

## Supplemental abstracts for Current Concepts in Internal Medicine, 3/16/11

[J Vet Emerg Crit Care \(San Antonio\)](#). 2009 Oct;19(5):484-8.

### Use of thromboelastography in dogs with immune-mediated hemolytic anemia: 39 cases (2000-2008).

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#### Abstract

**OBJECTIVE:** To analyze thromboelastograms (TEGs) of naturally occurring cases of immune-mediated hemolytic anemia (IMHA) in order to identify whether a hypercoagulable state was present and whether its presence was associated with differences in survival.

**DESIGN:** Retrospective study spanning January 2000 to June 2008. Medical records of dogs were evaluated. Endpoints were considered death or discharge from the hospital.

**SETTING:** Academic teaching hospital.

**ANIMALS:** Thirty-nine dogs with a diagnosis of IMHA and at least one TEG performed during hospitalization were included.

**INTERVENTIONS:** None.

**MEASUREMENTS AND MAIN RESULTS:** Four values were evaluated from the TEG: the R time (R), K time (K), alpha angle (alpha), and maximum amplitude. From these values, a coagulation index (CI) was calculated to classify patients as normocoagulable, hypercoagulable, or hypocoagulable. Thirty-three of 39 patients were hypercoagulable based on the CI. The 6 remaining dogs were normocoagulable. The patients with a normocoagulable CI had an increased mortality rate (100%) when compared with the hypercoagulable patients using Fisher's exact test ( $P=0.02$ ). Additionally, prolongation of partial thromboplastin time did not preclude hypercoagulable TEG values.

**CONCLUSIONS:** The majority of dogs with IMHA were hypercoagulable as measured by TEG. A normal CI was associated with a worse outcome in this patient population. TEG may provide additional and complementary information to prothrombin time and partial thromboplastin time relating to coagulation status in dogs with IMHA and may help predict prognosis and potentially guide clinical decisions to utilize anticoagulant drugs.

[J Am Vet Med Assoc](#). 2011 Feb 15;238(4):463-7.

### Identification of hypercoagulability in dogs with primary immune-mediated hemolytic anemia by means of thromboelastography.

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#### Abstract

**Objective-**To evaluate whole blood hemostasis by means of thromboelastography in dogs with primary immune-mediated hemolytic anemia (IMHA) to determine whether these dogs had evidence of hypercoagulability prior to the administration of immunosuppressant medications, blood transfusion products, or anticoagulant agents. **Design-**Evaluation study. **Animals-**11 client-owned dogs admitted to a teaching hospital for management of primary IMHA and 20 clinically normal dogs. **Procedures-**Citrated whole blood samples were obtained from all dogs for performance of kaolin-activated thromboelastography. Citrated plasma was harvested from blood samples of dogs with IMHA for plasma-based coagulation testing, including activated partial thromboplastin time, prothrombin time, D-dimer concentration, fibrinogen concentration, and antithrombin activity. **Results-**Compared with control dogs, dogs with primary IMHA had evidence of hypercoagulability as indicated by a significantly lower median (range) clot formation time (0.8 seconds [0.8 to 2.0 seconds] vs 1.9 seconds [1.3 to 3.8 seconds]), higher median angle ( $76.1^\circ$  [ $59.2^\circ$  to  $84.6^\circ$ ] vs  $64.0^\circ$  [ $45.4^\circ$  to  $71.0^\circ$ ]), higher median maximum amplitude (75.9 mm [66.3 to 86.3 mm] vs 55.7 mm [49.9 to 63.6 mm]), and higher median clot strength (15,000 dyne/cm<sup>2</sup> [9,900 to 31,400 dyne/cm<sup>2</sup>] vs 6,100 dyne/cm<sup>2</sup> [4,900 to 8,700 dyne/cm<sup>2</sup>]). **Conclusions and Clinical Relevance-**Dogs with primary IMHA had hypercoagulability as demonstrated by thromboelastography at the time of initial diagnosis and prior to treatment. Such hypercoagulability may be a precursor to clinically evident thrombosis as a complication of the disease process.

<http://avmajournals.avma.org/doi/full/10.2460/javma.238.4.463?prevSearch=allfield%253A%2528imha%2529&searchHistoryKey=>

[J Am Vet Med Assoc](#). 2005 Jun 1;226(11):1869-80.

### Evaluation of prognostic factors, survival rates, and treatment protocols for immune-mediated hemolytic anemia in dogs: 151 cases (1993-2002).

