



Blood morphology matters: common clinically significant findings you might miss if you don't smear

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IDEXX

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Disclosure:

I am an employee of IDEXX Laboratories Ltd.

Disclaimer:

The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.

IDEXX

Presentation overview:

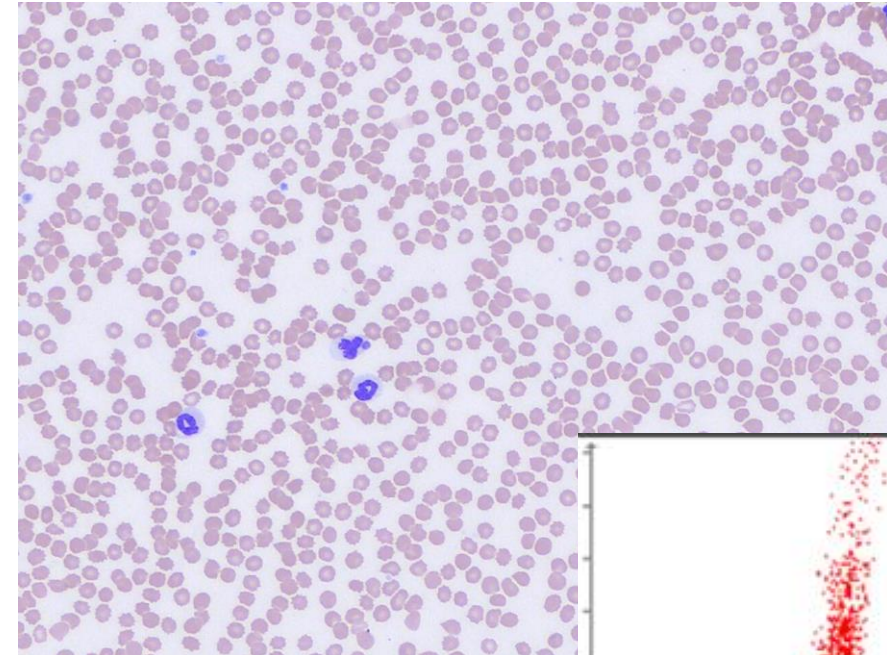
- Understand common limitations of the automated haematology counts to critically assess results
- Recognize common and significant changes in the blood smear morphology that are not identified by the haematology analysers
- Integrate information from the blood smear exam with the information from the haematology analyser in the clinical case context


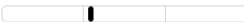




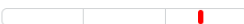

Haematology is an important diagnostic tool

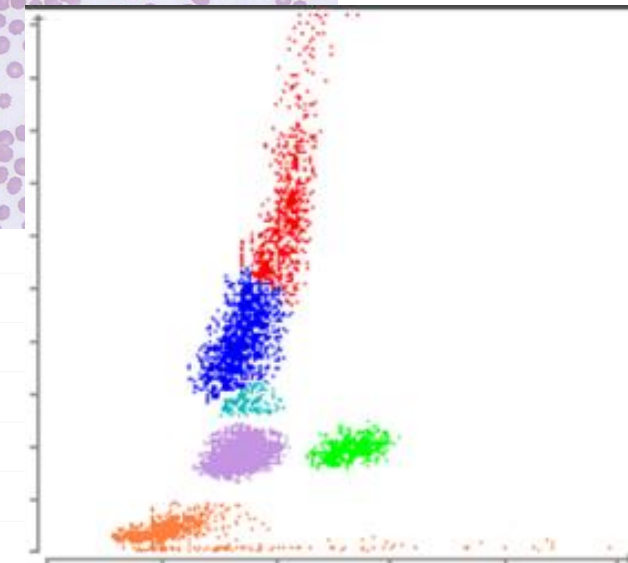
- Part of minimal data base
- Investigation of every sick patient

Components of haematology results

- Automated analysis
 - Numerical values
 - Dot plot analysis
- Blood film evaluation



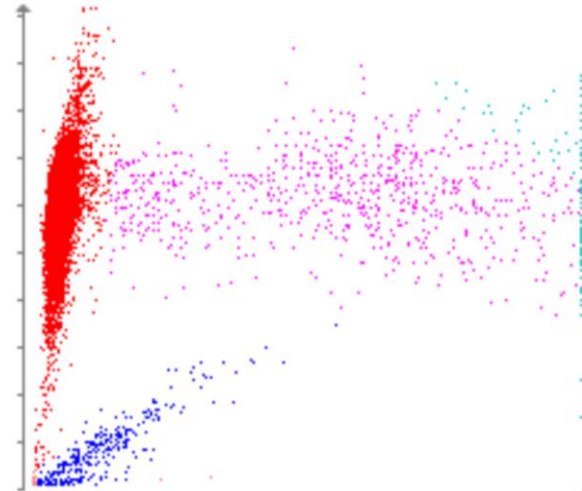
Neutrophils	*19.68	2.95 - 11.64 x10 ⁹ /L	
Lymphocytes	*1.29	1.05 - 5.10 x10 ⁹ /L	
Monocytes	*0.70	0.16 - 1.12 x10 ⁹ /L	
Eosinophils	*0.78	0.06 - 1.23 x10 ⁹ /L	
Basophils	*0.08	0.00 - 0.10 x10 ⁹ /L	
Nucleated RBC	*Suspected		
Platelets	*533	148 - 484 x10 ⁹ /L	
PDW	-	9.1 - 19.4 fL	
MPV	18.7	8.7 - 13.2 fL	
Plateletcrit	1.00	0.14 - 0.46 %	



