

# Hematological Disorders in Dogs and Cats



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# Goals of 5 weeks

- First 2 weeks
  - Heart disease
  - Respiratory tract
- Following 2 weeks
  - *Haematological disease*
  - Systemic infections
- Last week
  - Other remarkable notes



SIXTH EDITION

# Small Animal Internal Medicine



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ELSEVIER



# Anemia

- Anemia is defined as a decrease in the red blood cell (RBC) mass .
- In practical terms, it can be defined as a decrease in the packed cell volume (PCV), hematocrit (HCT), hemoglobin (Hb) concentration

CBC Results		References
WBC $10^9/l$	7.70	6.00 – 17.00
LYM $10^9/l$	1.17	1.0 – 4.80
MONO $10^9/l$	0.59	0.2 – 1.5
NEUT $10^9/l$	5.84	3.00 – 12.00
EOS $10^9/l$	0.1	0.1 – 19
LY %	15.2	12 – 30
MONO %	7.66	3 – 10
NEUT %	75.8	62 – 87
EOS %	1.29	0.1 – 19
RBC $10^{12}/l$	3.30	5.5 – 8.5
HGB <i>g/dl</i>	8.90	12 – 18
HCT %	26.0	37 – 55
MCV <i>fl</i>	79.0	60 – 77
MCH <i>pg</i>	26.9	19.5 – 24.5
MCHC <i>g/dl</i>	34.1	31 – 34
RDWc %	15.6	
PLT $10^9/l$	38.0	200 – 500
PCT %	0.04	
MPV <i>fl</i>	9.60	3.9 – 11
PDWc %	34.5	

# Etiology of Anemia

## Disorders Commonly Associated With Anemia, Hepatomegaly, Splenomegaly, and/or Lymphadenopathy

DISORDER	FREQUENCY
Lymphoma	F
Mycoplasmosis	F
Acute leukemias	F
Ehrlichiosis, anaplasmosis, leishmaniasis	F*
Systemic mast cell disease	R
Bone marrow hypoplasia	R
Immune-mediated hemolytic anemia	F

C, Cat; D, dog; F, frequent; R, rare.  
\*Geographic variation.

Iron deficiency anemia  
Leptospirosis

### Causes of Hemolytic Anemia in Dogs and Cats

DISORDER	SPECIES	BREED
<b>Congenital (Inherited?)</b>		
Pyruvate kinase deficiency	D, C	Dogs: Basenji, Beagle, West Highland White Terrier, Cairn Terrier, Poodle, Dachshund, Chihuahua, Pug, Beagle, Labrador Retriever, American Eskimo Cats: Abyssinian, Somali, Bengal, Egyptian Mau, La Perm, Maine Coon cat, Norwegian Forest cat, Savannah, Siberian, Singapura, domestic short-haired cat
PFK deficiency	D	English Springer Spaniel, Cocker Spaniel, Whippet, Wachtelhund
Stomatocytosis	D	Alaskan Malamute, Miniature Schnauzer
Nonspherocytic hemolytic anemia	D	Poodle, Beagle
<b>Acquired</b>		
IHA	D > C	All
Neonatal isoerythrolysis	C	British breeds, Abyssinian, Somali (other type B cats)
Microangiopathic hemolytic anemia	D > C	All
<b>Infectious</b>		
Mycoplasmosis	C, D	All
Babesiosis	D > C	All (Pitbulls and <i>Babesia gibsoni</i> )
Cytauxzoonosis	C	All
Ehrlichiosis (uncommon)	D > C	All
<b>Hypophosphatemia</b>		
	D, C	All
<b>Oxidants</b>		
Acetaminophen	C	All
Phenothiazines	D, C	All
Benzocaine	C	All
Vitamin K	D, C	All
Methylene blue	C > D	All
Methionine	C	All
Propylene glycol	C	All
Zinc	D	All
<b>Drugs That Can Cause Immune Hemolysis</b>		
Sulfa drugs	D > C	Doberman, Labrador Retriever
Barbiturates	D	All
Penicillins and cephalosporins	D > C	All
Propylthiouracil	C	All
Methimazole	C	All
Antiarrhythmics (?)	D	All
Zinc	D	All