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#### Abstract

**OBJECTIVE:** To evaluate prognostic factors, survival, and treatment protocols for immune-mediated hemolytic anemia (IMHA) in dogs.

**DESIGN:** Retrospective study.

**ANIMALS:** 151 dogs with IMHA not associated with underlying infectious or neoplastic disease.

**PROCEDURE:** Information recorded from review of medical records included signalment at the time of initial evaluation; vaccination history; 30-, 60-, and 365-day follow-up outcomes; laboratory data; results of imaging studies; and necropsy findings. Dogs were grouped according to the presence of spherocytes, autoagglutination, a regenerative erythrocyte response, and treatments received

(azathioprine, azathioprine plus ultralow-dose aspirin, azathioprine plus mixed-molecular-weight heparin [mHEP], or azathioprine plus ultralow-dose aspirin plus mHEP) for comparisons. All dogs received glucocorticoids.

**RESULTS:** Cocker Spaniels, Miniature Schnauzers, neutered dogs, and female dogs were overrepresented. Alterations in certain clinicopathologic variables were associated with increased mortality rate. Rates of survival following treatment with azathioprine, azathioprine plus ultralow-dose aspirin, azathioprine plus mHEP, and azathioprine plus ultralow-dose aspirin plus mHEP were 74%, 88%, 23%, and 70%, respectively, at hospital discharge; 57%, 82%, 17%, and 67%, respectively, at 30 days; and 45%, 69%, 17%, and 64%, respectively, at 1 year. In comparison, mean survival rates at discharge and at 30 days and 1 year after evaluation collated from 7 published reviews of canine IMHA were 57%, 58%, and 34%, respectively.

**CONCLUSIONS AND CLINICAL RELEVANCE:** Treatment with a combination of glucocorticoids, azathioprine, and ultralow-dose aspirin significantly improved short- and long-term survival in dogs with IMHA.

PMID: 15934255 [PubMed - indexed for MEDLINE]

<http://avmajournals.avma.org/doi/pdf/10.2460/javma.2005.226.1869>

[J Vet Intern Med.](#) 2010 May-Jun;24(3):597-605. Epub 2010 Apr 6.

## Treatment of immune-mediated hemolytic anemia with individually adjusted heparin dosing in dogs.

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### Abstract

**BACKGROUND:** A major cause of death in dogs with immune-mediated hemolytic anemia (IMHA) is thromboembolism. Previous studies suggest unfractionated heparin (UH) is not effective in preventing thromboembolism in IMHA; however, subtherapeutic dosing could explain the seeming lack of efficacy.

**HYPOTHESIS:** Providing therapeutic plasma concentration of UH by individually adjusting doses based on antifactor Xa activity would improve survival in IMHA.

**ANIMALS:** Fifteen dogs with primary IMHA.

**METHODS:** Randomized, prospective, controlled clinical trial. Dogs received standardized therapy for IMHA and either constant dose (CD) (150 U/kg SC) (n = 7) or individually adjusted dose (IAD) (n = 8) UH, monitored via an anti-Xa chromogenic assay, adjusted according to a nomogram. UH was administered every 6 hours until day 7, and every 8 hours thereafter. UH dose was adjusted daily in IAD dogs until day 7, weekly until day 28, then tapered over 1 week. Dogs were monitored for 180 days.

**RESULTS:** At day 180, 7 dogs in the IAD group and 1 in the CD group were alive (P = .01). Median survival time for the IAD group was >180 days, and 68 days for the CD group. Thromboembolic events occurred in 5 dogs in the CD group and 2 dogs in the IAD group. Doses of UH between 150 and 566 U/kg achieved therapeutic anti-Xa activity (0.35-0.7 U/mL).

**CONCLUSIONS AND CLINICAL IMPORTANCE:** This study suggests that IAD UH therapy using anti-Xa monitoring reduced case fatality rate in dogs with IMHA when compared with dogs receiving fixed low dose UH therapy.

PMID: 20384956 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2011 Jan-Feb;25(1):71-5. doi: 10.1111/j.1939-1676.2010.0656.x. Epub 2010 Dec 13.

## A prospective study of clopidogrel therapy in dogs with primary immune-mediated hemolytic anemia.

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### Abstract

**BACKGROUND:** A major cause of death in dogs with primary immune-mediated hemolytic anemia (pIMHA) is thrombotic disease. Ultralow-dose aspirin (ULDA) is commonly used to prevent thrombosis in dogs with pIMHA; however, the efficacy of antiplatelet agents in dogs with pIMHA is unknown.

