Update on IMHA in dogs

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Outline

- Introduction and definitions
- Pathogenesis
- Primary vs Secondary
- Diagnosis
- Prognosis
- Treatment

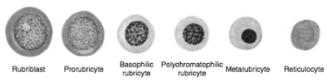
Great (free!) resources

- Balch, A. and A Mackin. Canine IMHA: Pathophysiology, Clinical Signs, and Diagnosis. Compendium 2007, 29:4. (Vetfolio.com)
- Journal of Veterinary Internal Medicine
  - **ALL** articles are **OPEN ACCESS**! ☺
  - Swann, J.W. and Skelly, B.J. (2015), Systematic Review of Prognostic Factors for Mortality in Dogs with Immune-mediated Hemolytic Anemia. Journal of Veterinary Internal Medicine, 29: 7–13.

What is IMHA?

Understanding your RBCs

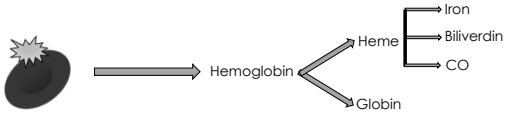
- Primary driver: erythropoietin (EPO) from peritubular renal instertitial cells
  - Need iron for synthesis of Heme
  - Copper for release of Iron from storage
  - Vitamin B6 for first step of heme synthesis



Stevens, A. et al. Veterinary Hematology (2012)

Normal RBC end of life

- Red blood cell (RBC) lifespan: 120 days
  - Humans: 0.05-0.5% turnover daily
- Oxidative injury → phagocytosis by macrophages of mononuclear phagocyte system (spleen, liver, etc.)



Causes of hemolytic anemia

- Intrinsic/Inherited RBC defects
  - Hereditary osmotic fragility
  - Idiopathic Heinz body anemia
  - Methemoglobin-reductase deficiency
  - Phosphofructokinase deficiency (ESS, ACS)
  - Pyruvate kinase deficiency (basenjis)

Causes of hemolytic anemia

- Intrinsic/Inherited RBC defects
- Chemical/toxin injury
  - Zinc (pennies post-1983, diaper cream, sunscreen)
  - Garlic/onion
  - Propylene glycol
  - Methylene blue
  - Castor bean

Causes of hemolytic anemia

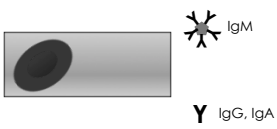
- Intrinsic/Inherited RBC defects
- Chemical/toxin injury
- Other
  - Severe hypophosphatemia (DKA treatment, malnutrition)
  - Snake envenomation

What is IMHA?

- Type II hypersensitivity reaction

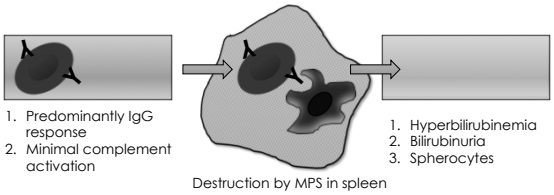
What is IMHA?

- Type II hypersensitivity reaction



What is IMHA?

- Type II hypersensitivity reaction
- Extravascular hemolysis



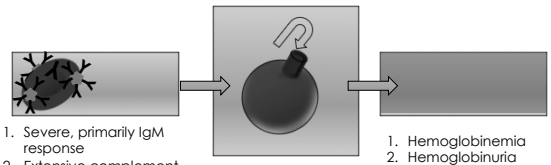
1. Predominantly IgG response
2. Minimal complement activation

1. Hyperbilirubinemia
2. Bilirubinuria
3. Spherocytes

Destruction by MPS in spleen

What is IMHA?

- Type II hypersensitivity reaction
- Intravascular hemolysis



1. Severe, primarily IgM response
2. Extensive complement activation

Membrane attack complex leads to destruction in circulation

1. Hemoglobinemia
2. Hemoglobinuria

Does it really matter?

- Maybe

What causes IMHA?

- The vast majority are primary or autoimmune idiopathic IMHA
  - No identifiable underlying cause

What causes secondary IMHA?

- Response to non-self antigens adhered to or altering RBC membranes
  - Many possible and reported causes

What causes secondary IMHA?