C, Cat; D, dog; IHA, immune hemolytic anemia; PFK, phosphofructokinase.  
Modified from Couto CG et al.: Hematologic and oncologic emergencies. In Murtaugh R et al., editors: *Veterinary emergency and critical care medicine*, St Louis, 1992, Mosby, p 359.

### Drugs and Toxins That Can Cause Anemia in Cats and Dogs

Acetaminophen  
Antiarrhythmics  
Anticonvulsants  
Antiinflammatories (nonsteroidal)  
Barbiturates  
Benzocaine  
Chemotherapeutic agents  
Chloramphenicol  
Cimetidine  
Gold salts  
Griseofulvin  
Levamisole  
Methimazole  
Methionine  
Methylene blue  
Metronidazole  
Penicillins and cephalosporins  
Phenothiazines  
Propylthiouracil  
Propylene glycol  
Sulfa derivatives  
Vitamin K  
Zinc



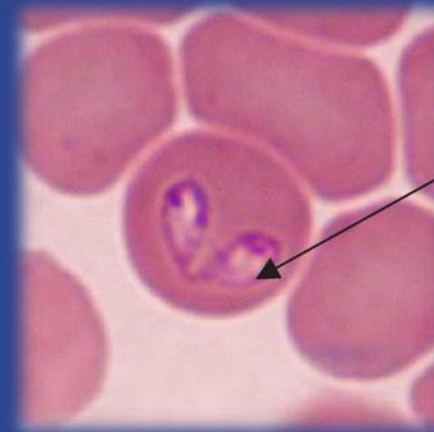
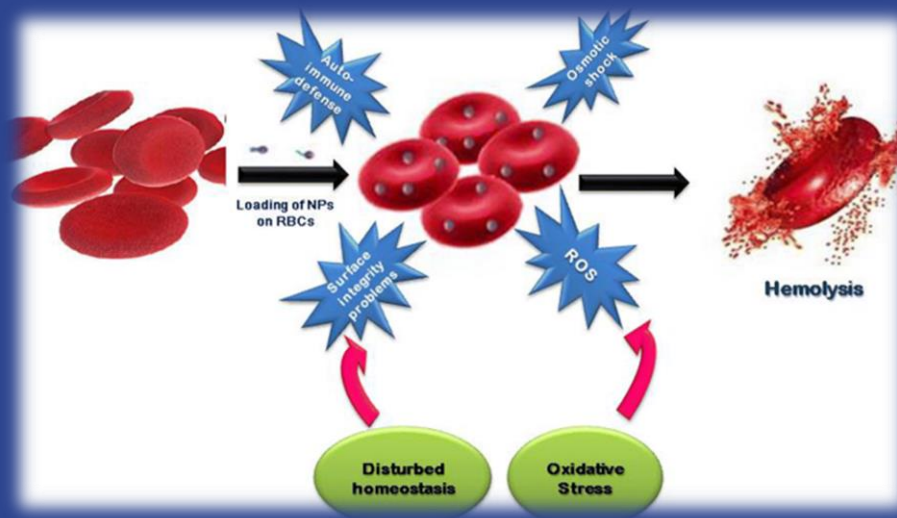
# Immune Hemolytic Anemia

- What is Hemolysis ?
  - Destruction of erythrocyte
- Why?
  - Erythrocyte surface antigens
  - Primary changes on ERY surface antigens
  - Secondary changes