**HYPOTHESIS:** The use of clopidogrel (CL), alone or in combination with ULDA, would improve survival to discharge and at 90 days without important adverse effects compared with ULDA alone in dogs with pIMHA treated with standard immunosuppressive therapy.

**ANIMALS:** Twenty-four client-owned dogs with pIMHA.

**METHODS:** Prospective, positive-controlled, unmasked clinical trial with dogs randomized in 3 treatment groups to receive PO ULDA or CL or both.

**RESULTS:** There was no identifiable adverse reaction, evidence of hemorrhage, or increase in transfusion requirements associated with CL therapy, either alone or combined with ULDA, compared with ULDA alone. There was no significant difference between treatment groups with respect to survival to discharge and at 90 days.

**CONCLUSIONS AND CLINICAL IMPORTANCE:** This study suggests that CL therapy, alone or in combination with ULDA, was safe and had similar short-term survival compared with ULDA alone in a small group of dogs with pIMHA able to tolerate oral medications and treated with standard immunosuppressive treatment.

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PMID: 21155892 [PubMed - in process]

Survival at discharge 90-day survival, hospitalization time, PRBC transfusion, hematologic response, evidence of hemorrhage, evidence of thrombosis, vomiting, diarrhea, relapse

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## Use of serum concentrations of interleukin-18 and monocyte chemoattractant protein-1 as prognostic indicators in primary immune-mediated hemolytic anemia in dogs.

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### Abstract

**BACKGROUND:** The cytokine response in immune-mediated hemolytic anemia (IMHA) is poorly characterized and correlation with outcome is unknown.

**HYPOTHESIS/OBJECTIVES:** To determine if cytokine activity is correlated with outcome in dogs with IMHA.

**ANIMALS:** Twenty dogs with primary IMHA and 6 control dogs.

**METHODS:** Prospective study on dogs with IMHA with blood sampling at admission. Serum activity of interleukin-2 (IL-2), IL-4, IL-6, IL-7, IL-8, IL-10, IL-15, IL-18, monocyte chemoattractant protein-1 (MCP-1), granulocyte-macrophage colony stimulating factor (GM-CSF), interferon-inducible protein-10, interferon-gamma, and keratinocyte chemoattractant (KC) was assessed.

**RESULTS:** Thirty-day case fatality rate was 25% (5/20 dogs). Increased concentrations (median [range]) of IL-2 (45.5 ng/L [0;830] versus 0 ng/L [0;46.8]), IL-10 (8.2 ng/L [0;60.6] versus 0 ng/L [0;88.2]), KC (1.7 µg/L [0.3;4.7] versus 0.5 µg/L [0.2;1.1]), and MCP-1 (162 ng/L [97.6;438] versus 124 ng/L [90.2;168]) were observed in dogs with IMHA compared with controls. The cytokine profile was indicative of a mixture of pro- and anti-inflammatory cytokines of various cellular origins. Cytokines/chemokines strongly associated with macrophage/monocyte activation and recruitment were significantly increased in nonsurvivors compared with survivors; IL-15 (179 ng/L [48.0;570] versus 21.3 ng/L [0;193]), IL-18 (199 ng/L [58.7;915] versus 37.4 ng/L [0;128]), GM-CSF (134 ng/L [70.0;863] versus 57.6 ng/L [0;164]), and MCP-1 (219 ng/L [135;438] versus 159 ng/L [97.6;274]), respectively. Logistic regression suggested increased IL-18 and MCP-1 concentrations were independently associated with mortality in this population ( $P < .05$ , Wald's type 3).

**CONCLUSIONS AND CLINICAL IMPORTANCE:** A mixed cytokine response is present in dogs with IMHA and mediators of macrophage activation and recruitment might serve as prognostic indicators.

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[J Vet Intern Med.](#) 2009 Sep-Oct;23(5):1071-8. Epub 2009 Aug 5.

## A prospective, randomized, double-blinded, placebo-controlled study of human intravenous immunoglobulin for the acute management of presumptive primary immune-mediated thrombocytopenia in dogs.

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### Abstract

**BACKGROUND:** Immune-mediated thrombocytopenia (IMT) is a common hematologic disorder in dogs. Human intravenous immunoglobulin (hIVIG) may have a beneficial effect in canine IMT.

