Hypoadrenocorticism

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Synonyms:

Addison's disease
Atypical, secondary Addison's disease
Iatrogenic hypoadrenocorticism

Disease description:

DEFINITIONS

Hypoadrenocorticism is a result of deficient secretion of mineralocorticoids (aldosterone), glucocorticoids, or both. Several terms have been used to describe the various forms of hypoadrenocorticism:
Primary hypoadrenocorticism is usually caused by immune-mediated destruction of the adrenal cortex in both cats and dogs.[1-7] Lymphomatous infiltration of the adrenals has been reported as a cause of hypoadrenocorticism in cats.[7]

Secondary hypoadrenocorticism, also commonly termed "atypical Addison's" disease, is due to inadequate production of adrenocorticotrophic hormone (ACTH). In the dog, the most common cause is chronic corticosteroid therapy with signs becoming present if the corticosteroids are abruptly stopped (see Iatrogenic hypoadrenocorticism below). Less common causes include tumors, trauma,[8] or congenital defects of the pituitary gland. Secondary hypoadrenocorticism is rare in both dogs and cats.

Atypical hypoadrenocortism describes glucocorticoid deficiency only. Secondary hypoadrenocorticism is always atypical. Primary hypoadrenocorticism can be atypical in the early stages of the disease prior to destruction of the zona glomerulosa.

Iatrogenic hypoadrenocorticism can occur in hyperadrenocorticism cases that are treated with mitotane or trilostane; signs of glucocorticoid or mineralocorticoid deficiency or both develop as the adrenal cortex is affected by the drugs. Some cases are reversible and some are not.

Another cause of iatrogenic glucocorticoid deficiency is the sudden withdrawal of corticosteroids from a patient who has been administered long term corticosteroids (also called secondary hypoadrenocorticism); such cases have adrenocortical atrophy that is reversible if the corticosteroids are slowly withdrawn over several months.

PATHOGENESIS

Glucocorticoid deficiency results in a decrease in gluconeogenesis and glycogenolysis, faulty energy metabolism, and decreased vascular sensitivity to catecholamines. Tolerance to stress is diminished. Mental depression and renal retention of water also occurs. Clinical signs include weakness, gastrointestinal hemorrhage, hypoglycemia, hyponatremia (due to impaired ability to excrete free water as antidiurectic hormone (ADH) release is not counteracted by glucocorticoids). Gastrointestinal signs are often waxing and waning in nature.

Mineralocorticoid deficiency results in sodium, chloride and water losses with potassium and hydrogen ion retention. Without aldosterone (main adrenal mineralocorticoid), potassium is no longer excreted adequately while there is increased sodium loss. Lack of sodium results in inadequate circulating blood volume, leading to decreased cardiac output and reduced perfusion of organs, especially kidneys. Hypovolemia, hypotension, hypoperfusion of tissue with reduced cardiac output are responsible for neurologic derangements, gastrointestinal disturbances, prerenal uremia, cardiac arrhythmias, and shock. The renal medullary gradient is also "washed out" leading to impaired urine concentration.

CLINICAL SIGNS

Signs can be acute in onset and intermittent or chronic in duration. Some signs mimic gastrointestinal diseases. Some signs are mild/subtle while other signs are severe. The more severe signs are usually found in patients with both glucocorticoid and mineralocorticoid deficiencies as opposed to only glucocorticoid deficiency.

Acute onset of signs is often due to hypovolemic shock. Vomiting, diarrhea, and collapse may be the presenting problems. Physical examination may reveal severe dehydration, abdominal pain, bradycardia, weak pulses, hypothermia, pale mucous membranes and obtundation.[2] Clinical features that should increase the index of suspicion of hypoadrenocorticism include a normal or slow heart rate in the face of circulatory shock, a prior positive response to corticosteroid or fluid therapy, and "waxing and waning" signs prior to collapse.

Chronic hypoadrenocorticism signs are often intermittent and vague in nature, and can be exacerbated or induced by stress. Anorexia, lethargy, shaking, polydipsia, polyuria, muscle twitching, weakness, diarrhea, vomiting and weight loss can occur.