- Infectious
  - *Ehrlichiosis*
  - *Babesiosis*
  - *A. phagocytophilum*
  - *Mycoplasma spp.*
  - *Leptosiprosis*
  - *Dirofilariasis*
  - *Histoplasmosis*

What causes secondary IMHA?

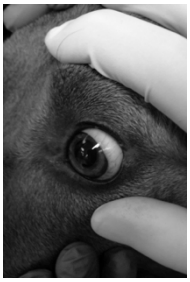
- Infectious
- Neoplastic
  - Lymphoma
  - Hemangiosarcoma
  - Histiocytic disease
  - Diffuse sarcoma
  - Multiple myeloma
  - Other solid tumors

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Acetaminophen
- Cephalosporins
- Heparin
- Penicillins
- Procainamide
- Sulfonamides
- Topical benzocaine
- Vitamin K
- Quinidine

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Other
- Bee-sting envenomation
- Recent vaccination (14-28d)
- Systemic lupus erythematosus



Signalment, History & Clinical signs

How do dogs with IMHA present?

Primary IMHA signalment

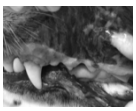
- Any breed possible
  - Cockers, English springer spaniels, poodles, OES, Irish setters, collies
- Females over-represented
- Median age 6yr
- Seasonality?

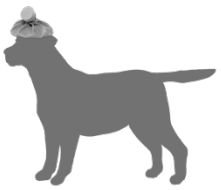
History and clinical signs

- History often indicative of hypoxia and amenia
  - Weakness
  - Collapse
  - Lethargy
  - Anorexia
  - Tachypnea
  - Jaundice

Physical exam findings

Physical exam findings





Physical exam findings

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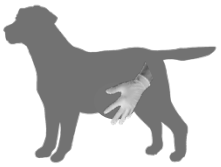

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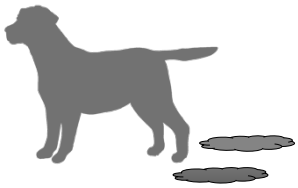

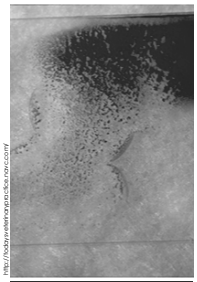

Diagnostics

The long road of rule-outs to primary IMHA

Suggested criteria for diagnosis of primary IMHA

- Severe anemia
- Evidence of hemolysis
- Evidence of immune response
  - Autoagglutination
  - Spherocytosis
  - Positive direct Coomb's test
- Lack of identification of an underlying cause
- Response to therapy

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Criteria #1: Severe Anemia

- How severe?

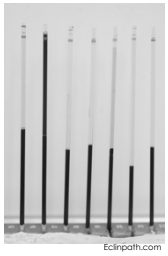
Criteria #1: Severe Anemia

- How severe?
  - 88% of dogs admitted for IMHA had a PCV <20%
  - Of 17 dogs admitted for IMHA
    - Mean PCV 15.7%
    - Range 6-35%

MK Klein et al. JAVMA 1989
E Miller CVT XIV 2009

Criteria #2: Hemolysis evidence

- Intravascular vs extravascular
  - Blood: plasma icteric or hemolyzed



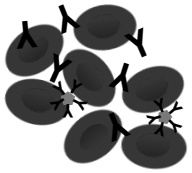
Eclinpath.com

Criteria #2: Hemolysis evidence

- Intravascular vs extravascular
  - Blood: plasma icteric or hemolyzed
  - Urine: hemoglubinuria versus bilirubinuria

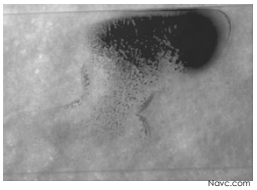
Criteria #3: Immune Response

- Autoagglutination



Criteria #3: Immune Response

- Autoagglutination
- Slide agglutination test
  - 1 drop anticoagulated whole blood + 1 drop physiologic saline



Criteria #3: Immune Response

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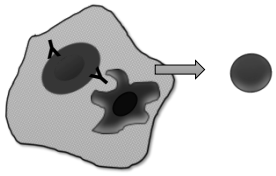
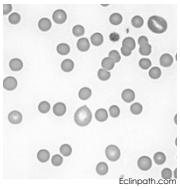


Criteria #3: Immune Response

- Autoagglutination
- Spherocytosis
- Identified in the **majority** of dogs with IMHA
  - Suggestive, not diagnostic



Evaluate a blood smear!