**HYPOTHESIS:** A single hIVIG infusion (0.5 g/kg) in dogs with presumed primary IMT (pIMT) is a safe adjunctive emergency treatment to accelerate platelet count recovery and shorten hospitalization time without increasing the cost of patient care.

**ANIMALS:** Eighteen client-owned dogs with a presumptive diagnosis of pIMT.

**METHODS:** Prospective, randomized, double-blinded, placebo-controlled clinical trial.

**RESULTS:** There were no identifiable immediate or delayed adverse reactions associated with hIVIG administration over a 6-month period. The median platelet count recovery time for the hIVIG group was 3.5 days (mean + or - SD: 3.7 + or - 1.3 days; range, 2-7 days) and 7.5 days (mean + or - SD: 7.8 + or - 3.9 days; range, 3-12 days) for the placebo group. The median duration of hospitalization for hIVIG group was 4 days (mean + or - SD: 4.2 + or - 0.4 days; range, 2-8 days) and 8 days (mean + or - SD: 8.3 + or - 0.6 days; range, 4-12 days) for the placebo group. There was no significant difference between groups with respect to expense of initial patient care, whereas significant reduction in platelet count recovery time ( $P = .018$ ) and duration of hospitalization ( $P = .027$ ) were detected in the hIVIG group.

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Compared with corticosteroids alone, adjunctive emergency therapy of a single hIVIG infusion was safe and associated with a significant reduction in platelet count recovery time and duration of hospitalization without increasing the expense of medical care in a small group of dogs with presumed pIMT.

PMID: 19674280 [PubMed - indexed for MEDLINE]

[J Vet Emerg Crit Care \(San Antonio\).](#) 2009 Apr;19(2):158-64.

## Use of human immunoglobulin in addition to glucocorticoids for the initial treatment of dogs with immune-mediated hemolytic anemia.

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### Abstract

**OBJECTIVE:** To determine the utility of human intravenous immunoglobulin (hIVIG) for the initial treatment of canine immune-mediated hemolytic anemia (IMHA).

**DESIGN:** Blinded, randomized, clinical trial.

**SETTING:** Veterinary teaching hospital.

**ANIMALS:** Twenty-eight, client-owned dogs with primary IMHA.

**INTERVENTIONS:** At enrollment, after diagnosis of IMHA, dogs were randomly assigned to receive either hIVIG or placebo, in a blinded fashion. For the next 14 days, all dogs received glucocorticoids as the sole immunosuppressant agent. All dogs received low-molecular-weight heparin as an anticoagulant. D-dimer concentrations were evaluated at the beginning and end of the study protocol to monitor for thromboembolic complications.

**MEASUREMENTS AND MAIN RESULTS:** Twenty-five of 28 dogs (89%) were discharged from the hospital. Thirteen of those received hIVIG and 12 received placebo. Twenty-four dogs (86%) were alive 14 days after enrollment, and of these 13 received hIVIG and 11 received placebo. D-dimer concentrations were elevated in 86% of all dogs at the time of diagnosis.

**CONCLUSIONS:** For initial treatment of dogs with IMHA, the addition of hIVIG to corticosteroid treatment did not improve initial response, nor did it shorten hospitalization.

PMID: 19691566 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2009 Nov-Dec;23(6):1164-9.

## Prothrombotic and inflammatory effects of intravenous administration of human immunoglobulin G in dogs.

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### Abstract

**BACKGROUND:** Intravenous administration of human immunoglobulin G (hIVIgG) has been suggested to potentiate thromboembolism in dogs, but supportive scientific reports are lacking. Objectives: To determine if hIVIgG therapy promotes hypercoagulability and inflammation in dogs.

**ANIMALS:** Twelve healthy Beagle dogs.

**METHODS:** Prospective, experimental trial. An hIVIgG/saline solution was infused IV at 1 g/kg BW over 8 hours to 6 dogs, and physiological saline was infused to the other 6 dogs. Blood samples were drawn before, during, and after infusion for serial measurement of indicators of coagulation and inflammation. Data were analyzed by 2-way repeated measures analysis of variance.