# Mechanism of Immune Hemolytic Anemia

- The normal life span of the canine RBC is approximately 100 to 120 days.
- Removal of aged RBCs normally occurs within the *liver and spleen* by the mononuclear phagocyte system.
- This system identifies antibodies directed against senescent membrane antigens and clears them from circulation.
- IMHA is a pathologic process that results in premature destruction of RBCs when an immune response directly or indirectly targets RBCs of all ages.
- Primary IMHA (Idiopathic)
- Secondary IMHA



# Socondary Causes of Immune Hemolytic Anemia

Causes of Secondary IMHA in Dogs <sup>1,7,8,10,13,14,17,18,23,a-c</sup>
<b>Infection</b> <ul style="list-style-type: none"><li>• Ehrlichiosis</li><li>• Babesiosis</li><li>• <i>Anaplasma phagocytophilum</i> infection</li><li>• <i>Haemobartonella canis</i> infection</li><li>• Leptospirosis</li><li>• Dirofilariasis</li><li>• Histoplasmosis</li></ul>
<b>Neoplasia</b> <ul style="list-style-type: none"><li>• Lymphosarcoma</li><li>• Hemangiosarcoma</li><li>• Lymphocytic leukemia</li><li>• Gastric and lung carcinoma</li><li>• Diffuse sarcoma</li></ul>
<b>Drugs</b> <ul style="list-style-type: none"><li>• Trimethoprim-sulfonamide</li><li>• Penicillins</li><li>• Cephalosporins</li><li>• Levamisole</li><li>• Phenylbutazone</li><li>• Dipyron</li><li>• Chlorpromazine</li></ul>
<b>Intrinsic RBC defects</b> <ul style="list-style-type: none"><li>• Phosphofruktokinase deficiency</li><li>• Pyruvate kinase deficiency</li><li>• Hereditary osmotic fragility</li></ul>
<b>Miscellaneous</b> <ul style="list-style-type: none"><li>• Onion</li><li>• Garlic</li><li>• Zinc</li><li>• Bee-sting envenomation</li><li>• Vaccination</li></ul>





# Predisposed Breeds

Cocker Spanial,  
Bichon Frise,  
Miniature Pinscher,  
Miniature Schnauzer,  
English Springer Spaniel,  
Rough-coated collie,



# Clinical Manifestations

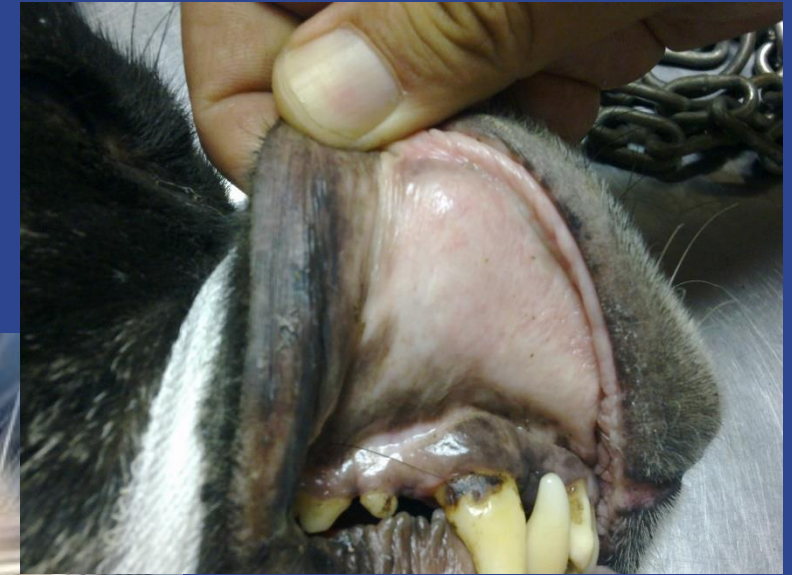
## Clinical Manifestations of Anemia in Cats and Dogs