- Should be done for EVERY dog with anemia
- Can be send-out or in-house
- Ability to assess:
  - Retiuculocytosis
  - Polychromasia
  - Anisocytosis
  - Spherocytes
  - nRBCs
  - Blood parasites
  - Platelet count

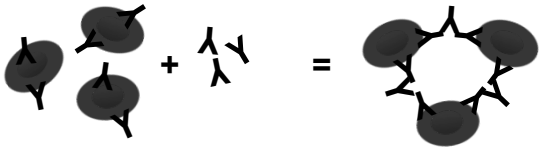
Criteria #3: Immune Response

- Autoagglutination
- Spherocytosis
- Coombs test

Criteria #3: Immune Response

- Autoagglutination
- Spherocytosis
- Coombs test
- Direct Coombs
  - Detects antibodies on patient's RBCs
  - Positive in 66-75% of dogs with IMHA
- Indirect Coombs
  - Detects antibodies in patient's serum

Direct Coombs testing



Patient's washed RBCs | Coombs reagent (antiserum) | Agglutination

Coombs limitations

False Positive

- Post-transfusion
- Non-specific coating
- Storage artifact

False Negative

- Antibody titer too low
- Prior steroid therapy
  - If still having signs, not as big a problem
- Elution of antibody during washing
- Sample aging resulting in antibody loss

What about regeneration?

- Is this anemia regenerative?
  - Dogs >60,000 absolute or greater than 1% corrected
  - Corrected percentage = $\frac{\text{(Patient's PCV x Retic \%)}}{45\%}$
- Approximately 1/3 are not regenerative at diagnosis
- Why?
  - Too early (recall pathway for RBC production)
  - Non-regenerative
    - Not immune-mediated
    - Precursor directed immune response

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- Lack of identification of an underlying cause
- Response to therapy

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Other
- PCR
- Serology
- Culture

Limitations of Serology & PCR

- PCR is highly **specific** (as long as you use a good lab)
  - Negative PCR NEVER rules out infection
  - Negative PCR NEVER rules out infection
- Antibiotic therapy can make PCR negative quickly depending upon organism
- Serology can be affected by time course of disease
  - Acute disease may need convalescent titers
  - Time for the body to mount an immune response
- TIME!
  - Especially applicable for culture (BAPGM)
  - Don't wait, start treatment

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Other
- Chemistry panel
- Urinalysis and culture
- Imaging
  - Thoracic radiographs
  - Abdominal ultrasound
- Don't be surprised if the liver and spleen look unusual

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Other
- History
  - Medications or vaccinations
  - Owner medications
  - Supplements
  - Treats

What causes secondary IMHA?

- Infectious
- Neoplastic
- Drug/toxin
- Other
- History
- ANA
- Bone marrow

Suggested criteria for diagnosis of primary IMHA

- Severe anemia
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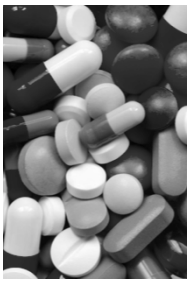


Treatment

Immunosuppressive, supportive care & newly available modalities

Glucocorticoids

- Mainstay of treatment
- Immunosuppressive dose: 2 mg/kg/d (divided)
  - Exception: Large and giant breed dogs
  - Smaller dogs may need higher doses
- Mechanism of action: many!
  - Stabilize cell membranes
  - Decreased T-cell activation and cytotoxicity
  - Suppress cytokine activity and macrophage function

Glucocorticoid dosing

- Prednisone 1-2 mg/kg BID
- Dexamethasone
  - Potency of **7-10x** prednisone
  - Divide dose of prednisone by 7-10
    - 0.1-0.2 mg/kg BID

Glucocorticoids

- Drawbacks: Many!
  - PU/PD/PP
  - Iatrogenic HAC
  - Muscle wasting
  - Lethargy
  - Panting
  - Gastric ulceration

mybullseyeview.com

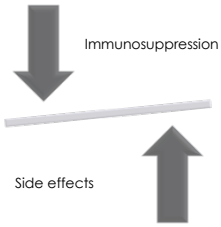
Additional immunosuppressives

- Goal: decrease the amount of prednisone needed
  - Minimize drug side effects
- No study has shown a benefit over prednisone alone in treating IMHA
  - Azathioprine
  - Mycophenolate
  - Cyclophosphamide