**RESULTS:** Dogs administered hIVIgG developed mildly decreased blood platelet concentrations without thrombocytopenia (median,  $200 \times 10^3/\mu\text{mL}$ ; range,  $150\text{-}302 \times 10^3/\mu\text{mL}$ ;  $P < .01$ ), leukopenia (median,  $3.5 \times 10^3/\mu\text{mL}$ ; range,  $20\text{-}62 \times 10^3/\mu\text{mL}$ ;  $P < .001$ ), and mildly increased plasma total protein concentrations (median, 6.3 g/dL; range, 5.6-6.7 g/dL;  $P < .001$ ). Administration of hIVIgG was also associated with increases in fibrin/fibrinogen degradation products in all dogs (either 5 microg/mL or 10 microg/dL), thrombin-antithrombin III complexes (median, 7.2 ng/mL; range, 4.9-14.2 ng/mL;  $P < .001$ ), and C-reactive protein concentrations (median, 2.5 mg/dL; range, 0.5-4.3 mg/dL;  $P < .01$ ).

**CONCLUSION AND CLINICAL IMPORTANCE:** Administration of hIVIgG to dogs promotes hypercoagulability and an inflammatory state. This should be further evaluated and considered when using hIVIgG in dogs with IMHA or other prothrombotic conditions.

PMID: 19909427 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Jul-Aug;24(4):819-24. Epub 2010 May 11.

## Antimicrobial resistance impacts clinical outcome of granulomatous colitis in boxer dogs.

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### Abstract

**BACKGROUND:** Escherichia coli have recently been identified within the colonic mucosa of Boxer dogs with granulomatous colitis (GC). Eradication of invasive E. coli is associated with clinical and histological remission.

**OBJECTIVES:** To determine antimicrobial susceptibility profiles of E. coli strains from GC and healthy dogs, and the association of antimicrobial resistance with clinical outcome.

**ANIMALS:** Fourteen Boxer dogs with GC and 17 healthy pet dogs.

**METHODS:** Prospective study: E. coli was cultured from GC biopsies and rectal mucosal swabs of healthy dogs. Individual strains were selected by phylogroup and overall genotype, determined by triplex- and random amplified polymorphic DNA-polymerase chain reaction respectively. Antimicrobial susceptibility was determined by broth microdilution minimal inhibitory concentration.

**RESULTS:** Culture yielded 23 E. coli strains from GC (1-3/dog, median 2) and 34 strains from healthy (1-3/dog, median 2). E. coli phylogroups were similar ( $P = .18$ ) in GC (5A, 7B1, 5B2, 6D) and healthy (2A, 10B1, 15B2, 7D). Resistance to ampicillin, amoxicillin-clavulanate, cefoxitin, tetracycline, trimethoprim-sulfa (TMS), ciprofloxacin, and chloramphenicol was greater ( $P < .05$ ) in GC (21-64%) than healthy (0-24%). Enrofloxacin resistant E. coli were isolated from 6/14 GC versus 0/17 healthy ( $P = .004$ ). Of the enrofloxacin resistant cases, 4/6 were also resistant to macrophage-penetrating antimicrobials such as chloramphenicol, rifampicin, and TMS. Enrofloxacin treatment before definitive diagnosis was associated with antimicrobial resistance ( $P < .01$ ) and poor clinical outcome ( $P < .01$ ).

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Antimicrobial resistance is common among GC-associated E. coli and impacts clinical response. Antimicrobial therapy should be guided by mucosal culture and antimicrobial susceptibility testing rather than empirical wisdom.

PMID: 20492483 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Jul-Aug;24(4):850-4. Epub 2010 Apr 16.

## Clinical efficacy of sildenafil in treatment of pulmonary arterial hypertension in dogs.

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### Abstract

**BACKGROUND:** Pulmonary arterial hypertension (PAH) in dogs carries a poor prognosis. Sildenafil increases exercise capacity and improves hemodynamics in people with PAH.

**HYPOTHESIS/OBJECTIVES:** Dogs receiving sildenafil will have lower pulmonary arterial pressure, increased exercise capacity, and better quality of life (QOL) than dogs receiving placebo.

**ANIMALS:** Thirteen dogs with echocardiographic evidence of PAH.

**METHODS:** Prospective short-term, randomized, placebo controlled, double-blind, crossover study. Dogs with PAH were randomly allocated to receive sildenafil or placebo for 4 weeks, followed by the alternative treatment for 4 weeks.

**RESULTS:** Dogs receiving sildenafil had a significantly lower estimated pulmonary arterial pressure (median, 56 mmHg; range, 34-83 mmHg) than at baseline (median, 72 mmHg; range, 61-86 mmHg;  $P=.018$ ), but not significantly lower than those receiving placebo (median, 62 mmHg; range, 49-197 mmHg). Exercise capacity was significantly greater in dogs receiving sildenafil than those receiving placebo (mean activity count per minute:  $101\pm 47$  versus  $74\pm 32$ ;  $P=.05$ ). QOL scores were significantly higher in dogs receiving sildenafil than dogs receiving placebo.

