

CHANGING FACE OF CUSHING'S DISEASE IN EQUINE PATIENTS

EQUINE Cushing's disease (ECD) is the most commonly encountered equine endocrine disorder (Frank and Geor, 2014), producing a range of symptoms. These symptoms traditionally include:

- excessively long coat (hirsutism; Lloyd et al, 2003; Figure 1);
- excessive sweating (Figure 2);
- secondary bacterial cutaneous infections; parasitism;
- oral ulceration and dental disease (Pascoe and Knottenbelt, 1999);
- recurrent bouts of laminitis (Figure 3);
- polydipsia and polyuria (PD/PU);
- bulging of the supraorbital fat pad (Figure 4);
- muscle wastage; and
- pendulous abdomen (pot belly; McGowan et al, 2013).

This article reviews the incidence of presenting signs in a group of 30 horses seen in general practice with sus-

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discusses the forms, signs, diagnosis and treatment of this endocrine disorder, using a study of 30 horses to identify any variation in typical presentations

pected ECD over a period of two years and reviews how this might differ from previous descriptions of ECD.

Disease forms

There are two forms of ECD (Tadros and Frank, 2013):

- **Pars pituitary intermedia dysfunction (PPID)**. Typically, dopamine from the hypothalamus inhibits production of adrenocorticotrophic hormone (ACTH) from the pars intermedia of the pituitary. In older horses, reduced production of dopamine due to ageing allows uncontrolled proliferation of the pars intermedia and excessive production of proopiomelanocortin-derived peptides including ACTH, alpha-melanocyte-stimulating hormone, beta-endorphin and corticotrophin-like intermediate peptide, which stimulate the pancreas to increase levels of insulin. PPID is seen more commonly in older horses (more than 15 years old).
- **Equine metabolic syndrome (EMS); peripheral Cushing's disease**. Insulin resistance (IR) develops due to excess deposition of fat and reduced



Clockwise from top: **Figure 1** - Hirsutism. **Figure 2** - Sweaty coat. **Figure 3** - Recurrent laminitis. **Figure 4** - Bulging of the supraorbital fat pad.



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Table 1. Diagnosis of equine Cushing's disease

| | 1 - 19 hour overnight dexamethasone suppression test (Sensitivity 89 per cent, specificity 88 per cent). | 2 - Measurement of basal plasma ACTH (Sensitivity 84 per cent, specificity 97 per cent). | 3 - Thyrotropin releasing hormone (TRH) response test (measures ACTH, not cortisol). ● Take basal cortisol level, inject 1mg TRH IV. ● Measure cortisol 15 minutes later - in PPID you see 50 per cent to 100 per cent rise in cortisol. ● The effect lasts one-and-a-half hours (in the normal horse you see a slight reduction in cortisol). ● Sensitivity 97 per cent, specificity 91 per cent. | 1 - Resting blood insulin (In normal horses <65µIU/ml measured at the lab by radioimmunoassay). | 2 - Combined glucose insulin test (IV glucose and insulin are given simultaneously. Both blood glucose and serum insulin are measured and in normal horses these levels return to within the reference range within 45 minutes). | 3 - In feed glucose (oral sugar) test (Horse is challenged with oral glucose and the insulinaemic response is measured). ● 1g/kg of glucose is given orally. ● After 120 minutes blood samples are taken and tested for insulin - levels more than 87µIU/ml indicate EMS. ● In the United States the oral sugar test uses corn syrup). |
|---|--|--|--|---|--|---|
| PPID | | | | | | |
| EMS (characterised by hyperinsulinaemia and normoglycaemia) | | | | | | |

Table 2. Incidence of symptoms in each group

| Total no. cases | Hirsutism | Excess sweating | Secondary infections | Parasitism | Dental disease | Laminitis | PP/PU | Dullness and lethargy | Bulging supra-orbital fat pad | Muscle wastage and pendulous abdomen |
|-----------------|-----------|-----------------|----------------------|------------|----------------|-----------|---------|-----------------------|-------------------------------|--------------------------------------|
| PPID 18 | 3 (16%) | 0 | 0 | 0 | 2 (11%) | 11 (61%) | 3 (16%) | 7 (39%) | 0 | 0 |
| EMS 7 | 0 | 0 | 3 (43%) | 0 | 0 | 4 (57%) | 2 (29%) | 0 | 0 | 0 |
| Non-ECD 5 | 0 | 0 | 0 | 0 | 0 | 5 (100%) | 0 | 0 | 0 | 0 |

activity (similar to type two diabetes in people), and is seen more commonly in younger horses and ponies (four to 15 years old).

Both conditions result in insulin dysregulation (Marr and Marr, 2014), affecting the health and well-being of the affected individual (Figure 5).

Diagnosis

The diagnosis is based on the presenting clinical signs and confirmed with blood tests (Table 1).

For PPID, elevated resting ACTH levels are helpful (specificity 97 per cent, sensitivity 84 per cent; Copas and Durham, 2012) and can be carried out at most commercial labs. The resting levels are affected by day length - from November to June normal levels are less than 35pg/ml and from July to October they are less than 45pg/ml, suggesting autumn is a good time to test (Copas and Durham, 2012). EMS can be diagnosed with resting insulin levels after a six-hour fasting period. In this study, levels exceeding 65µIU/ml were used at Dechra

Specialist Laboratories (DSL) to indicate IR; the specificity is high, but the sensitivity is low. Dynamic testing using a combined glucose-insulin tolerance test (in-feed glucose test) can be used to confirm the diagnosis, but requires overnight fasting and two blood samples (Tadros and Frank, 2013), which is not practical for many cases in general practice.