Disease description in this species:

CLINICAL SIGNS

In addition to the signs described earlier, other less common signs are hypoglycemic seizures, gastrointestinal tract hemorrhage and regurgitation (due to secondary mesaesophagus).[2,9] Muscle cramping has also been reported.[10]

An unusual feature of hypoadrenocorticism in dogs is severe gastrointestinal tract hemorrhage with melena, hematochezia and mild anemia.[11-14] Additionally, some dogs have concurrent arthritis, hepatitis, keratoconjunctivitis sicca, or myasthenia gravis; the relationship between these and Addison's disease is not understood.

DIAGNOSIS

While a variety of clinical signs and laboratory changes can be found with hypoadrenocorticism, none are specific enough to allow a definitive diagnosis. An ACTH stimulation test is needed.

Physical examination findings may include dehydration, weak pulses, prolonged capillary refill time, bradycardia, hypothermia, and weakness. Hematochezia and hematemesis are occasionally found.[1,2]

Hematological findings may include mild normocytic normochromic anemia; however, if dehydration is present, the underlying anemia may be masked. If anemia is due to gastrointestinal hemorrhage, it should be regenerative in nature within 5 days after onset. The absence of a stress leukogram is a subtle but important feature of glucocorticoid deficiency (atypical hypoadrenocorticism).[13] The presence of a normal or elevated eosinophil or lymphocyte count in a stressed animal should be viewed with suspicion for hypoadrenocorticism, particularly atypical Addison's disease. Eosinophilia and lymphocytosis are seen in 20% and 10% of dogs with primary hypoadrenocorticism, respectively.[2,15] However lymphopenia can occur in a small number of cases.[15]

Biochemistry results may have a variety of abnormalities. Hypoalbuminemia occurs in 6-12% of patients and may be due to impaired synthesis and impaired intestinal absorption; however a cause and effect relationship has not been defined.[16] In one large retrospective study of 225 cases, liver enzyme elevations occurred in 30% and mild hyperbilirubinemia occurred in 20%. These changes may have been due to decreased cardiac output and decreased liver perfusion.[15]

Hypoglycemia was noted in 17% of 225 affected dogs. In some cases, it can decrease sufficiently low enough to result in seizures.[15]

Azotemia and hyperphosphatemia are often present with primary hypoadrenocorticism making it difficult to differentiate it from acute renal failure. Azotemia associated with hypoadrenocorticism may be pre-renal as a result of dehydration, hypovolemia or gastrointestinal hemorrhage which results in reduced glomerular filtration rate and decreased renal perfusion.[2,15]

Electrolyte imbalances[17,18] are a common finding in patients with hypoadrenocorticism; however, 10% of patients with primary hypoadrenocorticism may have normal serum electrolyte levels. Those with normal

electrolytes may have secondary hypoadrenocorticism or may have early disease or incomplete destruction of the zona glomerulosa.[1]

Serum electrolyte abnormalities are the result of aldosterone deficiency, rendering the nephron unable to exchange sodium for potassium and resulting in massive losses of sodium and water into the urine which leads to hyponatremia, renal medullary washout, hemoconcentration, hypovolemic shock and death. Hyperkalemia, together with the profound hypovolemia and hypotension, can culminate in cardiac arrest. The Na:K ratio in patients with hypoadrenocorticism is typically lower than the normal ratio of 27:1-40:1. In one study of 76 dogs, use of an Na:K ratio of <27-28:1 correctly classified 95% of dogs as either affected with hypoadrenocorticism or not.[18] However, in another study of 162 dogs with an Na:K ratio <27:1, only 17% had hypoadrenocorticism.[19] The lower the Na:K ratio, the higher the chance that hypoadrenocorticism is present.[4] Other causes of a low Na:K ratio include chronic blood loss, trichuriasis, acute renal failure, post-renal azotemia and abdominal/thoracic effusions (third space disease).[4,20]

Hypercalcemia was reported in 30% of cases of hypoadrenocorticism.[21-22] Hemoconcentration, increased renal tubular reabsorption and decreased GFR may contribute to elevated calcium levels, but the exact mechanism for hypercalcemia is unclear.[2] In a study of 8 hypercalcemic dogs with hypoadrenocorticism, the majority of dogs had normal vitamin D levels, normal parathyroid levels, and normal parathyroid hormone-related protein levels.[22]

Mild to moderate metabolic acidosis may occur due to decreased hydrogen ion secretion in the renal distal tubule, (due to reduced aldosterone levels),[2] increased generation of acids secondary to reduced tissue perfusion, and renal retention of organic acids.

