Endocrine abnormalities of the horse
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Summary: Endocrine abnormalities occur frequently in the horse. The clinical presentation of common conditions may have significant overlap resulting in diagnostic confusion. It is important to arrive at an accurate diagnosis, as the successful therapy for endocrine abnormalities is contingent upon the correct diagnosis.

Hypothyroidism: Much of the confusion around hypothyroidism is a result of the erroneous association of this condition with obesity, laminitis and infertility. Research that is more recent indicates that hypothyroidism is actually quite rare. In the limited case reports of documented hypothyroidism in horses, the primary clinical signs are lethargy, exercise intolerance, and poor quality haircoat. In horses that had thyroids removed, neither weight gain nor laminitis were seen.

Diagnosis: The hypothalamus regulates the production of thyroid hormones through the actions of thyrotropin-releasing hormone (TRH), which stimulates the anterior pituitary gland to release thyroid-stimulating hormone (TSH). TSH then regulates the synthesis and release of thyroid hormones by the thyroid gland. In response to TSH stimulus, triiodothyronine (T3) and thyroxin (T4) are released from the thyroid gland into the bloodstream bound to either thyroglobulins or other proteins such as albumin. T4 has minimal activity and is essentially a prohormone. T3 is the primary active form of the hormone, and only unbound T3 can enter a cell and activate the vital functions attributable to this hormone. The common measurement of total T3 and T4 often provides erroneous values and does not provide a clear picture of thyroid function. Assessment of thyroid function requires thyroid stimulation tests that are difficult because of the lack of availability of TRH or TSH. To perform a stimulation test, a control blood sample is obtained, TRH (0.002 mg/kg) or TSH (0.01 IU/kg) is given intravenously and blood collected at 1, 2, and 4 hours after administration. In a normal horse, T3 should double at 2 hours and T4 should double at 4 hours. If a single blood collection to evaluate thyroid hormones is the only option, assays that determines the free fractions of the thyroid hormones are going to be more accurate than ones that only measure total concentrations of T3 and T4. Thyroid stimulation tests should not be performed on horses that are ill or receiving thyroid supplementation.

Numerous conditions are likely to result in low serum concentrations of circulating thyroid hormones despite normal thyroid function. It is well known that highly protein-bound drugs displace protein-bound T3 and T4 in the blood stream. This scenario results in a decrease in measured total serum T3 and T4, although the active unbound concentrations of these hormones remains unchanged. Fasting, strenuous exercise, and diets high in energy, protein, zinc and copper have all been demonstrated to decrease measured thyroid hormones. Additionally, nonthyroidal illness syndrome has been described, which results in a decline in measured thyroid hormone levels in proportion to the severity of disease. In conclusion, hypothyroidism is rare and should not be based off a single blood sample collected at random times throughout the day.

Equine Metabolic Syndrome (EMS): This condition is characterized as obesity or abnormal fat distribution, insulin resistance, and high risk of laminitis. In fact, most horses that were once thought to be hypothyroid actually suffer from this syndrome. There appears to be a genetic predisposition, and EMS occurs most frequently in pony breeds, Morgans, American Saddlebreds, Tennessee Walking Horses, and Spanish
breeds. Most of the affected horses are described as “easy keepers.” EMS can be described as a condition that results from interaction of genetics with environment. Horses with a genetic predisposition and access to sufficient feed are likely to develop this syndrome. This syndrome affects horses at a much younger age than seen with pituitary pars intermedia dysfunction. Affected horses will have a body condition score of ≥7 or regional accumulations of fat. Affected horses often present for sudden onset of laminitis and have concurrent hyperinsulinemia. Many horses demonstrate evidence of previous laminitis upon careful examination of the feet.

**Diagnosis:**
It is not possible to compare laboratory values for the same affected horse generated at two different laboratories. Be consistent.

1. **Resting insulin:** Fasting is not necessary, but grain should be withheld for at least 4 hours before testing. This test has a low sensitivity and can be negative in mildly affected animals.
   a. < 20 µU/ml = normal
   b. 20-50 µU/ml = suspect
   c. > 50 µU/ml = insulin dysregulation

2. **Oral sugar test:** Leave horse with one flake of hay at 10 pm and perform test next morning before feeding. Administer Karo Light corn syrup at a dosage of 0.15 ml/kg PO and collect blood sample for insulin and glucose determination at 60 and 90 minutes.
   a. Insulin < 45 µU/ml = negative
   b. Insulin 45-60 µU/ml = weak positive
   c. Insulin > 60 µU/ml = insulin dysregulation

3. **Insulin tolerance testing:** obtain baseline glucose, administer 0.10 IU/kg of regular insulin intravenously, and determine glucose 30 minutes later. A less than 50% decrease in baseline glucose is consistent with insulin dysregulation.

**Treatment:**
Diet and exercise are the primary methods of control. Levothyroxine (4 tsp PO, q 24hrs to 450 kg horse) can be used in horses that are resistant to weight loss, but supplementation will not work if calories are not restricted.

**Pituitary Pars Intermedia Dysfunction:** Oxidative injury to the dopaminergic neurons of the hypothalamus results in a loss of inhibition of the pituitary pars intermedia and excessive secretion of adrenocorticotropic (ACTH), as well as α-melanocyte-stimulating hormone (α-MSH), B-endorphin, and corticotropin-like intermediate peptide (CLIP). This syndrome is seen in older horses than is EMS, and typical clinical signs include lethargy, delayed shedding, regional adiposity, loss of muscle mass over topline, and a “pot-bellied” appearance. In severely affected horses, recurrent infections, abnormal sweating, infertility, laminitis, blindness, and insulin dysregulation may be seen.

**Diagnosis:**
Remember that there is significant seasonal variation to test results. Use laboratories with seasonally adjusted normals or avoid testing in late summer/fall.

1. **Resting ACTH:** sample must be kept cool at all times. The plasma should be separated within 2 hours of collection and frozen prior to shipping. Remember to ship overnight with icepacks.
   a. Mid-November to mid-July
      i. < 30 pg/ml = negative
      ii. 30 – 50 pg/ml equivocal
      iii. > 50 pg/ml positive
b. Mid-July to mid-November
   i. < 50 pg/ml = negative
   ii. 50-100 pg/ml = equivocal
   iii. > 100 pg/ml = positive

2. TRH stimulation test: for horses with equivocal results upon resting ACTH testing
   a. Feed hay but no grain overnight
   b. Baseline ACTH
   c. Administer 1 mg TRH IV
   d. Collect second ACTH at 10 minutes after TRH administration
      i. < 110 pg/ml = negative
      ii. 110-200 pg/ml = equivocal
      iii. > 200 pg/ml = positive

Treatment:
1. Pergolide (2 µg/kg daily) titrated to effect
   a. Adverse effects include decreased appetite, lethargy, and weight loss
   b. If adverse effects are severe, cut dose in half and slowly increase to optimal dose
   c. Retest in 30 days and adjust dose
   d. Twice annual testing recommended

2. Cyproheptidine
   a. Serotonin antagonist
   b. Used in conjunction with pergolide, but not as effective alone

3. Trilostane
   a. Inhibits cortisol synthesis at adrenal gland
   b. PPID does not affect adrenal gland, so limited expected benefit