanism of fat storage for survival during periods of nutritional scarcity and vary between winter and summer with lower levels at the end of winter. Crest fat takes longer to develop and to deplete than other fat stores and (as with abdominal fat in man) it has been implicated in providing signals that disrupt glucose and insulin, and is correlated with changes in blood and metabolism that accompany IR. Measurement of the girth to height ratio is a good indicator of overall fatness and while IR can also occur in normal and lean horses, they often have the abnormal accumulations and distribution of fat.

IR and Equine Metabolic Syndrome (EMS)

EMS is also known as insulin-resistance syndrome and includes a history of laminitis, IR and a characteristic physical appearance of cresty neck, bulging fat above the eyes and increased fat over the withers and back. Studies in herds of ponies shown EMS has a strong hereditary (ie genetic) component.

IR and Laminitis

Horses suffering from laminitis and insulin resistance seem to have a slow recovery process, but recovery is more likely if insulin sensitivity is improved Horses with insulin resistance have a higher risk of developing laminitis and to find and treat horses with insulin resistance would be a means of preventing laminitis.

Ponies predisposed to pasture-associated laminitis are metabolically different from ponies not at risk – they are IR. That pasture-associated laminitis is linked to underlying IR was discovered in the 1980's when ponies with a history of laminitis were found to be IR and have high blood pressure.

IR and Equine Cushing's disease
(ECD = Pituitary pars intermedia dysfunction (PPID))

The pituitary gland readies horses for winter – stimulation of appetite, acquisition of a winter coat and increased fat synthesis in autumn are all kindled by the pituitary gland. Dysfunction of the pituitary gland occurs in 30% of horses over 15yo, with ponies and Morgan horses most at risk. Factors contributing to PPID are unknown, although age, oxidative stress and chronic inflammation are risk factors. Most, but not all horses with PPID have IR. Signs include changes in fat distribution (pot belly, muscle wasting and bulging fat above the eyes), increased drinking and urine, and higher risk of infections and laminitis. PPID may arise as a result of chronic IR in obese horses and ponies that have been fed energy-dense rations over the course of many years. Many horses with a thrifty genotype and IR develop PPPID later in life.

IR Diagnosis

There is huge range of signs and symptoms of IR and a simple, reliable method of diagnosis is still not available. Since obesity is associated with IR, assessment of body condition (BCS) is a helpful tool for general obesity, but it misses the assessment of neck and local fat accumulation.

A BCS of >6 (scale 1—9) indicates high risk for IR and laminitis. Since local fat accumulations — especially in the neck region — are strongly associated with IR, a more specific scoring system based on neck fat has recently been developed. Scores range from 0 — 5 with 0 showing no signs of fat accumulation on the neck and 5 showing obvious signs of severe fat accumulation on the neck.

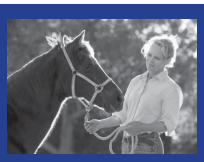
A score of >3 is described as “cresty neck”. Interestingly, changes in the “thickness” of the affected neck have been linked to changes in the severity of IR: as the neck thickens, signs of IR (such as laminitis) tend to increase (these signs decrease when treatments are associated with improvement in insulin sensitivity and a loss of neck crest thickness). Neck circumference relative to height and girth is a useful, practical index for suspicion of IR (similar to the use of waist circumference as an indicator of high BMI and IR in man).

Blood tests for insulin are useful to predict the risk and prognosis of laminitis. Other tests are needed to diagnose the range of IR-associated diseases, and may include ACTH and thyroxine levels.

IR Management

Methods to improve insulin sensitivity (ie reduce IR) include exercise, maintaining ideal body condition and avoiding of high-glycaemic feeds and pastures and molasses. This is because feeds rich in carbohydrates (carbs) + too little exercise collide with the natural way of horse and are the major reason for the development of insulin resistance. And, not surprisingly, the reasons that domesticated animals develop obesity are broadly similar to reasons why humans become overweight. The bottom line is that prevention and treatment of IR in horses must be based on changing the way they are managed and fed.

Pharmacologic agents that counteract IR can be part of the treatment of laminitis, PPID and ECD. These include chromium, metformin, levothyroxine, corticosteroids, pergolide and xylazine. The pros and cons of each, the most appropriate choice for your horse and the best treatment schedule, should be discussed with your veterinarian.



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Dr Jen Stewart has been an equine veterinarian for more than 40 years & an equine nutritionist for more than 10 years. Jen has been developing premium formulas for studs, trainers & feed companies in Australia & around the world & regularly consults to leading international studs & trainers in various countries. Jen has spent a fair bit of time researching & being involved in nutritional management of developmental orthopedic diseases, colic, tying-up, laminitis, performance problems, post-surgery & other conditions. And is currently the only practicing equine veterinarian & clinical nutritionist in Australia. ***Jen's promise is to continue to BRING SCIENCE TO YOUR FEED BIN***

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