

The Horse Ask the vet live: Equine Cushing's Disease (PPID)
Sept 18 2012 Nicholas Frank and Marian Little Sponsored by Boehringer Ingelheim

Dr Frank – has 25 year old Shetland pony with PPID

Dr Little – had advanced PPID horse

Q. What causes PPID and why is it so prevalent?

PPID is a progressive disorder – starts with dysfunction of pituitary gland (PG) – PG at base of brain sends out a number of different hormones – as PPID develops the pars intermedia sends out more of these hormones – this affects the horse in many different ways – increase in cortisol/stress hormones is one element of PPID. Dysfunction develops into small single or multiple tumours that produce excess hormones.

Common because changes happen with ageing – the pars intermedia is controlled by nerves that degenerate over time, but they degenerate faster in horses with PPID. Risk increases with age – about 1/3 of old (20+) horses have PPID

Q. What are the effects of PPID?

One component is that PPID weakens the immune system, white blood cells are not as effective, bacterial infections more likely to occur & harder to clear, e.g. hoof abscess, white line disease, tooth abscess, sinus infection. Increased susceptibility to infections is particularly seen with advanced PPID. Important to talk about early & advanced PPID.

Q 23 year old horse didn't shed until mid-Aug (others shed in May) – could this be a sign of PPID?

Yes – late shedding compared to other horses is a common sign of early PPID

Other early signs:

Subtle change in hair coat - regional hypertrichosis – areas of longer and lighter hair (the “woolly mammoth” i.e. general hypertrichosis is often a sign of advanced PPID);

Fat deposits – crest, tail head, above eye;

Subtle change in body conformation – losing top line despite regular exercise – common sign;

Easy keeper changes to hard keeper with no change in management ;

Subtle changes in behaviour – depressed, lethargic;

Footsoreness & chronic laminitis with no real reason;

Early signs of PPID are variable and subtle – discuss anything abnormal with vet

With horses that have had EMS then develop PPID, insulin often gets worse as PPID advances

Increased hormones in PPID can cause horses to drink and urinate excessively (PU/PD).

Abnormal sweating and recurrent infections tend to be more advanced signs

Late shedding, regional hypertrichosis, body conformation changes, laminitis or footsoreness are all red flags for early PPID.

Early signs often go unnoticed – need to be looking for PPID in horses much younger than mid 20s

Miller established 5 grades of the pituitary gland on histopathology – 1 being normal, 5 advanced PPID – diagnostic tests do a good job of detecting advanced PPID (grade 5 and some grade 4) but do not pick up mild to moderate disease – hopefully this will change as we develop better diagnostic tests.

Similar to Parkinson's disease and Alzheimer's disease in people, PPID has a slow insidious onset – by the time clinical signs are noticed the disease has progressed significantly.

Q. 29 year old mare with PPID now on pergolide – will horse regain muscle tone?

Takes time (several months) for body conformation changes – should notice significant change in 6 months – change in attitude and behaviour usually earliest sign – can take weeks to several months to really appreciate changes.

Q. What's the difference between PPID and IR? Is either disease hereditary?

EMS is hereditary in that there is a genetic predisposition towards IR which is influenced heavily by management, i.e. if the horse is put into situation where it can become obese, or doesn't get enough exercise, or has an incorrect diet

Horses that are obese and have EMS for many years are predisposed to PPID – we see them transition from EMS to PPID as the horse gets older.

Expect to see PPID in certain breeds & lines based on genetic predisposition for EMS

Q. Are certain breeds more prone?

As above, horses that have had EMS are likely to progress to PPID, and there appear to be certain genetic lines for EMS - easy keeper breeds, ponies....

Q. Do Overweight horses have a greater risk of PPID?

A history of obesity or EMS seems to predispose horses to PPID over time.

Theories as to why chronic (long-term) obesity may lead to PPID:

- may cause oxidative damage – presence of free radicals - leading to PPID,
- may interfere with WBC function & perhaps overstimulates the pituitary, leading to PPID,
- production of leptin from fat cells which may overstimulate hormone production from the pituitary.

We don't know the exact mechanism, but it appears that when a horse is obese for years and IR develops, the onset of PPID is not far behind.

Some obese horses never have a problem.

