

#### VITICUSGROUP<sup>™</sup> WVC ANNUAL CONFERENCE MARCH 2 - 5, 2025 | LAS VEGAS, NV

# 5 hematology abnormalities you should never ignore in your patients.

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## **Financial Disclosure**

I have a direct or indirect relationship with IDEXX. Because of the nature of the relationship, it **will not** influence my presentation.

## Three-part hematology...more than just the report



## 5 things to never ignore.

- 1. Trends and values that are within the reference interval.
- 2. The benefit of having reticulocytes with or without anemia.
- 3. Decreased reticulocyte hemoglobin concentration.
- 4. The value of dot plots (analyzer graphics).
- 5. Clues of inflammation



#### Established individual normals when young/healthy and trend.

#### Look at all numbers, not just ones flagged as high or low.

## Values in the normal range might not be 'normal.'





#### 10-year-old, spayed female mixed-breed dog, lethargic x 24 hours

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx					
RBC	6.2 x10^12/L	5.7 - 8.9			
HCT	43.2 %	37.5 - 61.7			
HGB	14.4 g/dL	13.1 - 20.5			
MCV	69.4 fL	61.6 - 73.5			
MCH	23.1 pg	21.2 - 25.9			
MCHC	33.3 g/dL	32.0 - 37.9			
RDW	19.1 %	13.6 - 21.7			
%RETIC	36%		75		

What if previous CBCs showed her normal HCT in mid 50s?







## Possible EEH:

- Gastrointestinal signs
  - Megaesophagus?
- Albumin:globulin <1.08
  - Over 1/3 hyperglobulinemic
  - Hypoalbuminemia more common w EEH
- Low cholesterol (<133 mg/dL)
- Lack of stress leukogram in sick animal
  - Lymphocyte count >1500-1750cells/µL
  - Eosinophil count >500 cells/μL
- Reticulocytosis without anemia
- Increasing Ca, decreasing BG, regurgitation...



# 

## ALIVE: Agreeing Language In Veterinary Endocrinology





## Then and now...



- Addison's disease Atypical Addison's disease Addisonian crisis
- Relative adrenal insufficiency

Primary hypoadrenocorticism

Eunatremic, eukalemic hypoadrenocorticism Adrenal crisis

Critical illness-related corticosteroid insufficiency



#### Why do we care so much about reticulocytes?

#### Immature cells in blood are earliest sign of change in patient status.

#### Changes in mature cells (indices, numbers) late indicators. RBC lifespan dog 100-120 d, cat 65-76 d.



### Immature cells in circulation = *current* bone marrow status.





Best indicator of regeneration?



MCHC

Reticulocyte percent

Absolute reticulocyte count





#### Regenerative or nonregenerative?



Test	Results	Reference Interva	I LOW	NORMAL	HIGH
ProCyte Dx (May 13, 2019 2:41 AM)					
RBC	2.28 M/µL	5.65 - 8.87 LOW			
HCT	15.9 %	37.3 - 61.7 LOW		-3.6	
HGB	5.1 g/dL	13.1 - 20.5 LOW			
MCV	69.7 fL	61.6 - 73.5			
MCH	22.4 pg	21.2 - 25.9	22	12 <u>0</u> 1	
MCHC	32.1 g/dL	32.0 - 37.9			

RBC indices **normal** in ≈90% with regenerative anemia.



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MCH	22.4 pg	21.2 - 25.9		22	105.0	
MCHC	32.1 g/dL	32.0 - 37.9		5		
RDW	18.7 %	13.6 - 21.7		2		
%RETIC	18.2 %			2 2		
RETIC	413.8 K/µL	10.0 - 110.0	HIGH			
RETIC-HGB	17.1 pg	22.3 - 29.6	LOW			

Retic counts >200-250K suggest hemolysis.





## Regenerative?

## Hemorrhage

• Hemolysis

# Nonregenerative?

- Chronic disease, e.g., CKD
- Acute hemorrhage/hemolysis
  - "pre-regenerative" (3-5 d to respond)



#### Differentiating hemorrhage from hemolysis. Cornell eClinpath



Finding	Hemorrhage	Hemolysis
Evidence of bleeding (internal or external) severe enough to cause anemia	Yes	No
Total protein (chemistry superior to refractometric measurement)	Usually low	Normal to high
RBC morphologic changes (e.g. spherocytes)	No	Usually
Total bilirubin (mostly indirect or unconjugated, exceptions given above)	Normal	Normal to increased

Retic counts >200-250K suggest hemolysis.



#### Hemolysis? Not always IMHA...







#### How do you determine if hemorrhage is due to coagulopathy?

Primary hemostasis - platelets (Surface hemorrhage)

↓ Platelet number, e.g., ITP ↓ Platelet function, e.g., vWD Secondary hemostasis - factors (Deep hemorrhage)





### Coag testing normal but suspect bleeding disorder?





## Normal PCV does not rule out hemorrhage or hemolysis.



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%RETIC	3.6 %				



#### Are they really reticulocytes? Check graphics to confirm the numbers...





#### What are these? And where to look to find out?





#### If dot plot abnormal $\rightarrow$ review blood smear.





Reticulocytosis without anemia

(≈10% of dogs & cats worldwide. Higher mortality.)



