

Equine Cushing's disease

Equine Cushing's disease is a disorder of the pituitary gland that results in hormonal imbalances, causing a variety of clinical signs: a long, wavy hair coat that fails to shed according to normal seasonal patterns; excessive sweating; lethargy and poor athletic performance; chronic recurrent laminitis; infertility; weight loss; muscle wasting, especially along the top line; abnormal distribution of fat, with accumulations in the crest of the neck, tail head, sheath and above the eyes; consumption of large volumes of water and passage of large amounts of urine; delayed wound healing; and increased susceptibility to infections. The disease tends to occur in middle-aged and geriatric horses, with an average age of approximately 20 years at the time of diagnosis. Without treatment, symptoms tend to worsen over time and many horses are euthanized as a consequence of laminitis, recurrent foot abscesses or complications related to bacterial infections.

In horses, the disease involves the intermediate part (pars intermedia) of the pituitary. This portion of the gland is comprised of hormone-secreting cells. In affected horses, the pars intermedia produces excessive amounts of hormones. Function of the pars intermedia is normally kept in check by hypothalamus, a nearby part of the brain that regulates a variety of body functions such as thirst, hunger, body temperature, water balance and blood pressure. In most cases of equine Cushing's disease, the pituitary gland is truly not a cancer, but rather enlarged and overactive as a result of faulty regulation by the hypothalamus. In fact, the most effective available medication for the disease, pergolide, works by mimicking the inhibitory effect of hypothalamic nerve cells on the pituitary.

Diagnosis

In advanced cases characterized by a long, wavy hair coat and other classical signs of Cushing's disease, diagnosis is relatively straightforward and may not require any specialized testing. Diagnosis of early cases or those characterized by few obvious clinical signs, however, is considerably more difficult. The two most practical and accurate tests currently available are (1) the dexamethasone suppression test, and (2) measurement of plasma ACTH concentration.

The dexamethasone suppression test is an overnight protocol in which a pretreatment blood sample is collected in the late afternoon, after which a low dose of dexamethasone is administered by intramuscular injection. A second sample of blood is collected the following day at around noon and both samples are submitted for measurement of plasma cortisol. In normal horses, administration of dexamethasone stimulates a negative-feedback response that suppresses secretion of cortisol from the adrenal glands, yielding a much lower concentration in the second blood sample. In horses suffering from Cushing's disease, however, the negative-feedback response is blunted and a lesser degree of suppression, if any, is observed.

The measurement of plasma ACTH involves collection and analysis of a single blood sample; the pituitary gland in affected horses often secretes excessive amounts of ACTH into the bloodstream as compared to normal horses. While useful, this test is generally considered to be somewhat less accurate than the dexamethasone suppression test, and blood samples must be handled very carefully to avoid degradation of ACTH and falsely lower measured values. Stress and pain due to other conditions may also result in falsely elevated values.

Supplemental tests that may be useful in suspect cases include measurements of blood glucose and insulin. Many affected horses are insulin resistant and some are significantly hyperglycemic; early recognition and tracking of these abnormalities will aid in nutritional management of the disease and provide additional criteria by which to evaluate the horse's response to treatment.

Treatment of Equine Cushing's disease

Optimal management of Cushing's disease involves a combination of both specific medication to normalize the function of the pituitary gland and supportive care to address and prevent complications associated with the disease. In both cases, management will be life-long as there is no way to reverse the disease process. In the early stages, specific medication may not be required and conservative measures such as body clipping to remove the long hair coat, strict attention to diet, and scrupulous attention to teeth, hooves and preventive care may be sufficient to provide good quality of life. Since affected horses are often insulin resistant, sweet feed and other feedstuffs high in soluble carbohydrates should be avoided in favor of diets emphasizing fiber and fat. Pelleted or extruded feeds designed specifically for older horses are strongly recommended, but those with high levels of sugar or molasses should be avoided unless needed to encourage the horse to eat. In both mildly and severely affected horses, the importance of early diagnosis and aggressive treatment of bacterial infections cannot be overstated.

The drug of choice is currently pergolide mesylate (Permax®), which is administered daily by the oral route. An initial dose of 0.002 mg/kg (approximately 1 mg for a 1000-lb horse) once daily is recommended; this dose may be gradually increased if clinical improvement fails to occur after one to two months of therapy. A favorable clinical response to therapy will be associated with improvement or normalization of results in the dexamethasone suppression and plasma ACTH tests. Occasional severe cases benefit from treatment with a combination of both pergolide and cyproheptadine (Periactin®).

In addition to these medications, a variety of nutritional supplements and alternative therapies have been advocated for the management of equine Cushing's disease. A comprehensive review of these strategies is beyond the scope of this article, but two that may be helpful and are unlikely to pose significant risks include dietary supplementation of magnesium (to achieve a target calcium:magnesium ratio of 2:1) and chromium picolinate. These nutrients are helpful in the management of type 2 diabetes and insulin resistance in humans, and may be beneficial in equine cases complicated by insulin resistance and hyperglycemia. An herbal product prepared from chaste berry extract (*Vitus agnus castus*) has also been recommended for the management of equine Cushing's disease, but a recent scientific study performed at the University of Pennsylvania's New Bolton Center found it ineffective.