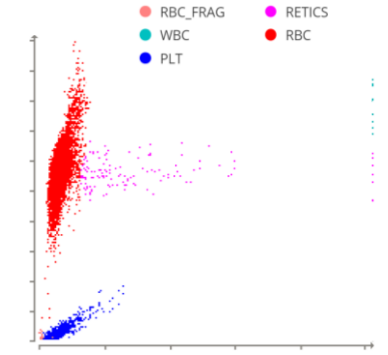
ProCyte Dx - Canine Normal WBC Dot Plot

...so much data!

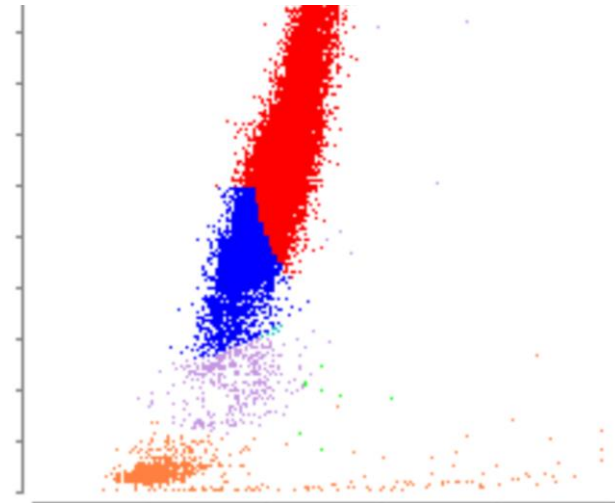
🔊 📉 RBC	3.75	5.65 - 8.87 x10 ¹² /L	
🔊 📉 Haematocrit	0.265	0.373 - 0.617 L/L	
🔊 📉 Haemoglobin	94	131 - 205 g/L	
🔊 📉 MCV	70.7	61.6 - 73.5 fL	
🔊 📉 MCH	25.1	21.2 - 25.9 pg	
🔊 📉 MCHC	355	320 - 379 g/L	
🔊 📉 RDW	18.0	13.6 - 21.7 %	
🔊 % Reticulocyte	3.1	%	
🔊 📉 Reticulocytes	114.8	10.0 - 110.0 K/ μ L	
🔊 📉 Reticulocyte Haemoglobin	26.7	22.3 - 29.6 pg	
🔊 📈 WBC	54.21	5.05 - 16.76 x10 ⁹ /L	
🔊 📉 Neutrophils	*0.82	2.95 - 11.64 x10 ⁹ /L	
🔊 📉 Bands	*Suspected		
🔊 📉 Lymphocytes	*10.93	1.05 - 5.10 x10 ⁹ /L	
🔊 📉 Monocytes	*42.44	0.16 - 1.12 x10 ⁹ /L	
🔊 📉 Eosinophils	0.01	0.06 - 1.23 x10 ⁹ /L	
🔊 📉 Basophils	0.01	0.00 - 0.10 x10 ⁹ /L	
🔊 📉 Platelets	*32	148 - 484 x10 ⁹ /L	
🔊 📉 PDW	-	9.1 - 19.4 fL	
🔊 📉 MPV	17.2	8.7 - 13.2 fL	
🔊 📉 Plateletcrit	0.06	0.14 - 0.46 %	



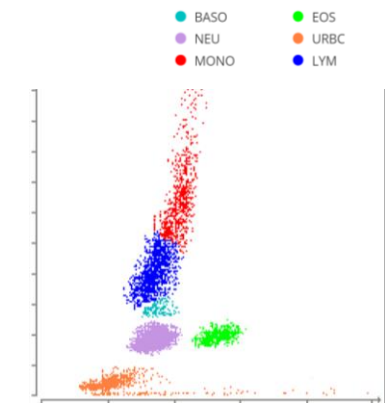
ProCyte Dx – Canine Patient RBC Dot Plot



