Glucocorticoid deficient hypoadrenocorticism in dogs: 18 cases (1986–1995)

Stephanie J. Lifton, DVM; Lesley G. King, MVB; Carole A. Zerbe, DVM, PhD

Objective—To characterize naturally developing glucocorticoid deficiency in dogs.

Design—Retrospective case series.

Animals—18 dogs with glucocorticoid deficiency defined by an inadequate response to stimulation with adrenocorticotropic hormone (ACTH), a normal Na:K ratio (> 27), and no history of receiving corticosteroids for at least 6 weeks.

Procedure—Information including signalment, body weight, clinical signs on admission, historical findings, physical examination findings, results of CBC and serum biochemical analyses, results of ACTH stimulation tests and other ancillary endocrine tests, diagnostic imaging findings, findings from other procedures such as endoscopy and surgery, and information on concurrent diseases, management, and outcome were retrieved from the medical records of dogs with glucocorticoid deficiency treated between 1986 and 1995 at the University of Pennsylvania's School of Veterinary Medicine and 2 dogs from private practices.

Results—Most dogs were young (< 7 years) and represented larger breeds (> 20 kg). Clinical signs were nonspecific: lethargy, weight loss, and gastrointestinal disturbances including regurgitation with radiographic evidence of megaesophagus. Hypocholesterolemia, hypoalbuminemia, hypoglycemia, and a mild, nonregenerative anemia were common. Ten of the 18 dogs responded well to glucocorticoid supplementation alone, with only 2 dogs developing electrolyte abnormalities. Four (22%) of the dogs died, with death usually occurring as a result of secondary disease processes rather than hypoadrenocorticism.

Clinical Implications—An ACTH stimulation test should be considered as part of the diagnostic plan in dogs with signs of weight loss, inappetence, and intermittent vomiting and diarrhea. Glucocorticoid-deficient dogs may not require supplemental mineralocorticoids. (*J Am Vet Med Assoc* 1996;209:2076–2081)

Hypoadrenocorticism is a well-recognized syndrome that classically includes mineralocorticoid and glucocorticoid deficiency. Clinical signs typically include debility and weakness, lethargy and signs of depression, vomiting, diarrhea, weight loss, hypotension, polyuria and polydipsia, and decreased appetite. Electrolyte imbalance (hyponatremia and hyperkalemia) caused by mineralocorticoid deficiency is the hallmark of this disease.

In previous reports of hypoadrenocorticism, 11 to 26% of affected dogs had serum concentrations of sodium, potassium, or both that were within reference ranges,[1-3] but such reports provide little specific information about this subgroup. Although iatrogenic glucocorticoid deficiency is fairly common in association with *o,p'*DDD or corticosteroid treatment, few reports in the literature focused on naturally developing deficiency of glucocorticoids alone, without concurrent mineralocorticoid deficiency. Therefore, the objective of the study reported here was to further characterize naturally acquired glucocorticoid deficiency in dogs.

From the Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104. Dr. Lifton's present address is VCA West Los Angeles Animal Hospital, 1818 S Sepulveda Blvd, Los Angeles, CA 90025.

Criteria for Selection of Cases

We retrospectively examined the medical records of 156 dogs with a diagnosis of hypoadrenocorticism that were admitted to the university veterinary hospital between March 1986 and December 1994. Sixteen dogs met the inclusion criteria. Two dogs from private veterinary practices also met the inclusion criteria and were included in this study. Hypoadrenocorticism was confirmed by an inadequate cortisol response to **adrenocorticotropic hormone (ACTH)** stimulation. Prestimulation plasma samples were obtained, 2.2 U/kg of body weight of ACTH gel[a] was injected, IM, and a second plasma sample was obtained 2 hours after stimulation. Cortisol concentration was determined by use of a previously validated radioimmunoassay method.[4,b] Reference values for the ACTH stimulation test were defined as pre- and poststimulation cortisol concentrations of 0.5 to 4 µg/dl and 8 to 18 µg/dl, respectively. The response to ACTH was considered inadequate if the post-ACTH cortisol concentration was < 4.5 µg/dl. Criteria for inclusion in this study were a confirmed diagnosis of hypoadrenocorticism, accompanied by a normal Na:K ratio (> 27) at admission, and no history of corticosteroid use for at least 6 weeks.