### History

- Breed (e.g., congenital enzymopathies, babesiosis in Pitbulls)
- Family history
- Exercise intolerance, syncopal episodes
- Pallor, jaundice
- Localized or generalized bleeding
- FeLV or FIV infection
- Vector-borne diseases (e.g., ehrlichiosis, anaplasmosis, babesiosis)
- Malnutrition, malabsorption
- Chronic inflammation, cancer
- Travel history

### Physical Examination

- Pallor, jaundice, petechiae, ecchymoses
- Lymphadenopathy
- Hepatomegaly, splenomegaly
- Tachycardia, heart murmur, cardiomegaly, left ventricular hypertrophy
- Occult blood in the stool
- Hematuria, bilirubinuria



FeLV, Feline leukemia virus; FIV, feline immunodeficiency virus.





# Physical examination



Tachycardia

Tachypnea

Mucosal pallor

Hypothermia

Lymphadenomagnaly

Lethargy

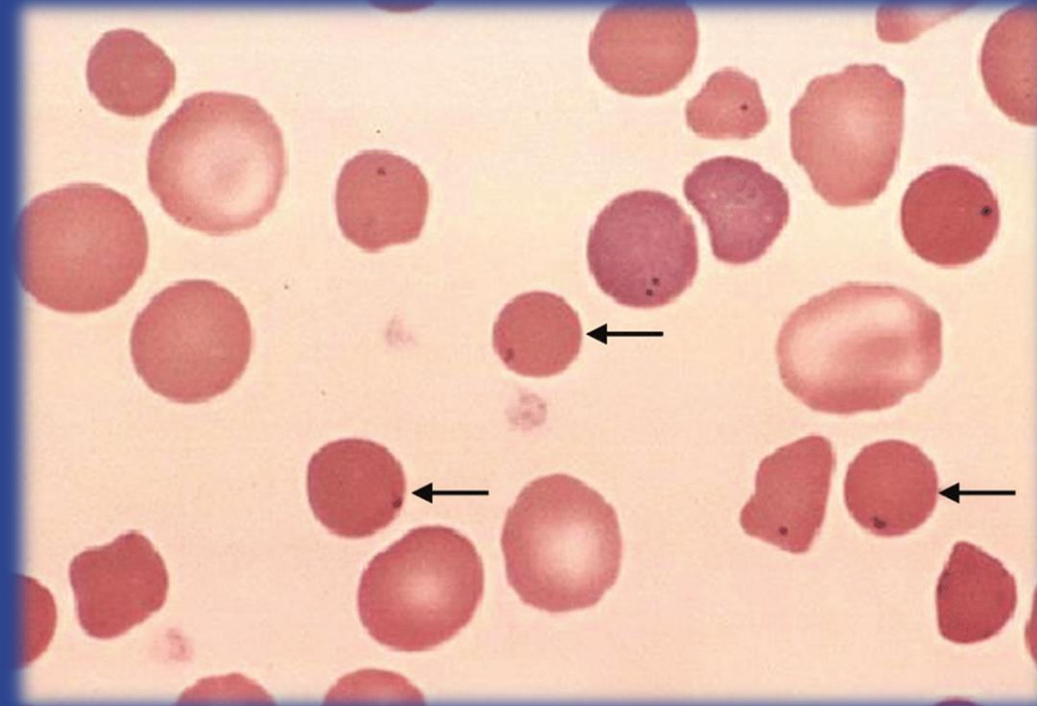


# Diagnosis of the IMHA

Table 1. First Evaluation of Blood Analyses

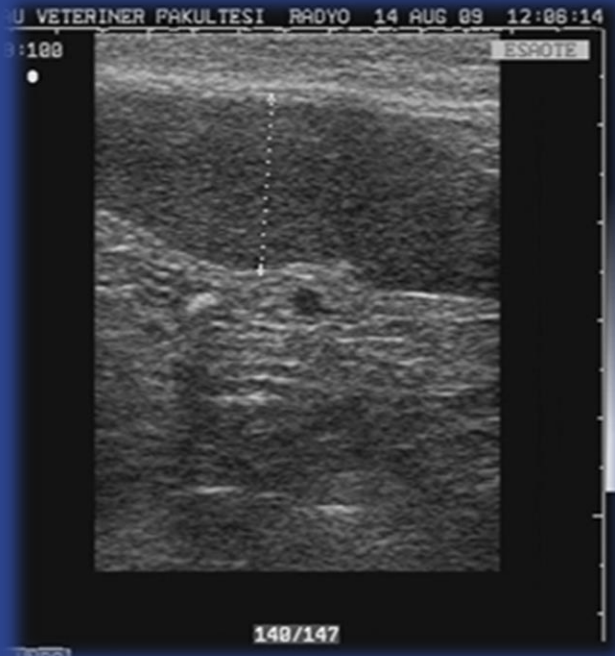
CBC Results		References	Serum Profiles		References
WBC $10^9/l$	7.70	6.00 – 17.00	Glucose <i>mg/dl</i>	73	65 – 118
LYM $10^9/l$	1.17	1.0 – 4.80	Urea <i>mg/dl</i>	28.6	15 – 60
MONO $10^9/l$	0.59	0.2 – 1.5	Creatinine <i>mg/dl</i>	0.72	0.5 – 1.5
NEUT $10^9/l$	5.84	3.00 – 12.00	Total Protein <i>g/dl</i>	7.1	5.4 – 7.1
EOS $10^9/l$	0.1	0.1 – 19	Albumine <i>g/dl</i>	3.6	3.1 – 4.0
LY %	15.2	12 – 30	Total Bilirubin <i>mg/dl</i>	0.42	0.1 – 0.3