ProCyte Dx - Canine Normal RBC Dot Plot



ProCyte Dx – Canine Patient WBC Dot Plot

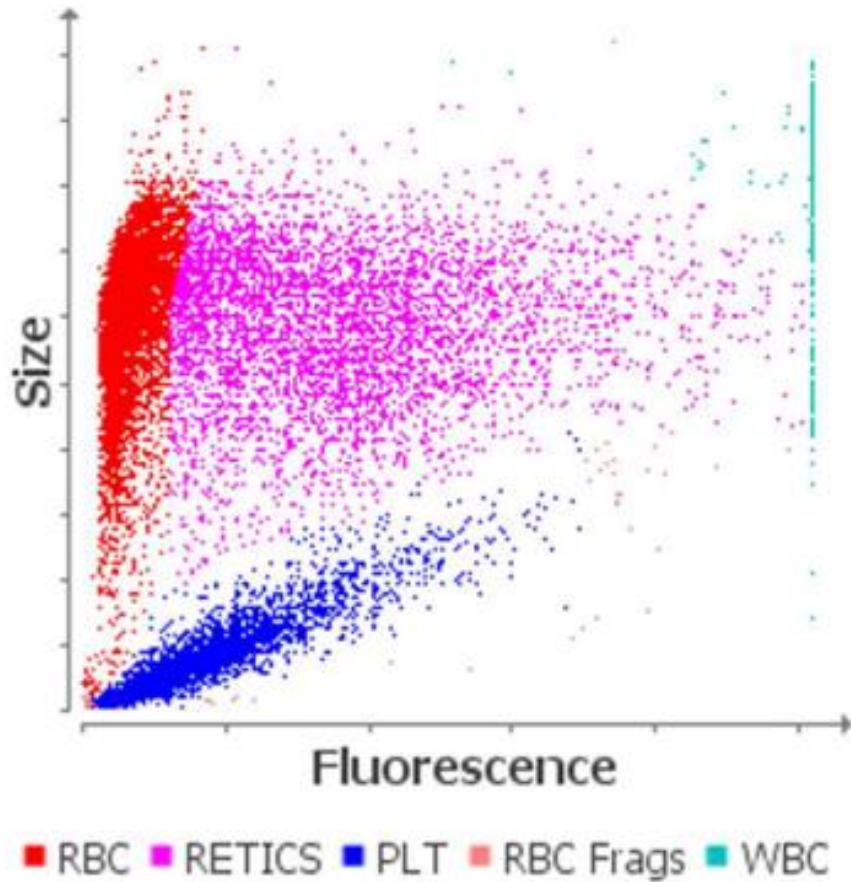


ProCyte Dx - Canine Normal WBC Dot Plot

... and many sample features that interfere with automated CBCs

- + Clots
- + Platelet clumps
- + Macroplatelets
- + RBC agglutination
- + nRBC
- + Heinz bodies
- + Lipemia
- + Leukocyte agglutination
- + Delay in sample handling (increase in MCV, haemolysis, changes in leucocytes, etc)

Why is morphological evaluation of cells important?



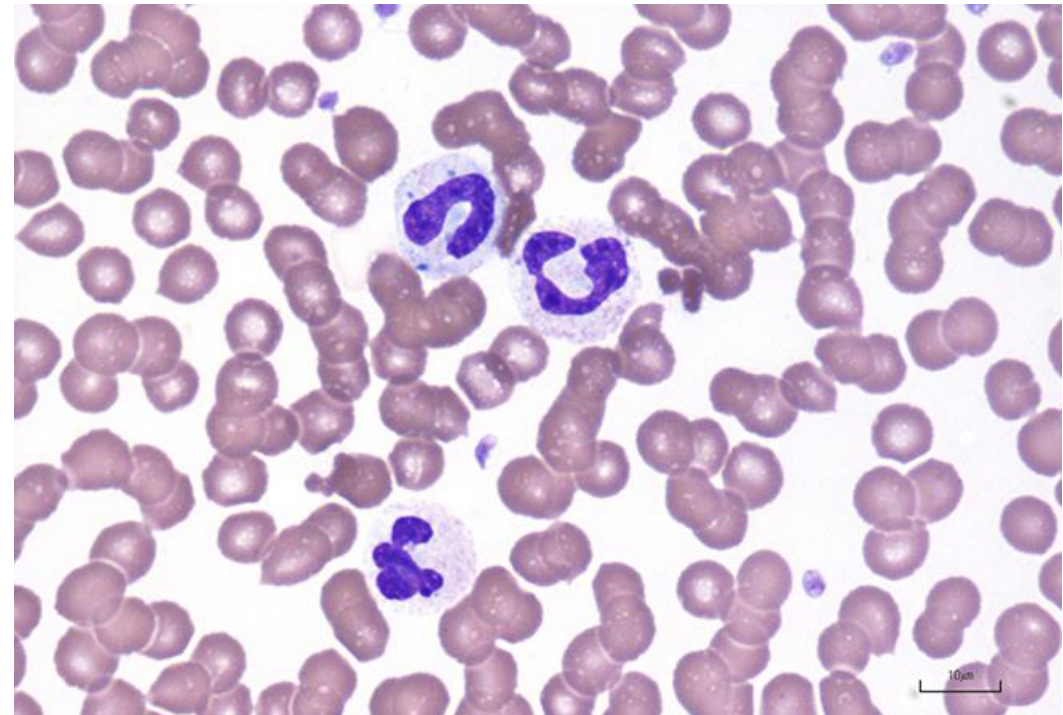
ProCyte Dx – Canine patient RBC Dot Plots