Glucocorticoid deficiency cases without mineralocorticoid deficiency do not show classic electrolyte imbalances but may have hypoglycemia as a result of impaired gluconeogenesis and glycogenolysis.[2,14,15] In one recent retrospective study, dogs with glucocorticoid deficiency were more likely to be anemic, hypoalbuminemic, and hypocholesterolemic than dogs with mineralocorticoid deficiency.[13]

Urinalysis may show a specific gravity that is low and is attributed to medullary washout (inadequate medullary gradient due to sodium depletion) and decreased medullary blood flow. Dilute urine in the face of azotemia and hyperkalemia may easily be mistaken for acute renal failure. An ACTH stimulation test is required to confirm the presence or absence of adrenal disease and to differentiate between hypoadrenocorticism and renal failure.

Basal cortisol levels can be useful to rule out hypoadrenocorticism but cannot confirm the diagnosis. A value >2 µg/dL makes hypoadrenocortism less likely.[23]

ACTH stimulation test is the gold standard for diagnosing hypoadrenocorticism. More than 90% of cases will have pre and post ACTH cortisol levels < 2.0 ug/dL and a majority of dogs have values well below 1 ug/dL on both the pre and post ACTH samples. The ACTH stimulation test does not differentiate between primary and secondary hypoadrenocorticism.[2,24]

Endogenous plasma ACTH levels can be used to distinguish between primary adrenocortical disease from the much less common pituitary disease. Patients with primary hypoadrenocorticism will have markedly elevated ACTH levels (>100 pg/mL) due to lack of negative feedback; such cases may develop mineralocorticoid deficiency at a later date. Those patients with secondary hypoadrenocorticism, which are caused by a pituitary deficiency of ACTH, have decreased endogenous ACTH concentrations (<20 pg/mL). Such cases do not develop mineralocorticoid deficiency.[2]

Plasma aldosterone assay results are primarily of academic interest.[25] Pre and post aldosterone levels are occasionally performed in atypical Addison's cases to determine if they’re becoming mineralocorticoid deficient. If results are normal, the animal is not mineralocorticoid deficient but if results are abnormal, the interpretation is still questionable since the dose of ACTH that causes maximal adrenocortical aldosterone secretion has not been unequivalently established and because the time of peak response has also not been fully evaluated. In one study, 1.0 µg/kg cosyntropin stimulated the highest serum aldosterone concentrations but the time of peak response was at 10 or 20 minutes, which is different from the 60-min sampling time currently recommended.[26]

Electrocardiography may confirm bradycardia and waveform changes that are associated with hyperkalemia. Classic electrocardiographic findings reported with hyperkalemia include prolonged QRS complexes, decreased R wave amplitude, increased T wave amplitude ("spiked" T waves), and prolonged or absent P waves. Sinoatrial standstill is the most common arrhythmia noted. Electrocardiographic changes should not be used to determine the exact serum potassium concentrations because serum potassium concentrations do not directly correlate with specific EKG changes; however, the EKG is useful in an emergency setting.[27]

Radiography may demonstrate findings associated with volume depletion or decreased tissue perfusion, such as microcardia, narrowed vena cava, and hypoperfused lungs. Megaesophagus has been reported uncommonly in dogs with both typical and atypical hypoadrenocorticism.[9,28] With typical hypoadrenocorticism the megaesophagus is thought to be due to generalized muscle weakness and changes in neuromuscular function from abnormal sodium and potassium levels on membrane potentials.[2]

Ultrasonography cannot be routinely used to identify "small" adrenal glands, particularly since the right adrenal may be difficult to image in normal animals.[29] But it may be used to evaluate the adrenal glands for neoplasia.

Laboratory Profile:
Sodikoff's Laboratory Profiles of Small Animal Diseases: Azotemia, Prerenal
Sodikoff's Laboratory Profiles of Small Animal Diseases: Hypoadrenocorticism, Addisons Disease
Sodikoff's Laboratory Profiles of Small Animal Diseases: Hypoadrenocorticism, Glucocorticoid Deficiency

Genetic Basis:
Portuguese Water Dog (PWD): Addison's disease is inherited as an autosomal recessive disorder in PWDs. An analysis of 11,384 PWDs surveyed between 1985 and 1996 suggests an incidence of 1.5%.[30-31]