Tests and Procedures

Information gathered from the medical records included signalment, body weight, clinical signs on admission and historical findings, physical examination findings, results of CBC and serum biochemical analyses, results of ACTH stimulation tests and other ancillary endocrine tests, diagnostic imaging findings, findings from other procedures such as endoscopy and surgery, and information on concurrent diseases, management, and outcome. Means and medians were calculated for all numerical data.

Results

Of 158 dogs with hypoadrenocorticism, 18 had a normal Na:K ratio. Of the 18 dogs, 10 were female. There were 5 mixed-breed dogs, 3 Standard Poodles, 3 German Shepherd Dogs, 2 Labrador Retrievers, and 1 each of 5 other breeds, including 1 Miniature Poo-

dle. Mean age was 6 years (range, 2.75 to 11 years), with 12 dogs < 7 years old. Mean body weight was 28.5 kg (range, 3.2 to 43 kg), with 14 dogs weighing > 20 kg.

Historical and physical examination findings—The most common historical signs were weakness, lethargy, and vomiting (n = 10). Other signs included weight loss (n = 8), polyuria/polydipsia (5), total or partial anorexia (5), diarrhea (5), and regurgitation (4). Three of the dogs were admitted because of acute collapse (2 dogs because of hypoglycemia and the other because of anemia secondary to a bleeding gastric ulcer). Miscellaneous signs included flatulence, nasal discharge, coughing, sneezing, and hip pain.

Two of the dogs had been previously treated with corticosteroids. One had received ear drops containing dexamethasone, but had not been medicated for at least 6 weeks. The other had received an injection of corticosteroid (type not specified) 2 months prior to admission. An ACTH stimulation test was not performed on this dog until 1 month after initial admission and the dog responded well to physiologic glucocorticoid supplementation. None of the other dogs had any history of receiving corticosteroids.

Physical examination findings varied from weakness and signs of depression to localized lymphadenopathy and muscle atrophy. No single physical examination finding was detected in more than 39% of the dogs. Findings included thin/cachexic body condition (n = 7), weakness (6), coat abnormalities (5), signs of a tense/painful abdomen on palpation (4), muscle atrophy (4), fever (3), weak/thready pulses (3), pale mucous membranes (3), and dehydration (2). One dog had bradycardia (48 beats/min), which resolved within 24 hours. Five dogs had localized lymphadenopathy and 2 had large tonsils. Signs consistent with concurrent diseases, such as regurgitation with megaesophagus, nasal discharge and fever with pneumonia, and weak pulses with presumptive sepsis, were observed in 13 dogs.

Laboratory findings—Anemia, the most common hematologic abnormality, was observed in 11 dogs (Table 1). Four dogs were anemic on admission. Three dogs had severe anemia: 1 had Coombs'-positive anemia (PCV, 13.8%) and 2 had gastrointestinal tract hemorrhage (PCV, 15 and 16%, respectively). The other dog was mildly anemic (PCV, 33%). Six of 14 dogs with PCV within the reference range were treated with fluids and 5 were found to have a mild normocytic, normochromic anemia after rehydration. Another of the 14 dogs was initially not treated in the hospital, but had developed a mild anemia 1 month later at the time of diagnosis. The median lowest PCV for all 18 dogs was 33.6% (range, 13.8 to 55.5%).

Five dogs had > 17,000 WBC/mm^3, with the highest counts in 2 dogs that had aspiration pneumonia and possible sepsis (41,200 and 22,900 WBC/mm^3, respectively; Table 1). Another of the 5 dogs had a mild increase in band cells (378 cells/mm^3; reference range, 0 to 378 cells/mm^3).

None of the dogs had absolute lymphocytosis and only 1 had a relative lymphocytosis (37% of the WBC were lymphocytes). Lymphocyte count was within the reference range in 15 dogs, and 3 dogs had lymphopenia (< 1,000 cells/mm^3). Likewise, eosinophil count was within the reference range in 11 dogs, 3 dogs had eosinophilia (> 1,250 cells/mm^3), and 4 dogs were eosinopenic (< 100 cells/mm^3).