Bands

* Suspected

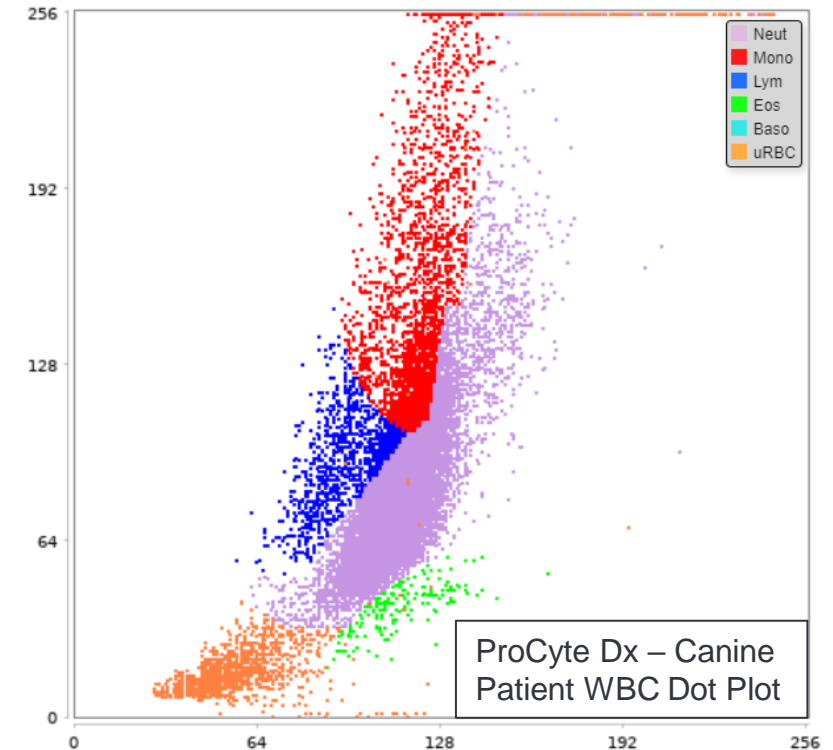
* Confirm with dot plot and/or blood film review.

Immature and/or toxic neutrophils likely present - consider inflammation



When should blood cell morphology be reviewed ?

- Ideally all smears should be evaluated
- Investigation of critically ill patient
- Moderately to severely anaemic patients
- Markedly high WBC counts
- Markedly low WBC/Plt counts
- Flags in dot plots/indistinct separation of clusters
- Unexpected or suspicious instrument results



Bands

*** Suspected**

*** Confirm with dot plot and/or blood film review.**

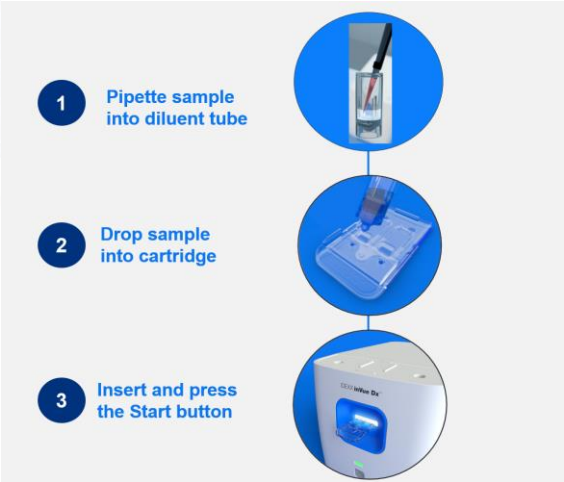
Immature and/or toxic neutrophils likely present - consider inflammation