Bearded Collie: In one study, hypoadrenocorticism in the Bearded Collie was demonstrated to be highly heritable but a pedigree study did not reveal the type of inheritance.[32]

Standard Poodles: In this breed, the heritability of hypoadrenocorticism was estimated to be 0.75 and complex segregation analyses suggested the disease was influenced by an autosomal recessive locus.[33]

Nova Scotia duck tolling retrievers: Studies have indicated an autosomal recessive mode of inheritance.[34-35]

Leonbergers, Labrador Retrievers, and other breeds: A familial predisposition to hypoadrenocorticism has been suggested. [36]

Etiology:
ACTH deficiency
Hypoadrenocorticism
Hypoadrenocorticism, secondary
Hypothalamic lesion
Idiopathic, unknown
Immune-mediated disease
Infection
Mitotane, o,p'-DDD
Pituitary lesion
Valvular disease

Breed predilection:
None, no breed signalment

Diagnostic procedures:
Hemogram (complete blood count)

Diagnostic results:
ANEMIA
Eosinophilia, eosinophils increased
Hemoconcentration or polycythemia
Leukocytosis
Lymphocytosis, lymphocytes increased

Serum chemistry	Alanine aminotransferase (ALT) increased Alkaline phosphatase (ALP) increased Aspartate aminotransferase (AST) increased Azotemia/uremia Blood urea nitrogen (BUN) increased Creatinine increased Gamma-glutamyl transferase (GGT) increased Hyperbilirubinemia, bilirubin increased Hypercalcemia Hyperkalemia Hyperphosphatemia Hypochloremia Hypoglycemia Hyponatremia Sodium:potassium ratio <25:1
Urinalysis	Urine specific gravity decreased Urine specific gravity increased
Radiography of thorax	Megaesophagus Microcardia, heart small
Adrenocorticotropic hormone stimulation test (ACTH)	Cortisol levels decreased
Blood pH measurement	Blood pH increased, alkalosis Blood/serum bicarbonate decreased, metabolic acidosis
Blood pressure measurement	Hypotension
Electrocardiography (ECG)	ARRHYTHMIA, CARDIAC IRREGULARITY BUNDLE BRANCH BLOCK ELECTROCARDIOGRAM ABNORMAL P wave decreased or absent P wave wide (>0.04 sec) P-R interval prolonged (>0.14 sec) Right bundle branch block S wave in lead II increased T wave in lead II increased (>0.7 mV)
Biopsy and histopathology of small intestines	Intestinal hemorrhage

Treatment/Management/Prevention:

ACUTE CRISIS

Acute adrenocortical insufficiency is a life-threatening emergency that necessitates immediate treatment. Treatment of the Addisonian crisis consists of four aspects: 1) fluid therapy and electrolyte stabilization 2) glucocorticoid replacement therapy 3) addressing gastrointestinal hemorrhage 4) mineralocorticoid replacement therapy.

1) **Fluid Therapy and Electrolyte Stabilization:** Large volumes of 0.9% NaCl delivered via a jugular catheter are ideal. Rapid administration of IV fluids restores blood volume and improves renal perfusion which decreases serum potassium concentration via dilution and promotion of renal potassium excretion. If hyperkalemia persists, serum potassium can be rapidly decreased by intravenous administration of regular, short-acting (crystalline) insulin at 0.03 to 0.06 units/lb followed by glucose (for every unit of insulin given, use 4 ml 50% dextrose) or intravenous administration of 10% calcium gluconate (0.4 to 1 mg/kg over a 10-20 minute period) to counteract the effects of hyperkalemia on the heart. [1-4,37]

2) **Glucocorticoid therapy** using ultra-short acting corticosteroids, such as dexamethasone sodium phosphate (0.1-2.0 mg/kg IV) or prednisolone sodium succinate (15-20 mg/kg IV), should be instituted

immediately. [1-4,37] Dexamethasone may be preferred in animals that require immediate glucocorticoid administration as it will not interfere with the ACTH stimulation assay; in addition, a single dose of short-acting corticosteroid will not suppress the hypothalamic pituitary adrenal axis.