Table 1—Laboratory findings in dogs with glucocorticoid-deficient hypoadrenocorticism

Variable	Median	Range	Reference
RBC X 10^6	6.04	1.97–8.08	5.00–8.00
Hb (g/dl)*	14.30	4.30–13.50	12.00–18.00
PCV (%)	39.90	13.80–55.50	37.00–54.00
Lowest value†	33.60	13.80–55.50	37.00–54.00
WBC/mm^3	13,250.00	5,100–41,200	6,000–17,000
Neutrophils/mm^3	10,696.00	2,754–40,376	3,000–11,500
Lymphocytes/mm^3	1,850.00	342.00–4,122	1,000–4,800
Eosinophils/mm^3	297.00	0.00–1,620	100.00–1,250
Total CO_2 (mmol/L)*	22.40	17.00–30.20	13.00–26.00
Cholesterol (mg/dl)*	116.00	25.00–355.00	150.00–250.00
Total protein (g/dl)	6.30	2.90–8.50	5.70–7.00
Albumin (g/dl)	2.60	1.40–4.50	2.70–3.60
Glucose (mg/dl)	90.60	20.00–125.00	65.00–135.00
ALT (U/L)	52.00	17.00–171.00	13.00–57.00
AP (U/L)	66.00	24.00–502.00	35.00–169.00
Calcium (mg/dl)	9.80	7.30–13.20	8.00–11.00
BUN (mg/dl)	18.50	4.00–42.00	7.00–27.00
Creatinine (mg/dl)	1.20	0.70–8.20	0.10–1.20
Na^+ (mmol/L)	145.50	130.00–156.00	135.00–155.00
K^+ (mmol/L)	4.40	2.90–5.00	3.50–5.50

*n = 17; otherwise, n = 18. †After rehydration or on follow-up examination.
Hb = hemoglobin; ALT = alanine transferase; AP = alkaline phosphatase.

Low serum cholesterol concentration was found in 13 of 17 dogs (Table 1). Serum total protein was less than the reference range in 4 dogs, and 10 dogs had serum albumin concentrations less than the reference range (< 2.7 g/dl). Six dogs were hypoglycemic (< 65 mg/dl) at admission. Six dogs had mildly high serum alanine transferase activity, and 2 dogs had mildly high serum alkaline phosphatase activity. Only 1 dog had hypercalcemia (13.2 mg/dl). All dogs had total CO_2 concentration within reference ranges.

Five dogs had high BUN concentration on admission, and 4 had high serum creatinine concentration; 3 dogs had high BUN and creatinine concentration. Four of these dogs (2 with high creatinine, 4 with high BUN concentration) were treated with fluids, and in all 4, serum BUN and creatinine concentrations decreased to reference ranges within 72 hours. Urine specific gravity was 1.040 in 1 dog with azotemia, 1.017 to 1.020 in 3 others. Obtaining pretreatment urine specific gravities for the other dogs was not possible.

Sodium:potassium ratios ranged from 28 to 47.9 (median, 33.3). One dog had a mildly low serum sodium concentration (130 mmol/L; reference range, 135 to 155 mmol/L), and 1 had a low serum potassium concentration (2.9 mmol/L; reference range, 3.5 to 5.5 mmol/L). Mean sodium and potassium concentrations were well within reference ranges.

Tests of adrenal function confirmed hypoadrenocorticism, with mean baseline serum cortisol concentrations of 0.77 (range, < 0.5 to 2.3 µg/dl), and mean poststimulation concentrations of 1.4 (range, < 0.5 to 4.4 µg/dl). Of the 6 dogs that were tested, 2 had antinuclear antibody titers of 1:80. Antiacetylcholine receptor antibody titers were measured in 4 dogs with

megaesophagus, and 1 had results (27.2 nmol/L; reference range, < 0.6 nmol/L) indicative of concurrent myasthenia gravis. Of 4 dogs tested, 2 had an inadequate response to thyroid stimulating hormone, suggestive of hypothyroidism. Another dog had a low baseline serum thyroxine concentration (0.9 µg/dl; reference range, 1.5 to 4 µg/dl). One dog was admitted with severe anemia (PCV, 13.8%) and had positive results for RBC antibodies (IgG) on a direct Coombs' test, indicative of immune-mediated hemolytic anemia.

Diagnostic imaging findings—Of the 11 dogs in which thoracic radiography was performed, 4 had evidence of megaesophagus. Two of these dogs had concurrent aspiration pneumonia. Abdominal ultrasonography revealed lymphadenopathy in 4 of the 13 dogs examined. Two of the dogs were believed to have small adrenal glands, although measurements were not obtained.