ASVCP guidelines

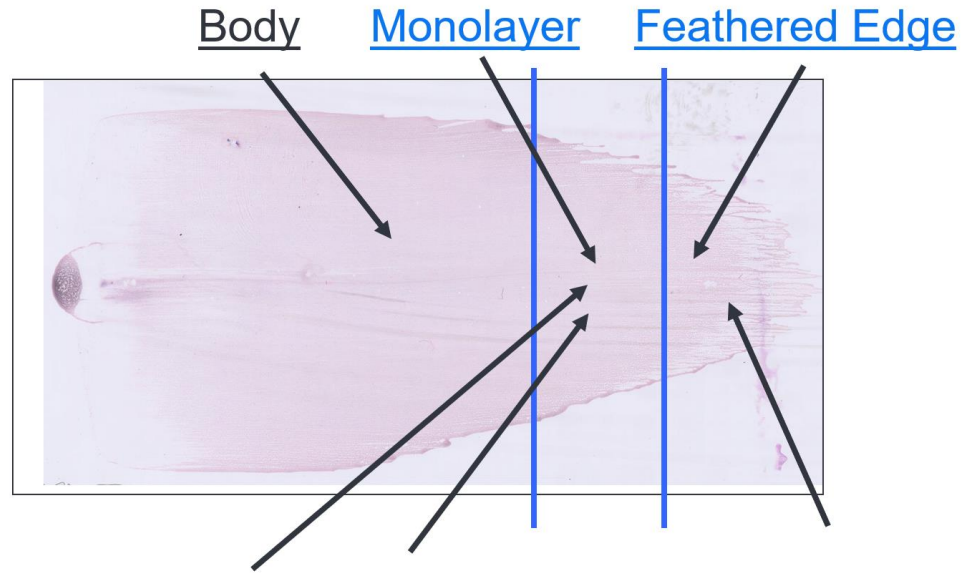
Some suggested numerical guidelines for medical review of blood smear and CBC data

	CRITERIA
WBC	Leukopenia < 3 x10e9/L
	Leukocytosis > 30 x10e9/L
	Lymphocytosis > 10 x10e9/L
	<i>Any unclassified cells</i>
Platelets	Thrombocytopenia < 100 x10e9/L
	Thrombocytosis > 900 x10e9/L
	Abnormal MPV (if reported by instrument)
RBC	Moderate to severe anaemia
	>5 nRBC/100WBC
	Abnormal MCV

Morphological evaluation of blood cells



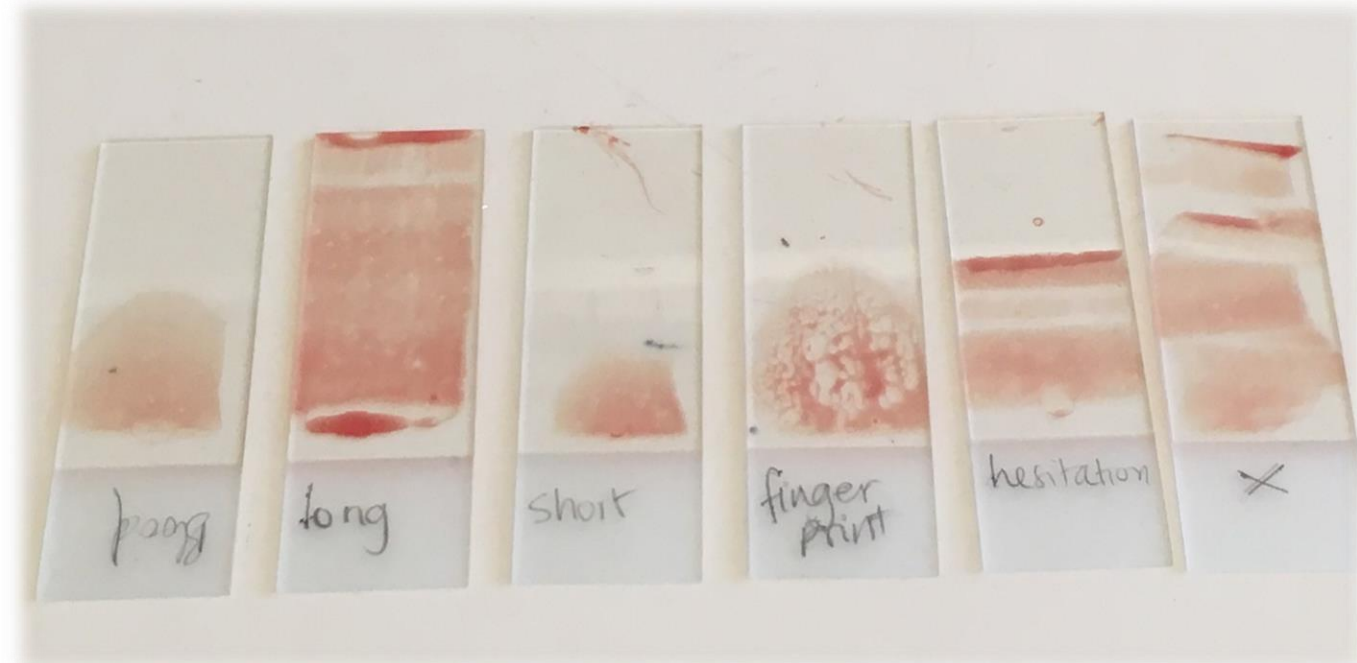
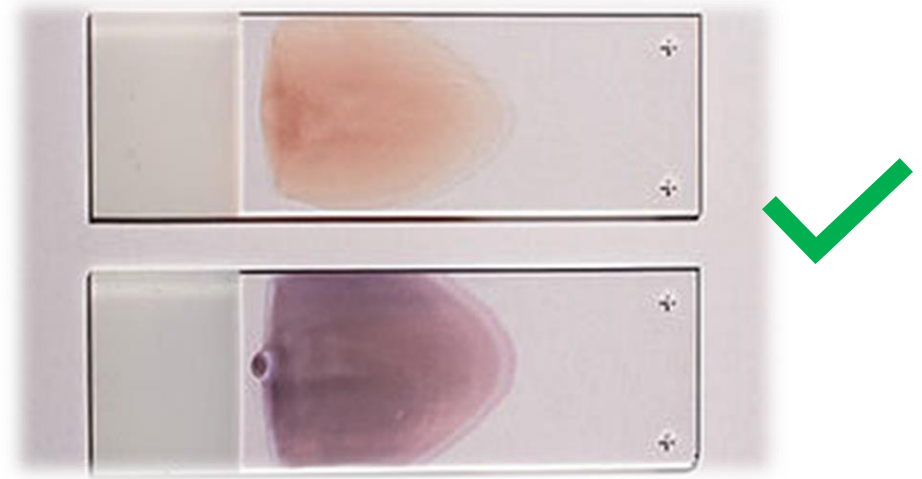
Blood smear