## Healthy excited pet

- Splenic contraction
- *Mild* bleeding/hemolysis
- Hookworms



- Neoplasia
- Occult bleeding/hemolysis
- Infection/inflammation
- Cardiac, respiratory, GI
- Neoplasia
- NSAIDs



#### Find more of these with retics on all CBCs









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## Find more of these with retics on all CBCs







Earliest indicator of iron deficiency?



#### MCHC

Reticulocyte hemoglobin concentration





#### RETIC-HGB indicates iron availability in bone marrow: *decreases* with...

*External* bleeding (true iron deficiency)

#### Inflammation (relative iron deficiency)







Detect decreased iron availability in **days** (not months).



#### 3 common leukogram patterns?

#### Inflammatory $\rightarrow$ increased bands, toxic change in neuts

#### Stress → lymphopenia (cortisol)

Physiologic → lymphocytosis (epinephrine)







## Total number of WBCs or neutrophils not that helpful

- Total counts normal in 50% dogs and cats with infection/inflammation
- Total counts high when no infection present
- Total counts low with acute suppurative infections
- Stress can raise neutrophils 2x normal (up to 35K in dogs!)
- CRP (dogs only) aids in determining systemic inflammation





## Toxic change in neutrophils is a big deal.

- Developmental abnormality caused by rapid maturation in bone marrow
  - Mistakes happen as cells rapidly divide and develop
  - NOT 'toxicity' as in exposure to toxin
- Abnormal granules, vacuoles (holes), Dohle bodies (RER), free ribosomes



• Important: indicates increased demand or endotoxin presence during maturation



## 14-yr-old, neutered male Labrador retriever

- Presenting complaint: acute vomiting, respiratory distress, severe suddenonset depression
- History:
  - Referred from boarding kennel
  - Gradual muscle mass loss over several years
- Physical examination findings:
  - Labored breathing harsh lung sounds
  - Weakness
  - Severe muscle wasting





Test	Results	Reference Interva	al LOW	NORMAL	HIGH		
ProCyte Dx (August 10, 2017 10:27 AM)							
WBC	7.16 K/µL	5.05 - 16.76					
NEU	* 0.16 K/µL	2.95 - 11.64 LOW					
BAND	* Suspected						
LYM	* 2.87 K/µL	1.05 - 5.10	80 1				
MONO	* 4.07 K/µL	0.16 - 1.12 HIGH	82- 				
EOS	0.06 K/µL	0.06 - 1.23	50 L				
BASO	0.00 K/µL	0.00 - 0.10	33) 				
Band neutrophils suspected							
WBC Abnormal	WBC Abnormal Distribution						

#### \* Qualified results—confirm with dot plot and/or blood film review



# WBC dot plot – bands/toxic change present (objective).









# Blood film (subjective).



- Bands and toxic neutrophils
- Severe infection present

ELEVATI

• Even though total WBC normal and neutrophils were *low* 



## Daily CBCs to monitor therapy...



Date	4/28/17	8/10/17	8/11/17	8/12/17	8/15/17	8/31/17
Band	-	+	+	+	+	-
WBC (K/µL) (5.05–16.76)	10.58	7.16	8.72	8.84	11.08	10.23



# What is C-reactive protein (CRP)?

- Positive acute phase protein
- Produce mainly in liver in response to proinflammatory cytokines
- Increased in serum within 4 hours of onset of systemic inflammation in dogs
- Peaks 24-48 hr (up to 1000x increase)
- T1/2 ≈18 hr
- Decreases within 18-24 hr of effective treatment
- Opsonizes pathogens, clears apoptotic cells, promotes leukocyte chemotaxis, phagocytosis, and release of inflammatory cytokines





# CRP has been evaluated in dogs with:

- Bacterial pneumonia
- Acute pancreatitis
- Immune-mediated disease
- Kidney disease
- Neurologic disease
- Musculoskeletal disease
- Gastrointestinal disease
- Cardiac disease
- Infectious disease (tick-borne, parvovirus, leptospirosis...)
- Sepsis, SIRS
- Pyometra
- Neoplasia...



# C-reactive protein in pneumonia in dogs

- Diagnostic and monitoring biomarker in humans with pneumonia
- Increased in dogs with bacterial pneumonia (v noninfectious disorders)
- Guide to duration of antibiotic therapy
  - Radiographic resolution lags
  - Prolonged antibiotic use may not be necessary
  - CRP normalized before radiographs in dogs, shorter treatment may be effective<sup>1</sup>
  - Treating for 5-7 days after CRP normal effective without increased relapse<sup>2</sup>



## What about platelets?

- They clump in the blood tube
- Clumps in the sample lowers all automated platelet counts
- Confirm all low platelet counts via graphics and peripheral blood smear
- Remember:
- It is possible for a pet to have a very low platelet count and show no signs
- Don't assume lack of signs means low platelet count is due to clumping...