Results from other procedures—Esophagogastroduodenoscopy performed in 2 dogs revealed that both had gastric erosions and 1 had concurrent duodenitis. Three dogs underwent exploratory laparotomy. One dog had chronic bloating, and the only abnormalities seen at surgery were dilated small intestines (gas filled), dilated lymphatics from the small intestine, and a decreased pyloric diameter. Another dog had a gastric ulcer. At surgery, multiple erosions were seen, as well as a 3-cm-diameter ulcer along the lesser curvature of the stomach. The third dog underwent surgery to explore the cause of worsening icterus and pancreatitis 5 months after the initial diagnosis of hypoadrenocorticism. A cholecystojejunostomy was performed, but further information was not available.

Concurrent diseases—Concurrent diseases were found in 13 dogs. Multiple abnormalities in a single dog were often detected. Four dogs had concurrent megaesophagus, which resolved in 2 dogs with glucocorticoid replacement treatment alone. The other 2 dogs with megaesophagus had aspiration pneumonia, probable sepsis, and concurrent hypothyroidism. One other dog also had concurrent hypothyroidism. Other concurrent diseases included gastrointestinal tract erosions or ulcerations (n = 3), pancreatitis (2), inflammatory bowel disease (2), and lymphangiectasia, mitral valve endocardiosis, Coombs'-positive anemia, urinary tract infection, myasthenia gravis, renal insufficiency, Horner's syndrome, ruptured cranial cruciate ligament, and possible hepatopathy (1 each).

Outcome—Of the 18 dogs, 10 responded well to glucocorticoid supplementation alone (follow-up period, 1 month to 4 years; median, 3.5 months). Two other dogs eventually received mineralocorticoid treatment. One of these 2 dogs was treated by a local veterinarian and was lost to follow-up after 3 weeks (serum electrolyte results during supplementation were unavailable). The other of these 2 dogs developed electrolyte abnormalities 1 month after the original diagnosis, and was additionally treated with mineralocorticoids. That dog was admitted to the emergency service 5 months later, in collapse and with severe hyperkalemia (8.6 mmol/L), and subsequently died. Findings at necropsy included severe diffuse bilateral adrenocortical atrophy, right middle lung lobe bronchopneumonia, and glomerular sclerosis.

Two of the dogs died during hospitalization. Both had megaesophagus, aspiration pneumonia, hypothyroidism, and probable sepsis. One was euthanatized 5 days after admission and the other died after 7 days of hospitalization. Another dog continued to have recurrent vomiting, then developed pancreatitis with icterus and high hepatic-associated enzyme activities. Cholecystojejunostomy and partial pancreatectomy were performed, but the dog was eventually euthanatized because of ongoing health problems. The owners denied necropsy on all 3 of these dogs.

One dog continued to lose weight and lymphangiectasia was eventually diagnosed. The dog with immune-mediated hemolytic anemia was treated with high doses of prednisone (after the ACTH stimulation test was performed). The dog subsequently had negative results on a Coombs' test and the anemia began to resolve after 1 month of treatment, and the dose of prednisone was gradually decreased. This dog was eventually maintained successfully on physiologic doses of corticosteroids. The remaining dog initially improved with prednisone treatment, but was lost to follow-up.

Discussion

Results of previous studies[1-3] suggested that up to 26% of dogs with hypoadrenocorticism may have normal mineralocorticoid function and, therefore, may have serum sodium and potassium concentrations within reference ranges. Although such cases have been reported,[5-7] detailed information about this atypical syndrome in a large group of dogs has not previously been reported.

This study revealed slightly higher prevalence of disease in female dogs. In reports of dogs with mineralocorticoid and glucocorticoid deficiency, approximately 70% of affected dogs are female.[1,3]

Familial hypoadrenocorticism has been reported in Standard Poodles,[8] and in human beings, hypoadrenocorticism is often familial.[9-11] Of the 18 dogs in this study, 3 were Standard Poodles, 1 of which subsequently developed electrolyte abnormalities in addition to the glucocorticoid deficiency. A familial glucocorticoid deficiency, in which a defect at the ACTH receptor or at a proximate postreceptor site in the adrenal membrane is the proposed mechanism, exists in human beings.[12,13]

Our population was young to middle-aged, with most dogs being < 7 years old, which is similar to that reported for typical hypoadrenocorticism in dogs.[1,3] Larger-breed dogs appeared to be predominate in this study, with 14 of 18 dogs > 20 kg.