3) **Gastrointestinal hemorrhage** is addressed via administering gastrointestinal protectants. Anemia of different degrees can be found and if it is severe, a blood transfusion may also be needed.[11]

4) **Mineralocorticoid replacement:** Rapid correction of hypovolemia with 0.9% NaCl is usually sufficient to correct most electrolyte abnormalities but injectable DOCP or oral fludrocortisone acetate (Florinef®) mineralocorticoid supplementation can be instituted (while waiting for diagnosis) without adverse effects should the case not be an Addisonian one. Metabolic acidosis often resolves after fluid therapy; however, severe acidosis (pH < 7.1) may be treated with sodium bicarbonate. Hypoglycemia, if present and symptomatic, should be treated with a slow intravenous bolus of 50% dextrose (0.5-1.0 ml/kg).

LONG-TERM MAINTENANCE

Without lifelong replacement therapy, dogs afflicted with hypoadrenocorticism invariably die. There are 2 choices of maintenance therapies.

1) **Desoxycorticosterone pivalate (DOCP) with maintenance prednisolone:** DOCP is a long acting ester of desoxycorticosterone acetate (DOCA), a synthetic corticosteroid with physiologic effects indistinguishable from aldosterone. DOCP is formulated in a microcrystalline suspension that, once injected IM, provides about 25 days of mineralocorticoid therapy. DOCP has no glucocorticoid activity.

DOCP dose and interval: Begin with the label dose of 1 mg/lb IM q 25 days, but adjustments, usually downwards in dose, can be made for most patients over the next few months as the dose and the duration are assessed. To assess the dose, check electrolytes on day 12 to 13 post-injection for the first 1-2 months. Potassium (K)should be towards the low end of the normal range and sodium (Na) toward the high end. If K is high, the next dose is increased by 10%. To determine the dose interval, electrolytes should be be checked at time of next injection (no need to wait for results). If K is low, or normal mid-range, increase the next dose interval by 2 days. If K is high, decrease the dose interval by 2 days.

If you adhere strictly to administering DOCP every 25 days, it will eventually have to be administered on a Saturday or Sunday. To avoid weekend injection appointments, stretch out the dose interval to 28 days so that the injection can be given the same day of every month (e.g. the first, second, third, or fourth Monday or whatever of every month) to make the appointments easier to remember. The dose interval can vary greatly among dogs, ranging anywhere from 14-35 days; however the median was 30 days in one study.[37] Careful electrolyte monitoring in the first 3-4 months of therapy is recommended.

Prednisolone: 0.1 to 0.2 mg/kg per day (or about 1 mg per 10 pounds). This dose is physiologic rather than pharmacologic; thus the average 40 pound dog would receive 4.0 mg of prednisone daily. During periods of stress, this dose may have to be increased 2-3 fold. Even though DOCP contains no glucocorticoid activity, some dogs on DOCP may not need the prednisolone unless there is stress or illness. If the electrolytes are normal yet the dog has a poor appetite, is less active, or has periodic vomiting or diarrhea, it is likely that glucocorticoid deficiency is present and physiologic doses of prednisolone will be required.

2) **Fludrocortisone**: 15-20 µg/kg P0 q 24 hrs or 0.1-0.5 mg/dog q12-24h depending on size of dog and Na and K values. The typical dose is 0.1 mg (one tablet) per 2.5 to 5 kg of body weight. A small percentage of dogs appear to be resistant to the drug regardless of the dose administered. Some dogs develop polydipsia, polyuria, and/or incontinence as side effects when administered doses necessary to maintain normal electrolytes.

Fludrocortisone provides some glucocorticoid activity and therefore, additional prednisolone supplementation isn't usually required except during periods of stress (i.e. boarding, disease, elective surgery, etc).

Special considerations:

Correction of a chronic hyponatremic state must be done cautiously. In one reported case, too rapid administration of sodium resulted in osmolar changes in cerebral cells and subsequent severe neurological signs.[38]

High dose trimethoprim-sulfa can interfere with renal potassium secretion and exacerbate the hyperkalemia of hypoadrenocorticism.[39]

Other Resources:
Medical FAQ on treating hypoadrenocorticism
Medical FAQ on diagnosing canine hypoadrenocorticism
Atypical Addisonian

Differential Diagnosis:
Causes of a low Na:K ratio: (pseudoAddison's)

Chronic blood loss
Gastrointestinal diseases
Trichuriasis
Acute renal failure
Post-renal azotemia
Abdominal effusion
Thoracic effusion (e.g. chylothorax)
Third space disease
Pregnancy[40]
Pyometra
Conditions causing severe acidosis (e.g. diabetic ketoacidosis)