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Sildenafil decreases systolic pulmonary arterial pressure from baseline in dogs with PAH and is associated with increased exercise capacity and QOL when compared to treatment with placebo.

PMID: 20412435 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Sep-Oct;24(5):1086-92. doi: 10.1111/j.1939-1676.2010.0566.x. Epub 2010 Jul 28.

## Association of iatrogenic hypothyroidism with azotemia and reduced survival time in cats treated for hyperthyroidism.

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### Abstract

**BACKGROUND:** Iatrogenic hypothyroidism can occur after treatment of hyperthyroidism, and is correlated with a reduced glomerular filtration rate in humans and dogs.

**HYPOTHESIS:** Cats with iatrogenic hypothyroidism after treatment for hyperthyroidism will have a greater incidence of azotemia than euthyroid cats.

**ANIMALS:** Eighty client owned cats with hyperthyroidism.

**METHODS:** Two retrospective studies. (1) Longitudinal study of 12 hyperthyroid cats treated with radioiodine (documented as euthyroid after treatment), to assess changes in plasma thyroid stimulating hormone (TSH) concentration over a 6-month follow-up period, (2) Cross-sectional study of 75 hyperthyroid cats (documented as euthyroid) 6 months after commencement of treatment for hyperthyroidism to identify the relationship between thyroid status and the development of azotemia. Kaplan-Meier survival analysis was performed to identify relationships between thyroid and renal status and survival.

**RESULTS:** Plasma TSH concentrations were not suppressed in 7 of 8 cats with hypothyroidism 3 months after radioiodine treatment. The proportion of cats with azotemia was significantly ( $P=.028$ ) greater in the hypothyroid (16 of 28) than the euthyroid group (14 of 47). Twenty-eight of 41 cats (68%) with plasma TT4 concentration below the laboratory reference range had an increased plasma TSH concentration. Hypothyroid cats that developed azotemia within the follow-up period had significantly ( $P=.018$ ) shorter survival times (median survival time 456 days, range 231-1589 days) than those that remained nonazotemic (median survival time 905 days, range 316-1869 days).

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Iatrogenic hypothyroidism appears to contribute to the development of azotemia after treatment of hyperthyroidism, and reduced survival time in azotemic cats.

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PMID: 20695989 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Jul-Aug;24(4):863-9.

## Survival and the development of azotemia after treatment of hyperthyroid cats.

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### Abstract

**BACKGROUND:** Hyperthyroidism complicates the diagnosis of chronic kidney disease (CKD) as it increases glomerular filtration rate. No practical and reliable means for identifying those cats that will develop azotemia after treatment for hyperthyroidism has been identified. Hyperthyroidism is associated with proteinuria. Proteinuria has been correlated with decreased survival of cats with CKD and with progression of CKD.

**HYPOTHESIS:** Proteinuria and other clinical parameters measured at diagnosis of hyperthyroidism will be associated with the development of azotemia and survival time.

**ANIMALS:** Three hundred client owned hyperthyroid cats treated in first opinion practice.

**METHODS:** Retrospective, cohort study relating clinical parameters in hyperthyroid cats at diagnosis to the development of azotemia within 240 days of diagnosis and survival time (all cause mortality). Multivariable logistic regression analysis was used to identify factors

that were predictive of the development of azotemia. Multivariable Cox regression analysis was used to identify factors associated with survival.

**RESULTS:** Three hundred cats were eligible for survival analysis and 216 cats for analysis of factors associated with the development of azotemia. The median survival time was 417 days, and 15.3% (41/268) cats developed azotemia within 240 days of diagnosis of hyperthyroidism. Plasma concentrations of urea and creatinine were positively correlated with the development of azotemia. Plasma globulin concentration was negatively correlated with the development of azotemia. Age, urine protein:creatinine ratio, and the presence of hypertension were significantly correlated with decreased survival time. Urine specific gravity and PCV were significantly correlated with increased survival time.

**CONCLUSIONS AND CLINICAL IMPORTANCE:** The proteinuria associated with hyperthyroidism is not a mediator of progression of CKD; however, it does correlate with all cause mortality.

PMID: 20649748 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Jul-Aug;24(4):870-4. Epub 2010 Jun 18.