In this study blood samples from 30 horses and ponies that presented with symptoms consistent with ECD were collected and put into diagnostic categories of PPID, EMS or no evidence of ECD. For financial reasons in many cases only an initial resting ACTH test was performed and if PPID was not diagnosed, a further laminitis profile test, which included insulin levels, was carried out to check for EMS. Laboratory samples for ACTH testing were taken in ethylenediaminetetraacetic acid tubes, the plasma separated and then sent in a plain tube in a chiller pack.

A diagnosis of PPID was made if ACTH levels were more than 35pg/ml on samples taken between November and June, and more than

Treatment of ECD includes management changes and medical therapy. Management changes include diet control - feeding a high fibre diet (soaking hay for 14 hours on a muzzle, strip grazing pasture and increasing the amount of exercise.)

45pg/ml July to October (Copas and Durham, 2012). Where possible, follow-up blood samples were taken four to six weeks later to monitor the response and adjust the dose of treatment. Insulin levels were tested on serum using radioimmunoassay at DSL and a diagnosis of EMS was made if insulin levels were more than 65µIU/ml.

Of the 30 horses studied, five had no evidence of ECD on blood results, 18 were diagnosed with PPID and seven with EMS. Laminitis was the most common presenting sign; 61 per cent (11/18) of the PPID cases and 57 per cent (4/7) of the EMS cases were found to be suffering from this. The other main symptom in ECD cases in this study was mental dullness and lethargy; 39 per cent (7/18) of the

PPID cases and 43 per cent (3/7) of the EMS cases were showing these symptoms. Only three cases (16 per cent) of the PPID group showed the classic hirsute coat - this may be because coat clipping is now popular, masking this symptom. Excessive thirst and urination were seen in three cases of PPID, secondary bacterial cutaneous infections were seen in three cases of EMS and dental disease was only seen in two cases of PPID. The other symptoms of excessive sweating, bulging of the supraorbital fat pad, pot belly and parasitism were not noted in any of the cases in this study.

Treatment

Treatment of ECD includes management changes and medical therapy. Management changes include diet control - feeding a high-fibre

From this study the most common symptom of ECD seen was laminitis. Mental dullness and lethargy were also common and secondary infections. The classic dermatological symptoms of hirsutism, excessive sweating, thirst and urination were not very common.

Symptoms

- 1 - Excessively long coat
- 2 - Excessive sweating
- 3 - Secondary bacterial cutaneous infections
- 4 - Parasitism
- 5 - Oral ulceration and dental disease
- 6 - Recurrent bouts of laminitis
- 7 - Polydipsia and polyuria
- 8 - Lethargy
- 9 - Bulging of the supraorbital fat pad
- 10 - Muscle wastage and a pendulous abdomen (pot belly)

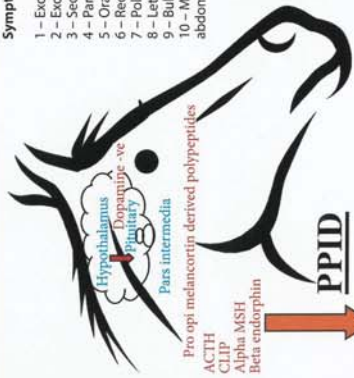


Figure 5. Insulin dysregulation resulting from both form of equine Cushing's disease.

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Of the 18 cases of PPID, one was lost to follow up, seven were managed on pergolide and 10 treated with management changes alone, and three were eventually euthanised due to poor control of the disease. Of the seven cases of EMS, three were treated with pergolide, one with metformin and three with management changes alone; one case treated with pergolide was eventually euthanised due to poor control.

Of the five cases of laminitis not found to have EMS or PPID on blood results, all recovered with supportive treatment. The popular trend of regular coat clipping by owners masks the symptom of hirsute coat and increased

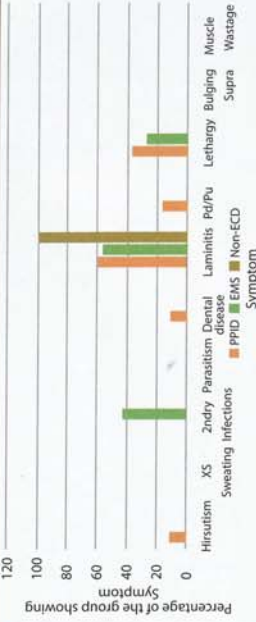


Figure 6. Incidence of symptoms as a percentage of the group.

owner awareness of the signs of ECD has led to cases being diagnosed before the classic symptoms are apparent. The traditional picture of equine Cushing's disease presenting as shaggy, sweaty ponies is no longer apparent. From this study, laminitis, mental dullness, lethargy and secondary infections were much more common and as new treatments become licensed the veterinary profession is able to improve welfare of the horse population, reducing the incidence of this crippling disease.

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From this study the most common symptom of ECD seen was laminitis (61 per cent of PPID cases, 57 per cent of EMS cases). Mental dullness and lethargy were also common (39 per cent of PPID cases, 29 per cent of EMS cases), and secondary infections (43 per cent of EMS cases). The classic dermatological symptom (soaking hay for 14 hours reduces the caloric content), putting on a muzzle, strip grazing pasture and increasing the amount of exercise. A range of medical treatments have been tried including metformin (Rendle et al, 2013) and pergolide (starting dose 0.002mg/kg). Only pergolide is licensed to treat equidae.

EMS
Reduced exercise
Increased feed intake