Some horses that have never been obese or had EMS develop PPID

Genetics are likely to play a role.

Best to avoid obesity – mainly to prevent laminitis.

Q. Can regular exercise prevent PPID?

Good to regularly work horses – min 20 mins 5 x wk, perhaps more for EMS types.

Diagnosing

New information from the Equine Endocrinology Working Group

http://www.prascend.com/Content/PDF/BIVM-12015%20Prascend%20Diagnosis%20Booklet_WEB.pdf

who agreed on clinical signs and diagnostics – many tests recommended in the past e.g. cortisol are no longer considered useful.

Tier 1 & 2 tests have been established:

Tier 1 – screening tests – ACTH (& DST) – DST has been referred to as gold standard but not considered any more accurate than ACTH, DST can't be used year round and there are considerations regarding injecting steroids.

ACTH is easier – sensitivity can be improved by taking more than 1 sample on a visit, seasonal reference ranges mean that ACTH can be performed all year.

NB Tier 1 tests likely to pick up moderate & more severe PPID but it's a challenge to diagnose early PPID. Dr Frank strongly recommends if you get a negative result but clinical signs are apparent and persist, keep testing, as horse gets older test result will generally become positive.

Tier 2 – TRH stimulation of ACTH – may be more sensitive for diagnosing early cases of PPID – not commercially available in USA but is available at referral institutions & some practices.

Pituitary gland is more active Aug-Oct – “seasonal rise” – both normal and PPID horses have increases in hormones in the autumn but PPID horses have greater increase and the difference between normal and PPID horses is greater, therefore a recent change is that the autumn is the best time to test. A horse that was negative in the spring may be positive in the autumn.

Q. PPID horse's symptoms seem to be getting worse in September – could this be due to seasonal rise?

Could be – many horses seem to get worse in the autumn. May need to increase pergolide dose in autumn, test ACTH in autumn to check how well PPID controlled.

Q. If a horse is showing classic clinical signs – is it necessary to test or just treat?

Ideally we want to diagnose in early stages before laminitis & other complications – once obvious clinical signs don't need lab test for diagnosis. However, treatment isn't always increased to a level that gets disease under control – lab results give idea of severity and response to treatment. If not responsive, increase dosage. Use blood tests plus clinical signs to establish dosage – ACTH.

Treatment & Management

Q. Can treatment with pergolide make horses more irritable/unpleasant?

Owners of PPID horses often say “the lights are on but no one's home” – over time PPID tends to make horses more lethargic & docile.

Often when treated with pergolide horses become much more energetic and perhaps bolshy – likely restoring the normal function of the pituitary that the horse lost some time ago – horses with advanced PPID are often very gentle with sweet personalities, and sometimes owners prefer their PPID horse to the one they find after treatment!

Also when some of the excess “feel-good” hormones are removed with treatment, some horses start to feel age-related aches & pains that were masked with PPID – need to rule these out.

Owners should provide an engaged environment, ensure horse eating well with appropriate nutrition. We often take horses off grass and isolate them - provide activity and companion. If behavioural changes persist, talk to vet, consider reducing dose if causing behavioural changes although this may not be possible if it might cause other symptoms to increase.

Q. What hoof care is necessary for a PPID horse?

Provide regular expert care – frequent trims – protect and maintain feet.

Advanced PPID – susceptible to infections like hoof abscesses, WLD, cracks that become infected – good environmental management e.g. dry areas to avoid mud/wet. Risks should reduce as PPID brought under control.

Q. How should PPID be managed?

Whole horse approach – drug therapy with pergolide, plus hoof care, nutrition – insulin status, deworming, clipping, dental checks, exercise if possible. Pergolide 1st line, if don't respond at higher doses cyproheptadine may be added. More than just drug therapy – stay on top of all issues that affect PPID horse.

Q. Why can't tumour be removed?

Location – expense, complications – the pituitary is at the base of the brain. We can image the pituitary gland with CT – but not routine. PPID occurs because of loss of dopaminergic neurons that enervate the pituitary – need to restore activity of dopamine medically not surgically. Not all PPID horses have visible pituitary lesions. Need pituitary for other functions in the body. Not sure surgery ever would be an option.