- Rouleaux
- Agglutination

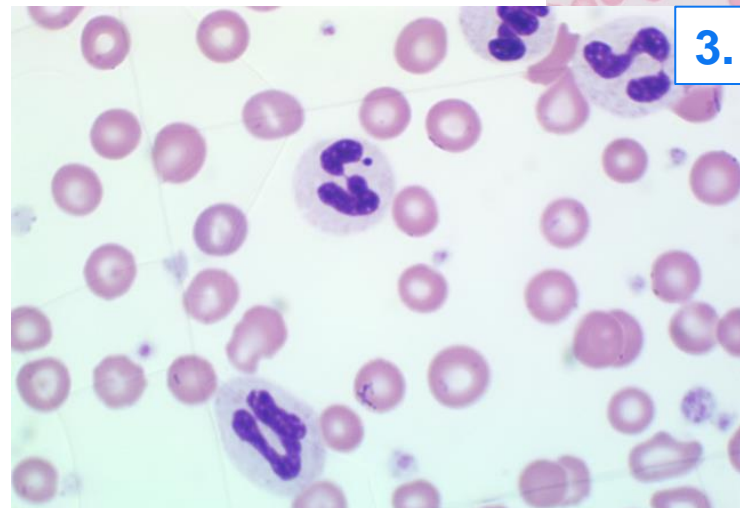
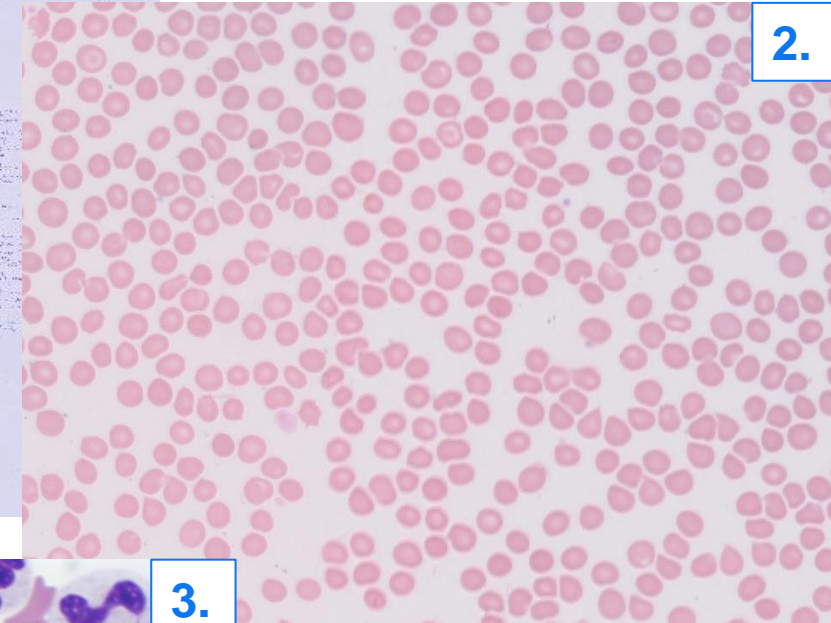
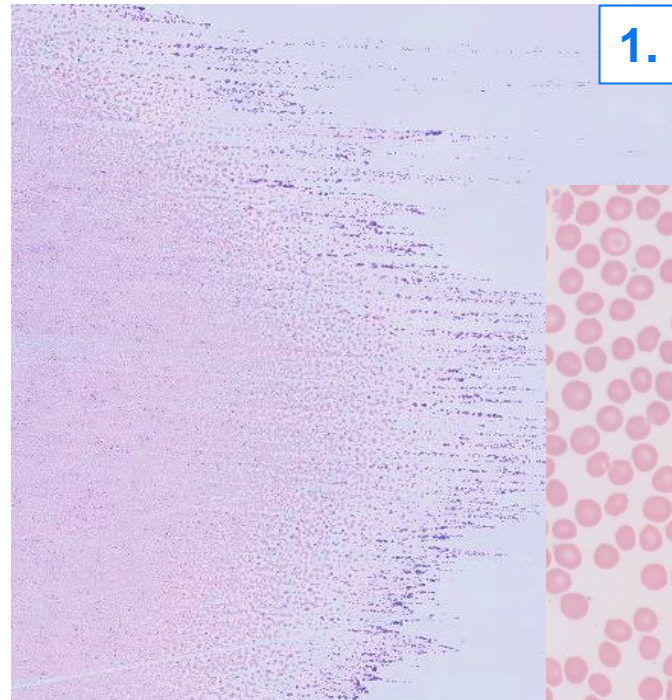
- Estimate numbers
- Morphology

