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Hall 3B ■ Saturday 10th September

09.50–10.15

Inter-relationships of hyperinsulinaemia and PPID

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Pituitary pars intermedia dysfunction (PPID, Equine Cushing's disease) and insulin resistance (IR) are the commonest endocrinopathies seen in equine practice and are both associated with increased risk of laminitis. The 2 conditions may be seen independently of one another or may coexist which may cause diagnostic and therapeutic confusion. Coexistence might be a pure coincidence given that they are both common conditions. Alternatively there might be a causal inter-relationship of the 2 conditions such that IR might predispose to PPID and/or *vice versa*.

It is recognised that PPID arises as a result of oxidative damage to hypothalamic dopaminergic neurons. Years of obesity and IR in earlier life might possibly create chronic inflammatory and oxidative challenge adequate to lead to neuronal damage and PPID. Furthermore, long-term management of obese, insulin resistant, laminitis-prone ponies might also inadvertently lead to deficiencies that could also promote disease, for example, lack of antioxidants present in fresh grass or vitamin D from exposure to sunlight resulting from restricted turnout. Conversely, it is also possible that PPID might be a cause of IR as a result of endocrine factors that might promote IR (e.g. cortisol, ACTH) and hyperinsulinaemia (e.g. corticotrophin-like intermediate lobe peptide).

Data from 744 cases of PPID seen between January 2009 and December 2010 were examined to look for associations between several variables including signalment data (age, breed, gender, time of year) and results of blood tests (ACTH, insulin, glucose, triglycerides) with the aim of providing information that might help clarify putative inter-relationships between PPID and IR. Cases of PPID were defined as a combination of a clinical suspicion of PPID and a plasma ACTH concentration greater than the reference interval for that time of year (Nov–Jul 29 pg/ml; Aug–Oct 47 pg/ml).

More PPID cases were seen in ponies than horses (61% vs. 39%). Comparison of ponies vs. horses revealed that PPID horses were significantly older and had lower serum insulin concentrations than PPID ponies. It was also found that several other associations examined (below) were different in horses and ponies and therefore these 2 populations were examined separately.

Comparison of laboratory data derived at different times of year was performed. In both PPID horses and PPID ponies it was found that plasma ACTH was significantly greater between the months of August and October than the rest of the year. It was also found that, in horses only, plasma glucose was significantly greater between August and October than during the rest of the year.

When data were compared between genders, the only significant finding was that plasma glucose was significantly higher in PPID pony geldings than in PPID pony mares. No significant gender effects were found in PPID horses.

Using a cutoff of 20 years of age, older PPID horses were found to have significantly higher plasma ACTH and lower plasma glucose than younger PPID horses. Older PPID ponies were found to have significantly higher plasma ACTH and lower serum insulin than younger PPID ponies.

Hyperglycaemia was found in similar numbers of PPID horses and PPID ponies (7% vs. 9%). Hyperglycaemic PPID horses had significantly higher plasma ACTH, serum insulin and serum triglycerides than normo-glycaemic PPID horses; whereas hyperglycaemic PPID ponies only differed from normo-glycaemic PPID ponies in having higher serum insulin.

Hyperinsulinaemia was more prevalent in PPID ponies than PPID horses (49% vs. 36%). Hyperinsulinaemic PPID horses had significantly higher plasma ACTH, plasma glucose and serum triglycerides than normo-insulinaemic PPID horses; whereas no significant differences were found between hyperinsulinaemic and normo-insulinaemic PPID ponies.

Hypertriglyceridaemia was more prevalent in PPID ponies than PPID horses (53% vs. 28%). Hypertriglyceridaemic PPID horses had significantly higher plasma ACTH and serum insulin than normo-triglyceridaemic PPID horses; whereas no significant differences were found between hypertriglyceridaemic and normo-triglyceridaemic PPID ponies.

The median ACTH concentration of all PPID cases was 65 pg/ml (all cases had plasma ACTH > seasonal reference interval). This value was then used as a cutoff to define 'high-ACTH' (>65 pg/ml) and 'low ACTH' (<65 pg/ml) PPID cases. PPID horses with high ACTH were significantly older and had higher serum insulin and plasma glucose than PPID horses with low ACTH. PPID ponies with high ACTH only differed from those with low ACTH in being significantly older.

These data indicate several interesting epidemiologic and pathophysiological inter-relationships within 2 complex endocrinopathic conditions and are illustrated in **Figure 1**. Further targeted investigation is required to further elucidate inter-related factors although the following appear to be plausible theories consistent with the findings.

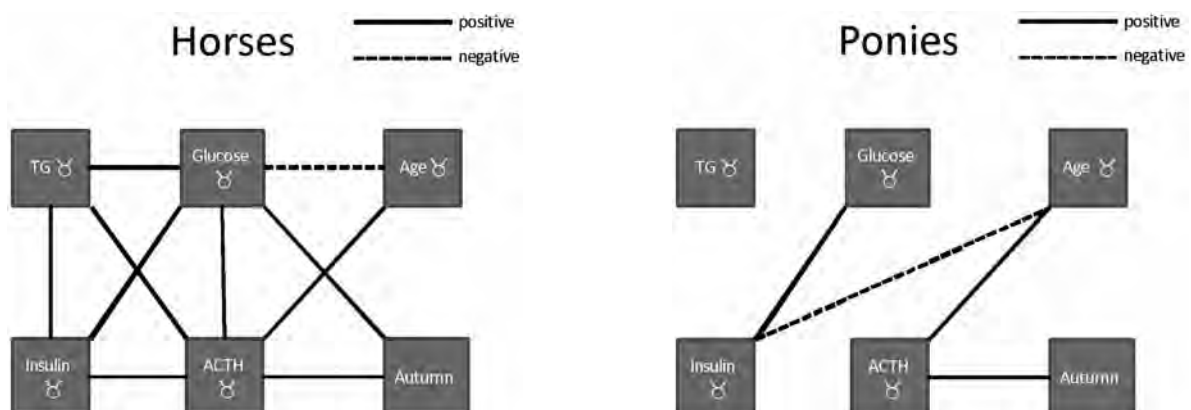


Fig 1: Illustrations of significant associations demonstrated in the study (gender effects not included for clarity).



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PPID causes IR in horses?

In horses there appeared to be close associations between ACTH (a marker of PPID) and insulin, glucose and triglycerides (markers of IR) consistent with the possibility that PPID is a cause of IR in horses. In contrast, ponies had no significant relationship between ACTH and markers of IR casting doubt on PPID being a common cause of IR in ponies.

IR causes PPID in ponies?

The fact that ponies developed PPID at a younger age than horses is consistent with there being a predisposing factor or factors that are more common in ponies than horses. Possible candidates might include hyperinsulinaemia and IR. Interestingly insulin was higher in young vs. old PPID ponies which is consistent with them being IR at the onset of PPID with subsequent weight loss as a result of PPID gradually improving insulin sensitivity.

NOTES