Glucocorticoids affect every organ of the body. They play a role in the metabolism of glucose, fats, and proteins; they influence hematopoiesis; and they help to maintain vascular integrity.[14] Thus, when glucocorticoids are deficient, multiple systems are affected. The historical signs in this study were primarily vague ones, such as weakness, lethargy, and weight

loss, or gastrointestinal signs such as vomiting and diarrhea. These findings are similar to those of previous reports in dogs and human beings with typical and atypical hypoadrenocorticism.[1-3,5,15,16] Additionally, 4 of the dogs in this study were admitted with regurgitation secondary to megaesophagus. Three dogs were admitted with acute collapse, caused by profound hypoglycemia, or in hemorrhagic shock because of acute gastrointestinal tract hemorrhage. Despite the collapse, typical of classic hypoadrenocorticism, these dogs had electrolyte concentration within reference ranges and their respective conditions (hypoglycemia and bleeding) most likely resulted from glucocorticoid deficiency.

In dogs, experimental studies revealed that sudden withdrawal of corticosteroid influence leads to a decrease in migrating motor complexes, and therefore, decreased gastrointestinal tract motility.[17] Increases in retrograde giant contractions and giant migrating contractions also were documented.[17] These increases, together with decreased migrating motor complexes and decreased gastrointestinal tract motility, may have led to the nausea and vomiting observed in glucocorticoid-deficient dogs.

Glucocorticoids also play a role in the maintenance of vascular tone and blood pressure, and in the distribution of total body water within the intravascular compartment.[18-21] Gastrointestinal tract mucosal hemorrhages and ulcers can develop because of hypovolemia and vascular stasis.[22] Cortisol deficiency may have potentiated these effects on the gastrointestinal tract mucosa, possibly because of compromised vascular integrity, and therefore could have contributed to the tendency toward gastrointestinal tract bleeding in these dogs.[22]

The physical examination findings in these dogs were rather nonspecific. The most common findings included weakness, a tense or apparently painful abdomen, and thin or cachectic body condition. Most dogs were well hydrated, in contrast to those with typical hypoadrenocorticism, in which hypoaldosteronism leads to dehydration and volume depletion. An explanation for the bradycardia seen in 1 of the dogs could not be found, but the dog had been vomiting, so perhaps vagal tone was increased. The dog was treated with fluids IV, but no specific treatment for the bradycardia was instituted and the heart rate was normal within 24 hours. Other physical examination findings reflected concurrent disease processes, rather than hypoadrenocorticism.

Although all of the dogs were ill, the lack of stress leukograms was notable. In earlier studies,[5] lymphocytosis and eosinophilia were common findings in dogs with hypoadrenocorticism. Our results were similar to those from subsequent studies in which lymphocytosis and eosinophilia were inconsistently seen.[1,3,14] None of our dogs had lymphocytosis, and 13 of 18 had eosinophil counts within reference ranges. A stressed dog would be expected to have low lymphocyte and eosinophil counts. Cortisol deficiency, however, results in an inability to mount an adequate stress response, thus leading to the lymphocyte and eosinophil counts observed in many of the dogs in this study.

Glucocorticoids have several effects on erythropoiesis. They play a permissive role for the heme synthesis enzyme, delta-aminolevulinic acid,[23] and they enhance the effect of erythropoietin in adrenalectomized animals.[15] Therefore, we would expect a decrease in glucocorticoids to lead to bone marrow inhibition, resulting in normocytic, normochromic, nonregenerative anemia. Only 4 of the dogs were anemic on admission, but mild anemia was often evident after IV fluid treatment in those dogs with marginal hydration status on admission.

Fewer dogs in this study had azotemia than in reports of typical hypoadrenocorticism,[1,3] reflecting the lack of volume depletion with glucocorticoid deficiency, compared with that of mineralocorticoid deficiency. Of the 18 dogs, 5 (28%) had a history of polyuria and polydipsia. Although the cause of polyuria in dogs with hypoadrenocorticism is not well understood, glucocorticoids may be required for a full response to vasopressin by the renal collecting tubules,[24-27] and cortisol seems to play a role in the development and maintenance of medullary hypertonicity.[28] All dogs had total CO_2 concentration within reference ranges, suggesting normal acid-base status.