## Pharmacodynamics of insulin detemir and insulin glargine assessed by an isoglycemic clamp method in healthy cats.

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### Abstract

**BACKGROUND:** Insulin detemir and insulin glargine are synthetic long-acting insulin analogs. In people, insulin glargine is longer acting and has a relatively flat time-action profile, while insulin detemir has significantly less within-subject variability. Insulin detemir is also associated with less undesired weight gain and decreased frequency of hypoglycemic events.

**OBJECTIVES:** To compare the pharmacodynamics of insulin detemir and insulin glargine in healthy cats.

**ANIMALS:** Ten young, healthy, neutered, purpose-bred cats.

**METHODS:** Randomized, cross-over design. Pharmacodynamics of insulin detemir and insulin glargine were determined by the isoglycemic clamp method after a 0.5 U/kg SC injection.

**RESULTS:** The only significant difference in the pharmacodynamics of insulin detemir and insulin glargine was onset of action (1.8+/-0.8 and 1.3+/-0.5 hours for insulin detemir and insulin glargine, respectively, P=.03). End of action of insulin detemir was reached at 13.5+/-3.5 hours and for insulin glargine at 11.3+/-4.5 hours (P=.18). Time-to-peak action of insulin detemir was reached at 6.9+/-3.1 hours and for insulin glargine at 5.3+/-3.8 hours (P=.7). The time-action curves of both insulin analogs varied between relatively flat curves in some cats and peaked curves in others.

**CONCLUSION AND CLINICAL IMPORTANCE:** Insulin detemir and insulin glargine have shorter durations of action than in people when assessed by the clamp method, but in some cats these insulin analogs could be useful as once-a-day drugs. Peak effects of both insulin analogs are pronounced in some cats.

PMID: 20561185 [PubMed - indexed for MEDLINE]

[J Vet Intern Med.](#) 2010 Nov-Dec;24(6):1314-21. doi: 10.1111/j.1939-1676.2010.0598.x. Epub 2010 Sep 14.

## Predictors of clinical remission in cats with diabetes mellitus.

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### Abstract

**BACKGROUND:** Clinical remission is frequent in cats with well-controlled diabetes mellitus, but few studies explored predictors of this phenomenon.

**HYPOTHESIS:** Data retrieved from medical records at admission might be valuable to identify likelihood of remission and its duration in diabetic cats.

**ANIMALS:** Ninety cats with newly diagnosed diabetes, followed-up until death or remission.

**METHODS:** Retrospective cohort study. Data were collected from records at admission, including history, signalment, physical examination, haematology, and biochemical profile, and the occurrence and duration of remission, defined as normoglycemia without insulin for  $\geq 4$  weeks. Predictors of remission were studied with univariate and multivariate logistic regression. Factors associated with remission duration were analyzed with Kaplan-Meier and Cox proportional hazard models.

**RESULTS:** Forty-five (50%) cats achieved remission, after a median time of 48 days (range: 8-216). By study end, median remission duration was 114 days (range: 30-3,370) in cats that died and 151 days (range: 28-1,180) in alive cats. Remission was more likely with higher age (OR: 1.23, 95% CI: 1.04-1.46; P=.01) and less likely with increased serum cholesterol (OR: 0.36, 95% CI: 0.11-0.87; P=.04). Remission was longer with higher body weight (HR: 0.65, 95% CI: 0.42-0.99; P=.04) and shorter with higher blood glucose (HR: 1.01, 95% CI: 1.00-1.02; P=.02).

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Age, body weight, cholesterol, and glucose levels are suggested for prediction of remission or its duration in diabetic cats. Older cats developing diabetes may have a better outcome, possibly suggesting a slower disease progression.

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## Urinary catecholamine and metanephrine to creatinine ratios in dogs with hyperadrenocorticism or pheochromocytoma, and in healthy dogs.

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### Abstract

**BACKGROUND:** Urinary catecholamines and metanephrines are used for the diagnosis of pheochromocytoma (PHEO) in dogs. Hyperadrenocorticism (HAC) is an important differential diagnosis for PHEO.

**OBJECTIVES:** To measure urinary catecholamines and metanephrines in dogs with HAC.

**ANIMALS:** Fourteen dogs with HAC, 7 dogs with PHEO, and 10 healthy dogs.

**METHODS:** Prospective clinical trial. Urine was collected during initial work-up in the hospital; in dogs with HAC an additional sample was taken at home 1 week after discharge. Parameters were measured using high-pressure liquid chromatography and expressed as ratios to urinary creatinine concentration.