#### CONSENSUS STATEMENT 🔂 Open Access

# ACVIM consensus statement on the diagnosis of immune thrombocytopenia in dogs and cats

Dana N. LeVine, Linda Kidd 🔀, Oliver A. Garden, Marjory B. Brooks, Robert Goggs, Barbara Kohn, Andrew J. Mackin, Erin R. B. Eldermire, Yu-Mei Chang, Julie Allen ... See all authors 🗸

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CONSENSUS STATEMENT  $\bigcirc$  Open Access  $\bigcirc$   $\bigcirc$   $\bigcirc$   $\bigcirc$   $\bigcirc$   $\bigcirc$ 

# ACVIM consensus statement on the treatment of immune thrombocytopenia in dogs and cats

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# ITP by the numbers

- >100,000/uL  $\rightarrow$  unlikely
- <100,000/uL  $\rightarrow$  consider
- <50,000/uL  $\rightarrow$  consider more strongly
- <20,000/uL  $\rightarrow$  consistent
- <10,000/uL  $\rightarrow$  5x more likely primary v secondary



## Evaluation if suspect ITP

- History for travel, drugs, vaccination...
- PT, PTT (+/- D-dimer, FDP)
- DOGiBAT bleeding severity score
- CBC, biochemistry, UA
- Infectious disease screen (next slide)
- Bone marrow, immunologic testing not routine







#### Dogs: ITP: *Ehrlichia, Babesia, Anaplasma Leishmania, Rangelia, Angiostrongylus,* distemper

IMHA: Babesia, heartworm Anaplasma, Ehrlichia, Bartonella, Leishmania

Cats: ITP: **FeLV/FIV** *A. phagocytophilum, Ehrlichia spp., B felis* 

IMHA: FeLV/FIV, Hemotropic mycoplasma



## Bone marrow ever?

- Not routine diagnostic or monitoring
- Other unexplained cytopenias
- Suspect neoplasia
- +/- Treatment failure
- Megakaryocyte hypoplasia does not affect outcome
  - Doing bm to confirm megakaryocytes therefore unnecessary





#### ITP treatment



- Stable
  - Prednisone 2 mg/kg/day; >25 kg 40-50 mg/m<sup>2</sup>/day (s)
  - VDB treatment
  - Stop unnecessary drugs
- Active bleeding add:
  - Vincristine 0.02 mg/kg IV once (s)
    - Not in collies, Shetland sheepdogs, Australian shepherds, long-haired whippets (ABCB1 mutation)
    - Delay cyclosporine several days if using
  - hIVIg 0.5–1.0 mg/kg IV, over 6 hr (s)
  - Platelet transfusion if life-threatening bleeding (w)
  - Packed RBCs if anemic
  - Antifibrinolytics EACA or TXA (w)
  - Gastroprotectants if melena





# Second immunosuppressive drug? (w)

- Not routine, no evidence one superior to another
- Hemorrhage requiring multiple transfusions
- Active refractory haemorrhage after vincristine or hIVIg
- Inadequate response to glucocorticoids w/in 5 d
- Severe glucocorticoid side effects
- Concurrent disease requiring rapid dose reduction
  - Diabetes mellitus, Cushing's syndrome, urinary incontinence, cardiac disease, prior thrombotic event
- ITP recurs while on glucocorticoids



## Treatment outcome?



**No response:** Plts <30 000/μL, or ongoing bleeding

**Partial response:** Plts ≥30 000/μL but <100 000/μL, 2-fold increase in Plts, no bleeding

Complete response: Plts ≥100 000/µL, no bleeding

- Most have platelet count >50,000-100,000 within 7 d starting glucocorticoids
- Full remission plt count ≥100K/uL without bleeding off all treatment



# Tapering medication and relapse

- When platelet count normal or >100,000/uL x 1-2 months
- Taper prednisone 25-50% q2-4 wk
  - Platelet count stable and confirmed immediately before taper
- CBC/blood smear at taper and 1-3 weeks later ideal
- CRP aids monitoring remission
- Relapse 9-47% early in disease (median 79 d, up to 3 yr)
- Mild relapse  $\rightarrow$  last effective dose
  - CBC/blood smear, biochems, UA, infectious disease/neoplasia screening, cytology, imaging
- Severe relapse  $\rightarrow$  starting dose
- Monitoring in remission q3 mo, then extend, CBC before vax or procedure



## Splenectomy?

- Refractory to all else
- Sustained remission without drugs in some (70%)
- Relapse after splenectomy common
- Well-tolerated but must rule out vector-borne disease
- Therapeutic plasma exchange before splenectomy if available?
- Subsequent vaccine based on life-style, risk, titers...
  - Risk of relapse minimal to zero\*



\*Sparrow et al. JVIM 2024



## Thank you!