Q. Does chasteberry help?

Pennsylvania University study – Vitex not effective. Anecdotal reports of improvements in horses with chasteberry – may help some horses and not others, but it's not a substitute for pergolide, may be additional help. Pergolide clearly effective in controlling PPID.

Q. Will PPID horse be able to compete again?

Don't give up – manage nutritional aspects – control sugar/starch, minimize glycaemic response but provide enough energy. If recovering from laminitis, low s/s feeds, add rice bran, corn oil, molasses free beet pulp.... Nutrition plays important role in getting horses back into work. Also address hoof care if previously laminitic.

Q. If pergolide is safe for horses, why was it removed from the market for humans?

Pergolide in humans – people developed heart problems with higher dose than used for horses, over long time. Only some patients. We use a lower dose for horses, different pharmacokinetics, no evidence in vet literature of problems with heart – horses that have been on pergolide for years have had post mortems and no adverse signs have been seen. No reason to be concerned. What we find in one species doesn't necessarily translate into other species. Unless we see issues arising, we can be comfortable with pergolide use in horses.

Prascend safety study – screened for cardiac abnormality with exaggerated doses – no signs.

Q. Why is Prascend more expensive than compounded pergolide?

Consistent validation of manufacturing and packaging, plus submission for FDA approval and proof of efficacy, stability & potency – establishes a minimum cost to bring product to market.

Ongoing stability testing, monitoring of safety and efficacy – Prascend offers something you are not assured of with compounding products.

BI does not establish a recommended price for the product.

Compounded pergolide is not an inexpensive treatment if it fails to control clinical signs.

Prascend offers best chance of controlling the clinical signs of the disease

Get backing of team of people at BI – safety net that owner and vet doesn't get with compounded pergolide.

Phil Johnson said smaller quantities of Prascend doing as much or more as larger doses of compounded pergolide. Prascend is more cost effective, better control of clinical signs over time.

Q. What is the best way to feed a PPID horse?

PPID horses have different needs – those with acceptable body condition and those that need to gain weight.

Consider Insulin status – IR or not?

Feed to ideal BW if ok BC & no IR. Grass hay and vit/min supplement/balancer.

Gain weight – more calories – senior feeds, add corn oil, beet pulp, flaxseed oil

IR – lean horse – more calories – need to put weight on without making IR worse - hay analysis, low NSC - around 10%, low carb/starch feeds, limit access to pasture until IR controlled

If severely IR permanently take off grass – if IR controlled perhaps return to grass over time

Vit E good for any PPID horse - anti-oxidant

Not all PPID horses are IR – need to know to make best nutritional recommendations – many older PPID horses being calorie restricted as if IR when they aren't. Insulin should be tested as well as ACTH.

Q. Is it OK to turn horse out on pasture?

Regarding diet, important to know situation with each individual horse – need to test insulin in order to make informed decisions:

- basal insulin & glucose
- or oral sugar test (corn syrup) – see how horse might respond to sugars in grass and feed.

Some PPID horses have IR problems, some don't.

e.g. pony – had IR whole life, probably due to genetics, PPID at 25, could make IR worse – need to know what insulin levels are and insulin responses to diet;

TB – 25-30, never had IR, now PPID, once checked and insulin ok, different diet needed.

Check insulin resting or even better after OST, then will know whether safe to graze. If can get out with grazing muzzle for limited time, perhaps twice a day, moving around. May be possible to leave horse out all day all the time – many older horses do better on grass.

So monitor insulin and then make decisions about grazing/diet.

Q. Do PPID horses always get laminitis?

No! Laminitis much more tied to IR – previous IR, more likely to get laminitis. IR can get worse when PPID develops.

Horses with advanced PPID have poorer quality feet because of problems PPID causes, but not always due to laminitis. Horses with laminitis are the ones vets see more of, but there are many others that have PPID but no laminitis that vets don't tend to see.

Wrap up:

Dr Little: Owners – recognise management is a process and individual – there isn't one management scheme that works for every horse and every situation, individual management strategies needed – it's a learning process and a very individual experience.

Dr Frank: Great progress has been made in this area – we're better at recognising PPID in the early stages, we're better at managing and controlling it, we can do more for PPID horses. Older horses can remain active, can do much more now than 10 – 20 years ago.

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