MONO %	7.66	3 – 10	Direct Bilirubin <i>mg/dl</i>	0.37	
NEUT %	75.8	62 – 87	ALP <i>IU/L</i>	172.0	20 – 156
EOS %	1.29	0.1 – 19	ALT <i>IU/L</i>	105.7	21 – 102
RBC $10^{12/l}$	3.30	5.5 – 8.5	AST <i>IU/L</i>	41.6	23 – 66
HGB <i>g/dl</i>	8.90	12 – 18	GGT <i>IU/L</i>	6.0	6 – 28
HCT %	26.0	37 – 55	Phosphore <i>mg/dl</i>	3.1	2.9 – 6.2
MCV <i>fl</i>	79.0	60 – 77	Calcium <i>mg/dl</i>	9.5	9 – 11.3
MCH <i>pg</i>	26.9	19.5 – 24.5	Sodium <i>mmol/l</i>	145	140 – 154
MCHC <i>g/dl</i>	34.1	31 – 34	Potassium <i>mmol/l</i>	3.9	3.8 – 5.6
RDWc %	19.6		<b>Coagulation Variables</b>		
PLT $10^9/l$	38.0	200 – 500	PT <i>seconds</i>	7.9	6.2 – 7.7
PCT %	0.04		aPTT <i>seconds</i>	19.4	9.8 – 14.6
MPV <i>fl</i>	9.60	3.9 – 11	D-dimer <i>µg/ml</i>	0.53	0.01 – 0.34
PDWc %	34.5				

WBC – White blood cell; LYM – Lymphocyte; MONO – Monocyte; NEUT – Neutrophile; EOS – Eosinophile; RBC – Red blood cell; HGB – Hemoglobin; HCT – Hematocrit; MCV – Mean corpuscular volume; MCH – Mean corpuscular hemoglobin; MCHC – Mean corpus cular hemoglobin concentration; RDW – Red blood cell distribution width; PLT – Platelet; PCT – Plateletcrit; MPV – Mean platelet volume; PDW – Platelet distribution width; ALP – Alkaline phosphatase; ALT – Alanine transaminase; AST – Aspartate aminotransferase; GGT – Gamma-glutamyltransferase; PT – prothrombin time; aPTT – Activated Partial Thromboplastin Time.