**RESULTS:** Dogs with HAC had significantly higher urinary epinephrine, norepinephrine and normetanephrine to creatinine ratios than healthy dogs. Urinary epinephrine, norepinephrine, and metanephrine to creatinine ratios did not differ between dogs with HAC and dogs with PHEO, whereas the urinary normetanephrine to creatinine ratio was significantly higher ( $P = .011$ ) in dogs with PHEO (414, 157.0-925.0, median, range versus (117.5, 53.0-323.0). Using a cut-off ratio of 4 times the highest normetanephrine to creatinine ratio measured in controls, there was no overlap between dogs with HAC and dogs with PHEO. The variables determined in urine samples collected at home did not differ from those collected in the hospital.

**CONCLUSION AND CLINICAL IMPORTANCE:** Dogs with HAC might have increased concentrations of urinary catecholamines and normetanephrine. A high concentration of urinary normetanephrine (4 times normal), is highly suggestive of PHEO.

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## Efficacy of oral famotidine and 2 omeprazole formulations for the control of intragastric pH in dogs.

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### Abstract

**BACKGROUND:** Little is known about the efficacy of commonly used acid suppressants on intragastric pH in dogs.

**OBJECTIVE:** To compare the effect of oral famotidine, 2 formulations of omeprazole, and placebo on intragastric pH in dogs with a catheter-free, continuous pH monitoring system.

**ANIMALS:** Six healthy adult mixed-breed colony dogs.

**METHODS:** Utilizing a randomized, 4-way cross over, open-label study, dogs were administered famotidine PO (1.0-1.3 mg/kg q12h), omeprazole tablet (1.5-2.6 mg/kg q24h), omeprazole reformulated paste (RP) (Gastrogard, 1.5-2.6 mg/kg q24h), and placebo for 7 days followed by a 10-day washout period. Radiotelemetric pH capsules were placed with gastroscopy assistance to continuously record intragastric pH for 4 days (days 4-7 of dosing). The percentage of time that intragastric pH was  $\geq 3$  and  $\geq 4$  was compared among treatment groups using repeated measures of analysis of variance. Tukey's Studentized range test was used to determine which groups were different with  $\alpha = 0.05$ .

**RESULTS:** Mean  $\pm$  SD percent time intragastric pH was  $\geq 3$  and  $\geq 4$  was  $22 \pm 8\%$  and  $14 \pm 6\%$  for famotidine,  $63 \pm 14\%$  and  $52 \pm 17\%$  for omeprazole tablet,  $54 \pm 17\%$  and  $44 \pm 18\%$  for omeprazole RP, and  $6 \pm 6\%$  and  $5 \pm 5\%$  for placebo. Both omeprazole formulations significantly increased intragastric pH compared with famotidine and placebo, but omeprazole tablet and RP was not significantly different from each other.

**CONCLUSION:** Oral omeprazole tablet and RP provide superior gastric acid suppression to famotidine, and should therefore be considered more effective for the treatment of acid related disorders in dogs.

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## Ivermectin and milbemycin oxime in experimental adult heartworm (*Dirofilaria immitis*) infection of dogs.

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### Abstract

**BACKGROUND:** The US Food and Drug Administration reports an increase in the frequency of reports of lack of effectiveness claims for heartworm (HW) prevention products.

**HYPOTHESIS:** At their labeled doses, single doses of commercially available HW prevention products are not completely effective against all field isolates of HW.

**ANIMALS:** Forty-two HW-free dogs experimentally inoculated with a recent HW field isolate.

**METHODS:** Placebo-controlled, blinded laboratory clinical trial. Dogs randomly allocated to 1 of 3 treatment groups with 14 dogs per group. Groups were untreated control or p.o. dosed with milbemycin oxime (MBO) or ivermectin (IVM). Dogs were inoculated with 50 HW third stage larvae 30 days before dosing and necropsy was performed on Day 123 after treatment to enumerate adult HW.

**RESULTS:** Thirteen of 14 control dogs had adult HW detected at necropsy with a geometric mean worm count of 22.3. One HW was found in 1 dog in each of the MBO and IVM treatment groups.

**CONCLUSIONS AND CLINICAL IMPORTANCE:** Two currently approved macrocyclic lactone HW preventives used at their labeled dose rates were <100% effective against a recent HW field isolate, supporting the hypothesis that the effectiveness of a single dose of these preventives can vary. This is important in guiding clients on expectations of product effectiveness.

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