N Mason et al JVIM 2003
E Miller CVT XIV 2009

Additional immunosuppressives

- Not all sunshine and roses
  - Adverse effects with other drugs
  - Serious adverse effects with combined immunosuppressive therapies
    - Fungal infection
    - Bacterial infection
    - Marrow suppression
    - Neoplasia



Other immunosuppressives

- Azathioprine
  - Purine analog
    - Metabolized to ribonucleotide monophosphates
    - Incorporation into DNA leads to faulty transcription
  - Dose: 2.2mg/kg SID for 1 week, then q48hr

Other immunosuppressives

- Azathioprine
  - Drawbacks:
    - GI upset most commonly
    - Uncertain levels in all dogs
      - Differences in metabolism by breed
    - Hepatotoxicity
      - 15% of dogs in median 14 days
      - ALT > 2-fold increase
    - Bone marrow suppression
      - Thrombocytopenia or neutropenia in 8%
      - Median onset 53 days

K Wallish and L Trepanier JVIM 2015

Other immunosuppressives

- Azathioprine
  - Drawbacks:
    - Uncertain levels in all dogs
    - Hepatotoxicity
    - Bone marrow suppression
  - Recommendations
    - Check chemistry panels occasionally
    - Recheck full CBC
    - Avoid in dogs with known liver/marrow disease

Other immunosuppressives

- Azathioprine
- Mycophenolate

Other immunosuppressives

- Azathioprine
- Mycophenolate
  - MOA similar to azathioprine
    - Inhibits inosine monophosphate dehydrogenase
    - Affects purine synthesis
    - Developed as an alternative to azathioprine
  - Dose: 10 mg/kg q12h

Mycophenolate mofetil

- Retrospective study
- n=64
  - Mycophenolate n=30, mean dose 20.5 mg/kg q24h
- One dog experienced diarrhea
- Mycophenolate with prednisone has similar efficacy to other combinations
  - Cyclosporine, azathioprine, IVIg
- Prospective study
- n=5, dose 10-15 mg/kg q8h
- All dogs developed diarrhea
  - One euthanized for GI toxicity
  - Two discontinued drug
- 3/5 longterm survival
- Cannot recommend without further studies

KA Creevy et al JSAP 2013
JR Hart et alJVECC 2013

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine

- Calcineurin inhibitor
  - Suppresses T cell function
- Monitoring: Trough whole-blood cyclosporine levels between 400 ng/mL and 600 ng/mL
  - Mississippi State
- Dose: 5 mg/kg PO q12h

Cyclosporine

- Abstract from 1996
  - Effective in combination with prednisone
- Adverse effects
  - GI upset (typically self limiting)
  - Gingival hyperplasia
  - Opportunistic infections
  - Lymphoproliferative disorders
  - Hepatotoxicity
  - Nephrotoxicity

JS Wohl et al JVIM 1996

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine
- Leflunomide

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine
- Leflunomide

- Selective pyrimidine synthesis inhibitor
  - Inhibits dihydroorotate dehydrogenase
  - B and T cells lack pyrimidine salvage pathway
- Dose: 2-4 mg/kg q24h

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine
- Leflunomide

- No randomized, controlled studies on IMHA in dogs
  - Effective in IMPA
- Generic available now so more affordable
- Adverse effects
  - Lethargy, GI upset (can be severe)
  - Bone marrow suppression
    - Case reports of necrosis

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine
- Leflunomide
- Intravenous immunoglobulin

MF Whelan et al JVECC 2009

Other immunosuppressives

- Azathioprine
- Mycophenolate
- Cyclosporine
- Leflunomide
- Intravenous immunoglobulin

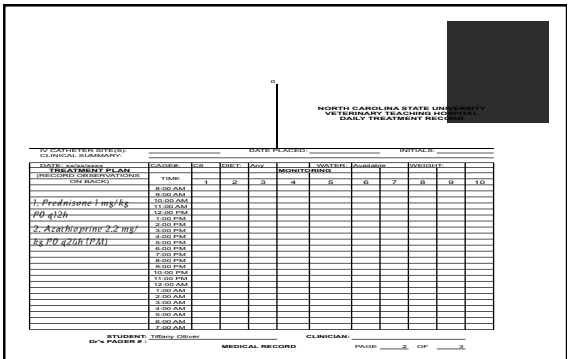
- Modulation of expression and function of Fc receptors
- Interference with activation of B and T cells and complement
- Decrease in immunoglobulin production
- Dose: 0.5-1.0 g/kg once as a slow infusion