Glucocorticoids increase gluconeogenesis and decrease the peripheral uptake and use of glucose[14]; thus, lack of glucocorticoids could result in hypoglycemia. In this study, 6 of 18 (33%) dogs were hypoglycemic (serum glucose concentration $<$ 65 mg/dl), and 1 of the 6 had collapsed on admission because of hypoglycemia. In human beings with secondary hypoadrenocorticism (and thus, glucocorticoid deficiency), 32% have hypoglycemia on initial examination.[29]

Serum total protein concentration was markedly low in 1 of the dogs with gastrointestinal tract bleeding, and mildly decreased in 2 others. Serum albumin concentration, however, was low in 10 of 18 (56%) dogs. Possible explanations for hypoalbuminemia include loss via the gastrointestinal tract, anorexia, and loss into the interstitium.

Hypocholesterolemia, which was reported in only 1 dog with glucocorticoid deficiency,[5] was a common finding in this study. Glucocorticoids facilitate fat absorption, and steatorrhea is observed in some people with hypoadrenocorticism.[30] This was not documented in any of our dogs, but subclinical decreases in fat absorption may have contributed to the hypocholesterolemia. In addition, cholesterol is the primary precursor for adrenocortical hormones.[15,31] If adrenal gland synthesis of these hormones is subnormal, there may be a lack of stimulation to absorb cholesterol or to take it up from storage. Adrenocorticotropic hormone is known to increase free cholesterol by increasing cholesterol esterase activity and decreasing cholesteryl synthetase.[31] Low plasma ACTH concentration might, therefore, be associated with decreased cholesterol concentration in animals with secondary hypoadrenocorticism. Further testing to differentiate primary from secondary hypoadrenocorticism would be necessary to ascertain whether ACTH plays a role in cholesterol metabolism in dogs with an altered pituitary-adrenal axis.

In this study, 4 dogs had megaesophagus, which is consistent with previous reports of hypoadrenocor-

ticism in dogs.[6,7,14,32,33] One dog with megaesophagus had a high antiacetylcholine receptor antibody titer; thus, myasthenia gravis may have contributed to the development of megaesophagus in this dog. Two of the dogs with megaesophagus may have had concurrent hypothyroidism. Physiologic quantities of cortisol are needed for muscle strength. Adrenalectomized animals have muscle weakness that is reversed by glucocorticoid supplementation, but not completely restored by mineralocorticoid supplementation.[20,34]

Abdominal ultrasonography revealed lymphadenopathy in 4 of the dogs. One of these dogs and 5 others also had evidence of large tonsils or peripheral lymphadenopathy. One effect of glucocorticoids is to decrease the size and weight of the thymus gland, lymph nodes, spleen, and Peyer's patches.[34] Possible explanations for lymphadenopathy in dogs with hypoadrenocorticism include concurrent disease or infection, translocation of bacteria and endotoxin secondary to gastrointestinal tract mucosal compromise, or lymph nodes that react more readily without the anti-inflammatory effect of glucocorticoids.

Thirteen of the dogs had other diseases in addition to adrenal insufficiency. Some disorders probably developed as a result of glucocorticoid deficiency, such as gastrointestinal tract erosions and megaesophagus. Others, such as hypothyroidism, lymphangiectasia, and pancreatitis, were probably concurrent primary diseases.

By definition, all of our dogs had electrolyte concentrations within reference ranges, a normal Na:K ratio, and an inadequate response to ACTH stimulation. Although the ACTH stimulation test is considered the definitive diagnostic test for hypoadrenocorticism, only cortisol, not aldosterone, reserve is typically tested. Similarly, the ACTH stimulation test does not differentiate primary from secondary disease. Tests that could be used to differentiate primary, secondary, and tertiary disease include measuring endogenous ACTH concentrations, the prolonged ACTH stimulation test, and the corticotropin-releasing hormone stimulation test.[15,35,36]

Although this was a small sample of dogs, some interesting conclusions can be drawn. In absence of serious concurrent disease, long-term glucocorticoid supplementation alone may be an effective treatment. Serum electrolyte concentrations should be monitored to determine whether mineralocorticoid supplementation becomes necessary, but many dogs with this disease did not develop mineralocorticoid insufficiency.