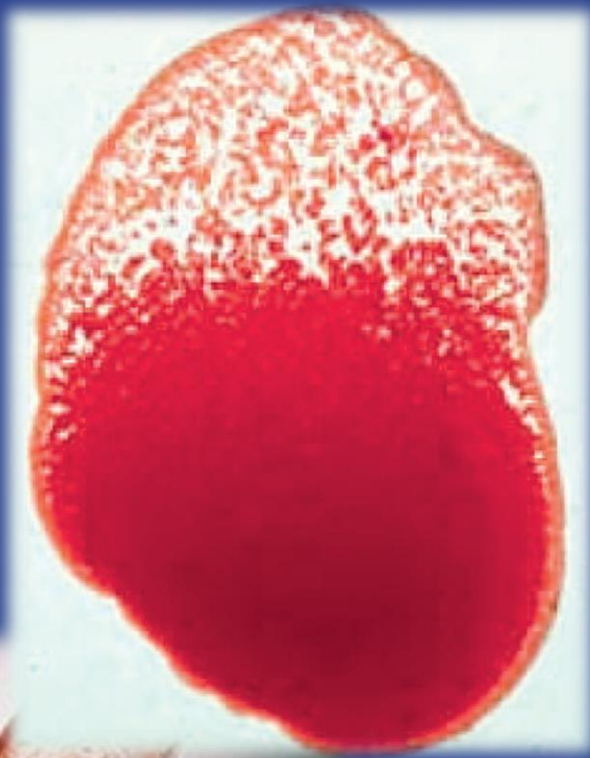


- Spherocytes are small, round, intensely stained RBCs that lack central pallor and are created by MPS phagocytosis of a portion of antibody-coated RBC membrane
- Marked spherocytosis is certainly highly suggestive of the diagnosis.
- Evans syndrome





# Diagnosis of the IMHA





# Treatment

- Primary
  - Supportive care
    - Fluid therapy (isotonic saline %0.9 iv)
    - Oxygenation
    - Vitamin C increases erythrocyte membrane resistance
  - Immunosuppressive therapy
    - Prednisolone (2 mg/kg q12h) 2-4 weeks
    - If HCT levels increases, possible to reduce the first doses
- Secondary
  - Ehrliciosis, Babesiosis, Anaplasmosis, Dirofilariosis, Lymphoma



# Treatment

- Blood transfusion
  - The criteria for transfusion are not rigid but may include the presence of severe tachypnea, dyspnea, tachycardia, cold extremities, weakness, mental depression, or a hematocrit under 15
  - Blood volume = HCT x kg CA x 2
  - Blood volume = 12-20 ml/kg
- Transfusion Rate
  - Adult dogs: maximum rate of 3 to 6 ml/minute
  - Cats, kittens, puppies: maximum rate of 1 to 2 ml/minute



# Other Therapy Applications

- Splenectomy
  - Last-choice treatments in canine IMHA.
  - The benefits arise from removing one source of B cells and splenic macrophages, the primary culprits in the removal of antibody-coated erythrocytes.
- IVIG (Intravenous human immunoglobulin)
  - 0.5 to 2 g/kg IV daily, given over six to 12 hours (single infusion)
  - The mechanism of action of IVIG is thought to be a blockade of the Fc receptors on macrophages, thereby reducing phagocytosis of antibody-coated RBCs, interfering with complement, and suppressing antibody production.
  - Unfortunately, IVIG is also costly and difficult to obtain.



# Long Term Management - Prognosis

- Need always prednisolone therapy
  - No otoagglutination
  - No spherocytes
  - Normal hematology
- Prognosis
  - Depends on blood marrow storage or how to blood marrow supports the erythrocyte levels.
  - Bone marrow histopathology are especially important to decide the prognosis.
    - If the marrow support is possible, prognosis nice
    - If the marrow support is not possible, prognosis poor.



# Hematological Disease in Dogs and Cats



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