MF Whelan et al JVECC 2009

Intravenous immunoglobulin

- Blinded, randomized, clinical trial
- n=28 (underpowered)
- hIVIG with glucocorticoids did not improve response or survival
  - Did not shorten length of hospitalization
  - Did not decrease the transfusion requirement
- Drawbacks
  - Can increase thrombotic tendencies
  - Anaphylaxis
  - Expensive
- Recommendations
  - Nonresponders?
  - ITP shows promise
    - Evans' syndrome dogs?

MF Whelan et al JVECC 2009



NORTH CAROLINA STATE UNIVERSITY
VETERINARY TEACHING HOSPITAL
DAILY TREATMENT RECORD

IV CATHETER SITE(S): _____ DATE PLACED: _____ INITIALS: _____
CLINICAL SUMMARY: _____

DATE: mo/day/yr	CAGE#	Cs	DIET:	Rx:		WATER: Available			WEIGHT:		
TREATMENT PLAN (RECORD OBSERVATIONS ON BACK)	MONITORING										
TIME:	1	2	3	4	5	6	7	8	9	10
8:00 AM										
9:00 AM										
10:00 AM										
11:00 AM										
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7:00 AM										

1. Prednisone 1 mg/kg PO q12h
2. Azathioprine 2.2 mg/kg PO q24h (PM)

STUDENT: Tiffany Olliver CLINICIAN: _____
Dr's PAGER # : _____
MEDICAL RECORD PAGE 2 OF 3

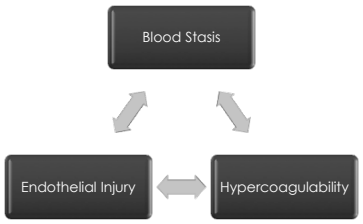
What kills dogs with IMHA?

Hypercoagulability in IMHA

- Thromboembolism presence estimated 30-50%
  - May be much higher based on necropsy studies
- Mix of venous and arterial thrombosis (PTE > other locations)
  - Dysregulation of platelets and coagulation
- What drives the thrombosis?

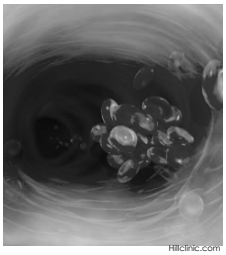
M Kjelgaard-Hansen et al. JVIM 2011
S Dow in Kirk's CVT XV 2014
L Kidd & N Mackman JVECC 2013

Virchow's triad



What drives thrombosis in IMHA?

- Platelet and endothelial activation
- Procoagulant microparticles
- Decreased antithrombin activity
- Treatment of the disease
  - Impair macrophage function decreases scavenging of MPs
  - Corticosteroids
  - IVIg
  - Cyclosporine?



How do we prevent it?

Platelet inhibition

- Low dose aspirin
  - Inhibits thromboxane A2
  - Non-responders (up to 30%)
  - Dose: 0.5-1 mg/kg q12h
- Clopidogrel
  - Platelet ADP receptor inhibitor
  - Dose: 2 mg/kg q24h

Coagulation inhibition

- Unfractionated heparin
  - 1.5x baseline aPTT
  - Anti-factor Xa measurement
  - Dose: 600U/kg/day as a CRI or divided into 200 U/kg TID
- LMW heparin
  - Expensive
- Direct Xa inhibitors
  - Rivaroxaban 0.5-1 mg/kg q24h

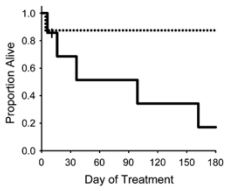
SE Helmund et al. JVIM 2010
AM Mellet et al. JVIM 2011
A Morassi et al. JVECC 2016

What's the cost? (18kg dog)

	Drug cost (30d)	Monitoring cost	Total
Aspirin (1 mg/kg/d)		N/A	
Clopidogrel (2 mg/kg/d)		N/A	
UFH (900 U/kg/d)			
LMWH		N/A	
Rivaroxaban (1 mg/kg/d)	$375 (#30, 15mg tabs) Target (GoodRx price)	N/A	$375/mo