References:

1) Scott-Moncrieff JC: : Hypoadrenocorticism in Dogs and Cats: Update on Diagnosis and Treatment. ACVIM Proceedings 2010.
2) Ettinger SJ, Feldman EC: Hypoadrenocorticism. Veterinary Internal Medicine, 2 ed. Elsevier Saunders 2005 pp. 1613-21.
3) Peterson ME, Greco DS: Primary hypoadrenocorticism in ten cats . J Vet Intern Med 1989 Vol 3 (2) pp. 55-8.
4) Behrend EN: Update on Diagnosis and Treatment of Canine Hypoadrenocorticism. Western Veterinary Conference 2010.
5) Stonehewer J, Tasker S: Hypoadrenocorticism in a cat. J Small Anim Pract 2001 Vol 42 (4) pp. 186-190.
6) Tasker S, MacKay AD, Sparkes AH: A case of feline primary hypoadrenocorticism. J Feline Med Surg 1999 Vol 1 (4) pp. 257-260.
7) Parnell NK, Powell LL, Hohenhaus AE, Patnaik AK, Peterson ME: Hypoadrenocorticism as the primary manifestation of lymphoma in two cats. J Am Vet Med Assoc 1999 Vol 214 (8) pp. 1208-1211.
8) Platt SR, Chrisman CL, Graham J, et al: Secondary hypoadrenocorticism associated with craniocerebral trauma in a dog. J Am Anim Hosp Assoc 1999 Vol 35 (2) pp. 117-122.
9) Bartges JW, Dielson DL: Reversible megaesophagus associated with atypical primary hypoadrenocorticism in a dog. J Am Vet Med Assoc 1992 Vol 201 (6) pp. 889-91.
10) Saito M, Olby NJ, Obledo L, Gookin JL: Muscle cramps in two standard poodles with hypoadrenocorticism. J Am Anim Hosp Assoc 2002 Vol 38 (5) pp. 437-443.
11) Medlinger TL, Williams DA, Bruyette DS: Severe gastrointestinal tract hemorrhage in three dogs with hypoadrenocorticism. JAVMA 1993 Vol 202 (11) pp. 1862-72.
12) Sadek D, Schaer M: Atypical Addison's disease in the dog: a retrospective survey of 14 cases. J Am Anim Hosp Assoc 1996 Vol 32 pp. 159-63.
13) Thompson AL, Scott-Moncrieff JC, Anderson JD: Comparison of classic hypoadrenocorticism with glucocorticoid-deficient hypoadrenocorticism in dogs: 46 cases (1985-2005). J Am Vet Med Assoc 2007 Vol 230 (8) pp. 1190-1194.
14) Lifton SJ, King LG, Zerbe CA: Glucocorticoid deficient hypoadrenocorticism in dogs: 18 cases (1986-1995). J Am Vet Med Assoc 1996 Vol 209 (12) pp. 2076-81.
15) Peterson ME, Kintzer PP, Kass PH : Pretreatment clinincal and laboratory findings in dogs with hypoadrenocortism: 225 cases (1979-1993). J Am Vet Med Assoc 1996 Vol 208 pp. 85-91.
16) Uanglais-Burgess U, Lumsden JH, Mackin A: Concurrent hypoadrenocorticism and hypoalbuminemia in dogs: a retrospective study.. J Am Anim Hosp Assoc 1995 Vol 31 pp. 307-311.
17) Roth L, Tyler RD: Evaluation of low sodium:potassium ratios in dogs. J Vet Diagn Invest 1999 Vol 11 (1) pp. 60-4.
18) Adler JA, Drobatz KJ, Hess RS: Abnormalities of serum electrolyte concentrations in dogs with hypoadrenocorticism. J Vet Intern Med 2007 Vol 21 (6) pp. 1168-73.
19) Nielson L, Bell R, Zoia A: Low ratios of sodium to potassium in the serum of 238 dogs. Vet Rec 2008 Vol 162 (14) pp. 431-5.
20) DiBartola SP, Johnson SE, Davenport DJ, et al.: Clinicopathologic findings resembling hypoadrenocorticism in dogs with primary gastrointestinal disease. J Am Vet Med Assoc 1985 Vol 187 pp.