An ACTH stimulation test should be considered as part of the diagnostic plan in dogs with signs such as weight loss, inappetence, and intermittent vomiting or diarrhea, especially when these signs are observed in young, larger-breed dogs. A higher index of suspicion is warranted when the CBC and serum biochemical testing reveal hypocholesterolemia, hypoalbuminemia, or mild anemia. In addition, all dogs with unexplained hypoglycemia, megaesophagus, or gastrointestinal tract hemorrhage should be tested for glucocorticoid deficiency.

[a]Butler ACTH gel, 40 USP unit/ml, The Butler Co, Columbus, Ohio.

[b]GammaGoat [^{125}I] cortisol radioimmunoassay kit, Incstar, Stillwater, Minn.

References

1. Willard MD, Schall WD, McCaw DE, et al. Canine hypoadrenocorticism: report of 37 cases and review of 39 previously reported cases. *J Am Vet Med Assoc* 1982;180:59–62.
2. Schaer M, Chen CL. A clinical survey of 48 dogs with adrenocortical hypofunction. *J Am Anim Hosp Assoc* 1983;19:443–452.
3. Rakich PM, Lorenz MD. Clinical signs and laboratory abnormalities in 23 dogs with spontaneous hypoadrenocorticism. *J Am Anim Hosp Assoc* 1984;20:647–649.
4. Zerbe CA, Refsal KR, Schall WD, et al. Adrenal function in 15 dogs with insulin-dependent diabetes mellitus. *J Am Vet Med Assoc* 1988;193:454–456.
5. Rogers W, Straus J, Chew D. Atypical hypoadrenocorticism in three dogs. *J Am Vet Med Assoc* 1981;179:155–158.
6. Bartges JW, Nielson DL. Reversible megaesophagus associated with atypical primary hypoadrenocorticism in a dog. *J Am Vet Med Assoc* 1992;201:889–891.
7. Bowen D, Schaer M, Riley W. Autoimmune polyglandular syndrome in a dog: a case report. *J Am Anim Hosp Assoc* 1986;22:649–654.
8. Shaker E, Hurvitz AI, Peterson ME. Hypoadrenocorticism in a family of Standard Poodles. *J Am Vet Med Assoc* 1988;192:1091–1092.
9. Baker J. Immunologic aspects of endocrine diseases. *JAMA* 1992;268:2899–2903.
10. Anderson PB, Fein SH, Frey WG III. Familial Schmidt's syndrome. *JAMA* 1980;244:2068–2070.
11. Spinner MW, Blizzard RM, Childs B. Clinical and genetic heterogeneity in idiopathic Addison's disease and hypoparathyroidism. *J Clin Endocrinol* 1968;28:795–804.
12. Thistlethwaite D, Darling JAB, Fraser R, et al. Familial glucocorticoid deficiency. *Arch Dis Child* 1975;50:291–297.
13. Spark RF, Etzkorn JR. Absent aldosterone response to ACTH in familial glucocorticoid deficiency. *N Engl J Med* 1977;297:917–920.
14. Feldman E, Nelson R. *Canine and feline endocrinology and reproduction*. Philadelphia: WB Saunders Co, 1987;144, 195–217.
15. Werbel SS, Ober KP. Acute adrenal insufficiency. *Endocrinol Metabol Clin North Am* 1993;22:303–328.
16. Nerup J. Addison's disease—a review of some clinical, pathological and immunologic features. *Dan Med Bull* 1974;21:201–217.
17. Phillips JD, Stelzner M, Zeng H, et al. Alterations in gastrointestinal motility during postoperative acute corticosteroid withdrawal. *Am J Surg* 1991;162:251–255.
18. Claussen MS, Landercasper J, Cogbill TH. Acute adrenal insufficiency presenting as shock after trauma and surgery: three cases and review of the literature. *J Trauma* 1992;32:94–100.
19. Fritz I, Levine R. Action of adrenal cortical steroids and norepinephrine on vascular responses of stress in adrenalectomized rats. *Am J Physiol* 1951;165:456–465.
20. Ramey ER, Goldstein MS, Levine R. Action of norepinephrine and adrenal cortical steroids on blood pressure and work performance of adrenalectomized dogs. *Am J Physiol* 1951;165:450–455.
21. Swingle WW, Brannick LJ, et al. Effect of glucocorticoid and mineralocorticoid adrenal steroids on fluid and electrolytes of fasted adrenalectomized dogs. *Proc Soc Exp Biol Med* 1957;96:446–452.
22. Medinger TL, Williams DA, Bruyette DS. Severe gastrointestinal tract hemorrhage in three dogs with hypoadrenocorticism. *J Am Anim Hosp Assoc* 1993;202:1869–1872.
23. Lane SE, Gidari AS, Levers RD. Glucocorticoid potentiation of delta-aminolevulinic acid synthetase in chick embryo liver cells: a "permissive" effect. *Biochem Biophys Res Commun* 1977;74:57–63.
24. Brand PH, Higgins JT Jr. Effect of adrenal hormones on water and electrolyte metabolism. In: Mulrow PJ, ed. *The adrenal gland*. New York: Elsevier Science Publishing Co, 1986;201–246.
25. Crow SE, Stockham SL. Profound hyponatremia associated