Thromboprophylaxis in IMHA

- We know this **improves outcome**!
  - Individually adjusted dose heparin versus continuous dose
    - 5/6 dogs in CD group had TEV
    - 1-2/6 dogs in IAD group
  - Doses of unfractionated heparin from 150-566 U/kg q8h



SE Helmund et al. JVIM 2010

DAILY TREATMENT RECORD

IV CATHETER SITE(S): _____ DATE PLACED: _____ INITIALS: _____
CLINICAL SUMMARY: _____

DATE: xx/xx/xxxx	CAGE#:	C6	DIET:	Any		WATER:	Available		WEIGHT:		
TREATMENT PLAN					**MONITORING**						
(RECORD OBSERVATIONS ON BACK)	TIME	1	2	3	4	5	6	7	8	9	10
1. Prednisone 1 mg/kg PO q12h	8:00 AM										
2. Azathioprine 2.2 mg/kg PO q24h (PM)	9:00 AM										
	10:00 AM										
	11:00 AM										
	12:00 PM										
3. Clopidogrel 2 mg/kg PO q24h	1:00 PM										
	2:00 PM										
4. UFH 200 U/kg SQ q8h	3:00 PM										
	4:00 PM										
– *Baseline aPTT*	5:00 PM										
– *aPTT q8h*	6:00 PM										
	7:00 PM										
	8:00 PM										
	9:00 PM										
	10:00 PM										

What about blood products?

- Necessary in 70-90% of patients
  - Most studies based on referral centers
- Indications:
  - Treatment of tissue hypoxia
    - Tachypnea, tachycardia, dyspnea, weakness
  - NOT treatment of PCV
- Packed RBCs
  - 10 ml/kg over 4h
    - 1 ml/kg raises PCV 1%
  - Vol = 90 x BW x (ΔPCV/donor PCV)
- When to crossmatch?
  - No transfusion history? Not necessary
  - Transfusion history? Absolutely
  - Give only DEA 1.1 negative products
  - NB: Autoagglutination may make interpretation of Xmatch impossible!

More on transfusions …

- S Haldane et al. Transfusion Medicine. Compendium. July 2004: 502-518. (vetfolio.com)
- Tocci, L. J. and Ewing, P. J. (2009), Increasing patient safety in veterinary transfusion medicine: an overview of pretransfusion testing. Journal of Veterinary Emergency and Critical Care, 19: 66–73.

Other supportive care

- Intravenous fluid support if needed
  - Dehydration
  - Hemoglobin-related nephropathy
  - Use caution when also giving pRBCs
- Antiemetics
  - Maropitant 2 mg/kg PO q24h
  - Ondansetron 0.5 mg/kg IV or PO q8h
- Gastroprotectants (high dose prednisone)
- Antibiotics
  - Doxycycline until known VBD status

DAILY TREATMENT RECORD

IV CATHETER SITE(S): _____ DATE PLACED: _____ INITIALS: _____
CLINICAL SUMMARY: _____

DATE: xx/xx/xxxx	CAGE#:	C6	DIET:	Any		WATER:	Available		WEIGHT:		
TREATMENT PLAN					**MONITORING**						
(RECORD OBSERVATIONS	TIME										
ON BACK)		1	2	3	4	5	6	7	8	9	10
1. Prednisone 1 mg/kg	8:00 AM										
PO q12h	9:00 AM										
2. Azathioprine 2.2 mg/	10:00 AM										
kg PO q24h (PM)	11:00 AM										
	12:00 PM										
3. Clopidogrel 2 mg/kg	1:00 PM										
PO q24h	2:00 PM										
4. UFH 200 U/kg SQ	3:00 PM										
q8h (100U/kg bolus)	4:00 PM										
– Baseline aPTT	5:00 PM										
– aPTT q8h	6:00 PM										
5. 0.65% NaCl + KCl	7:00 PM										
6. LRS for 5% deficit	8:00 PM										
7. Zofran 0.5 mg/kg q8	9:00 PM										
8. Doxycycline 5 mg/kg	10:00 PM										
PO q12h											

Plasmapheresis

- Exchange of patient's plasma and the IgG and IgM fractions within it
  - IgM 70% intravascular
  - IgG 45% intravascular
- Indicated in humans with IMHA, ITP, myasthenia gravis
- One dog refractory to standard treatment
  - Post exchange 37% and 75% reduction in IgG & IgM
  - No further transfusions needed – BUT only had 3d therapy prior to TPE

KL Crump & R Seshadri JVECC 2009

Prognosis

Not as clear as we'd like

General IMHA prognosis

- Widely variable mortality rate reported
- Approximately 50% die with in first 14 days
  - Majority of thromboembolic disease
  - Up to 90% survival after first 14 days
- Relapse rates from 15-30%

Prognostic indicators

Table 3. Prognostic factors for mortality identified by studies included in review.