60-63.
21) Peterson ME, Feinman JM: Hypercalcemia associated with hypoadrenocorticism in sixteen dogs. J Am Vet Med Assoc 1982 Vol 181 (8) pp. 802-4.
22) Gow AG, Gow DJ, Bell R, et. al: Calcium metabolism in eight dogs with hypoadrenocorticism. J Small Anim Pract 2009 Vol 50 (8) pp. 426-30.
23) Lennon EM, Boyle TE, Hutchins RG, et. al: : Use of basal serum or plasma cortisol concentrations to rule out a diagnosis of hypoadrenocorticism in dogs: 123 cases (2000-2005).. J Am Vet Med Assoc 2007 Vol 231 (3) pp. 413-16.
24) Hill K, Scott-Moncrieff C, Moore G: ACTH Stimulation Testing: A Review and Study Comparing Synthetic and Compounded ACTH Products . Vet Med 2004 Vol 99 (2) pp. 134-47.
25) Golden DL, Lothrop CD: A retrospective study of aldosterone secretion in normal and adrenopathic dogs. J Vet Int Med 1988 Vol 2 (3) pp. 121-5.
26) Behrend EN, Martin L, Lee HP, et al: Dose Response of Aldosterone to ACTH Stimulation in Clinically Healthy Dogs. ACVIM Proceedings 2007.
27) Riesen SC, Lombard CW: ECG of the month. Atrial fibrillation secondary to hypoadrenocorticism. J Am Vet Med Assoc 2006 Vol 229 (12) pp. 1890-1892.
28) Melian C, Stefanacci J, Peterson ME, et al: Radiographic findings in dogs with naturally-occurring primary hypoadrenocorticsm. J Am Anim Hosp Assoc 1999 Vol 35 (3) pp. 208-212.
29) Hoerauf A, Reusch C: Ultrasonographic evaluation of the adrenal glands in six dogs with hypoadrenocorticsm. J Am Anim Hosp Assoc 1999 Vol 35 (3) pp. 214-218.
30) Chase K, Sargan D, Miller K, et al: Understanding the genetics of autoimmune disease: Two loci that regulate late onset Addison's disease in Portuguese Water Dogs. Int J Immunogenet 2006 Vol 33 (3) pp. 179-184.
31) Oberbauer AM, Bell JS, Belanger JM, Famula TR: Genetic evaluation of Addison's disease in the Portuguese Water Dog. BMC Vet Res 2006 Vol 2 (1) pp. 15.
32) Oberbauer AM, Benemann KS, Belanger JM, et al: Inheritance of hypoadrenocorticism in bearded collies. Am J Vet Res 2002 Vol 63 (5) pp. 643-647.
33) Famula TR, Belanger JM, Oberbauer AM: Heritability and complex segregation analysis of hypoadrenocorticism in the standard poodle. J Small Anim Pract 2003 Vol 44 (1) pp. 8-12.
34) Hughes AM, Nelson RW, Famula TR, Bannasch DL: Clinical features and heritability of hypoadrenocorticism in Nova Scotia Duck Tolling Retrievers: 25 cases (1994-2006). J Am Vet Med Assoc 2007 Vol 231 (3) pp. 407-12.
35) Burton S, DeLay J, Holmes A, et al: Hypoadrenocorticism in young related Nova Scotia duck tolling retrievers. 1997 Vol 38 (4) pp. 231-234.
36) Smallwood LJ, Barsanti JA: Hypoadrenocorticism in a family of leonbergers. J Am Anim Hosp Assoc 1995 Vol 31 (4) pp. 301-5.
37) Kintzer PP, Peterson ME: Treatment and long-term follow-up of 205 dogs with hypoadrenocorticism. J Vet Intern Med 1997 Vol 11 (2) pp. 43-9.
38) Brady CA, Vite CH, Drobatz KJ: Severe neurologic sequelae in a dog after treatment of hypoadrenal crisis. J Am Vet Med Assoc 1999 Vol 215 (2) pp. 222-225.
39) Rubin SI, Toolan L, Halperin ML: Trimethoprim-induced exacerbation of hyperkalemia in a dog with hypoadrenocorticism. J Vet Int Med 1998 Vol 12 (3) pp. 186-188.
40) Schaer M, Halling KB, Collins KE, Grant DC: Combined hyponatremia and hyperkalemia mimicking acute hypoadrenocorticism in three pregnant dogs. J Am Vet Med Assoc 2001 Vol 218 (6) pp. 897-898.

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