with glucocorticoid deficiency in a dog. *J Am Anim Hosp Assoc* 1985; 21:303–400.

26. Jamison RL, Oliver RE. Disorders of urinary concentration and dilution. *Am J Med* 1982;72:308–322.

27. Schwartz MJ, Kokko JP. Urinary concentrating defect of adrenal insufficiency: permissive role of adrenal steroids on the hydroosmotic response across the rabbit cortical collecting tubule. *J Clin Invest* 1980;66:234–242.

28. Cooke RC, Steenburg RW. Effects of aldosterone and cortisol on the renal concentrating mechanism. *J Lab Clin Med* 1973; 82:784–792.

29. Yamamoto T, Fukayama J, Hsegawa K, et al. Isolated corticotropin deficiency in adults: report of 10 cases and review of the literature. *Arch Intern Med* 1992;152:1705–1712.

30. Koppers LE, Palumbo PJ. Lipid disturbances in endocrine disorders. *Med Clin North Am* 1972;56:1013–1020.

31. Tyrrell JB, Aron DC, Forsham PH. Glucocorticoids and adrenal androgens. In: Greenspan FS, ed. *Basic and clinical endocrinology*. 3rd ed. East Norwalk, Conn: Appleton & Lange, 1991;323–362.

32. Schaer M, Riley WJ, Buergelt CD, et al. Autoimmunity and Addison's disease in the dog. *J Am Anim Hosp Assoc* 1986;22:789–794.

33. Burrows CF. Reversible mega-oesophagus in a dog with hypoadrenocorticism. *J Small Anim Pract* 1987;28:1073–1078.

34. McPartland RP. Metabolic and pharmacologic actions of glucocorticoids. In: Mulrow PJ, ed. *The adrenal gland*. New York: Elsevier Science Publishing Co, 1986;85–116.

35. Orme SM, Belchetz PE. Isolated ACTH deficiency. *Clin Endocrinol* 1991;35:213–217.

36. Oelkers W, Diederich S, Bahr V. Diagnosis and therapy surveillance in Addison's disease: rapid adrenocorticotropin (ACTH) test and measurement of plasma ACTH, renin activity, and aldosterone. *J Clin Endocrinol Metabol* 1992;75:259–264.

Book Review:
Comparative Physiology of the Vertebrate Digestive System. Second Edition. *By C. Stevens and Ian Hume. 400 pages; illustrated. Press Syndicate of the University of Cambridge, 40 W 20th St, New York, NY 10011-4211. 1995. Price $79.95.*

The first edition of this book was published in 1988. The second edition has been updated to include recent advances in our understanding of the digestive system of vertebrates. The authors have done an excellent job presenting a concise and well-organized approach to comparative physiology of the digestive system.

The textbook contains basic chapters on energy, nutrient requirements, and general aspects of the digestive system of vertebrates. Additional chapters compare general anatomic and physiologic characteristics of the major groups of vertebrates. There also is a comprehensive concluding chapter that summarizes the information and suggests some areas in which research should be pursued.

Many figures and tables provide hard-to-find comparative aspects of vertebrate digestive systems. This book provides excellent information for graduate students in nutrition, physiology, and zoology. This is a physiology textbook and, therefore, will be beneficial in that light. I think this would be an excellent addition to the library of basic scientists and graduate students who are interested in the area of digestive system physiology. This book also may help advanced veterinary students who are pursuing specific interests in gastroenterology. The major strength of this book is the valuable comparative aspects, which would be difficult to find in any other single textbook. The only weakness of this textbook is that it is fairly expensive.

Steven L. Marks, BVsc, MS