References	Study Design	Outcome Measure	Statistical Method	Prognostic Factors Identified: Factor	OR/HR	95% CI
Piek et al[10]	Retrospective cohort	Survival time (death because of IMHA)	Cox proportional hazards analysis	Serum [urea] (>56 mg/dL)	2.56	1.729–3.789
				Icterus	2.94	1.60–5.42
				Spherocytosis	0.38	0.20–0.72
Ishihara et al[12]	Retrospective cohort	Survival time (death because of IMHA)	Cox proportional hazards analysis	Sex (male)	1.59	*
				Season (warm)	1.68	*
				PCV (<20%)	1.56	*
				Platelet count (<200,000/μL)	1.63	*
				Total protein (<6 g/dL)	1.78	*
Reimer et al[13]	Retrospective cohort	Survival time (all-cause mortality)	Cox proportional hazards analysis	Serum [bilirubin]	*	*
				Serum ALP activity	*	*
Swann & Skelly[14]	Retrospective cohort	Survival time (all-cause mortality)	Cox proportional hazards analysis	Serum [urea]	1.211	1.073–1.367
				Serum [bilirubin]	1.014	1.003–1.024
Piek et al[15]	Prospective cohort	Survival time (death because of IMHA)	Cox proportional hazards analysis	Serum [creatinine] (>0.23 mg/dL)	1.15	1.00–1.35
				Monocyte count (>100/μL)	2.32	1.34–6.05
				APTT	1.12	1.03–1.26
Kjelgaard-Hansen[16]	Prospective cohort	Mortality at 30 days (all-cause mortality)	Multivariable logistic regression	IL-18	*	*
				MCP-1	*	*

OR, odds ratio; HR, hazard ratio; CI, confidence interval; APTT, activated partial thromboplastin time; PCV, packed cell volume; ALP, alkaline phosphatase; IL-18, interleukin 18; MCP-1, monocyte chemoattractant protein 1.
*Not stated.

Swann, J.W. and Skelly, B.J. (2015), Systematic Review of Prognostic Factors for Mortality in Dogs with Immune-mediated Hemolytic Anemia. Journal of Veterinary Internal Medicine, 29: 7–13.

Prognostic indicators

Table 3. Prognostic factors for mortality identified by studies included in review.

"There are few pieces of high-quality evidence available to enable estimation of prognosis for dogs presenting with primary IMHA."

Swann, J.W. and Skelly, B.J. (2015), Systematic Review of Prognostic Factors for Mortality in Dogs with Immune-mediated Hemolytic Anemia. Journal of Veterinary Internal Medicine, 29: 7–13.

Prognostic indicators in IMHA

- **Reported** prognostic indicators
  - Increased BUN
  - Increased bilirubin
  - Thrombocytopenia
  - Leukocytosis with bands
  - Azotemia, petechiation, hypoalbuminemia
- **NOT** associated with worse outcome
  - Degree of anemia
  - Degree of spherocytosis
  - Reticulocyte response

The PCV is normal!

Now what?

Decreasing medications

- What I do when the PCV is normal?
  - Nothing. For another month.
- Well, not nothing.
  - Stop heparin when no longer autoagglutinating
  - Continue platelet inhibitor until off prednisone
- Recheck full CBC and Chemistry panel after 30 days normal PCV
  - Taper prednisone by 25%
  - Recheck PCV/TS in one week, full CBC three weeks later
  - Repeat until off immunosuppressives

Your plan may vary

- Lots of ways to taper immunosuppressive drugs
- Things I look for before tapering
  - Spherocytes
  - Agglutination
  - Reticulocyte count
  - Medication side effects
    - Physical and biochemical
- These may necessitate a shorter or longer duration of therapy

Questions?

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