- Platelet clumps
- Large cells
- Microfilaria



Systematic approach to blood smear review

1. Start small – with low magnification (10x) and then feathered edge
2. Go deeper - Go two to three fields back to the body of the smear into the monolayer
3. Go bigger – Increase to oil and evaluate morphology
4. Have a consistent approach:
 - + Platelets
 - + Erythrocytes
 - + Leukocytes



Blood smear evaluation steps - Systematic stepwise approach



Cell distribution

For all cell types:
Agglutination/
aggregation



Platelets

Estimate plt numbers
Examine morphology



Red Blood cells

Evaluate:

- size,
- shape,
- color,
- inclusions.

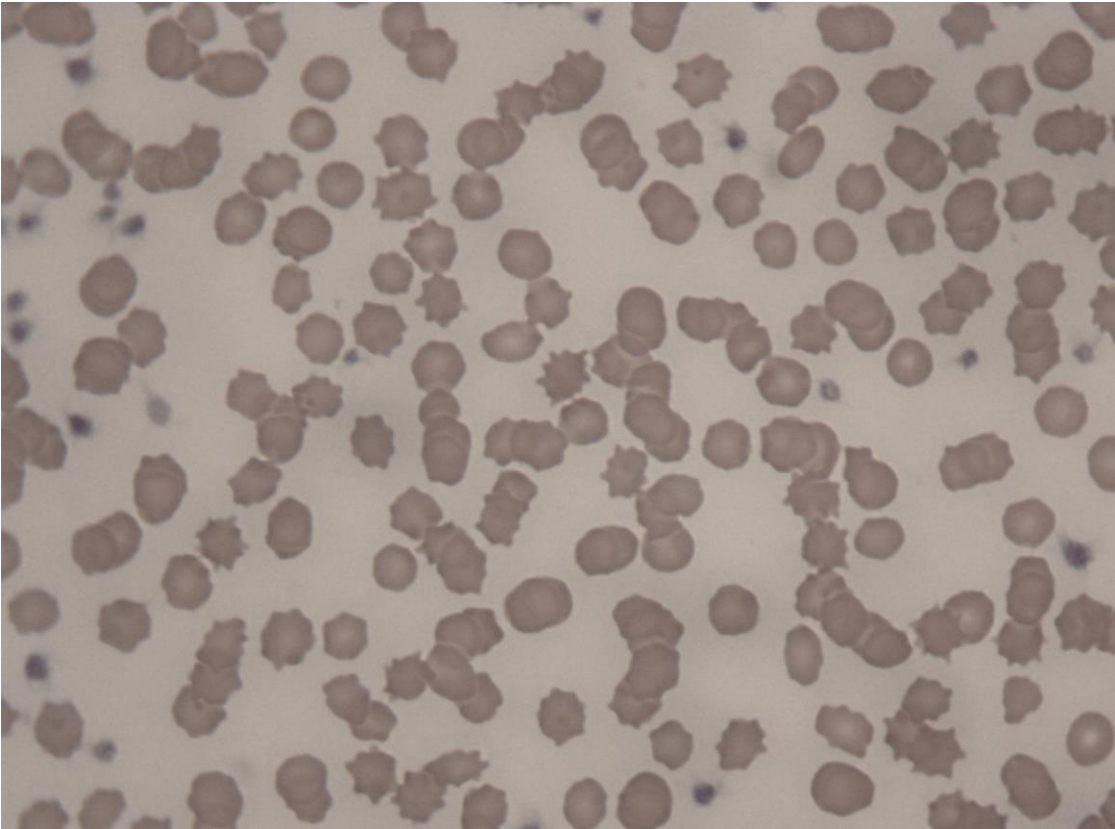


White blood cells

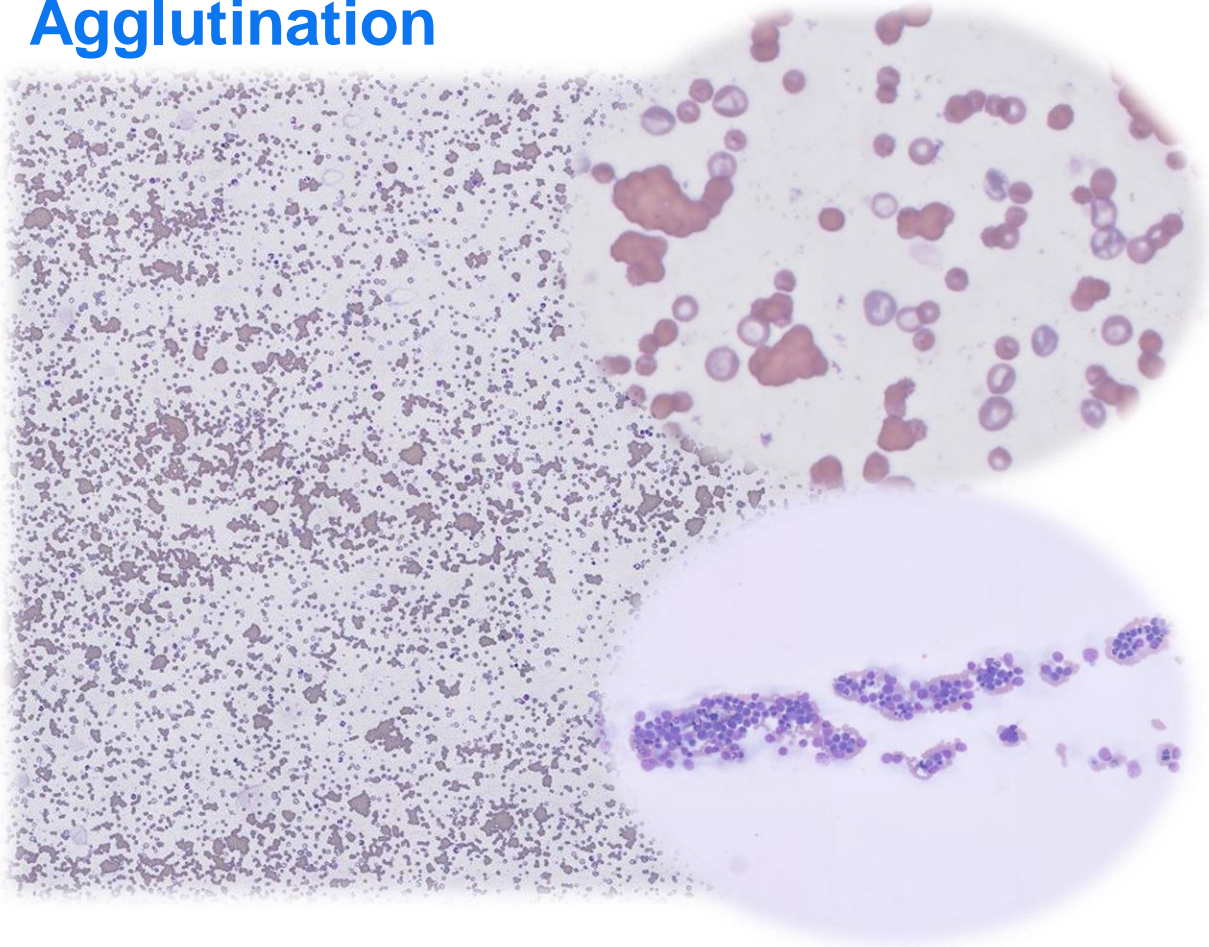
Do or verify differential
cell count
Evaluate morphology
changes and inclusions

Cell distribution

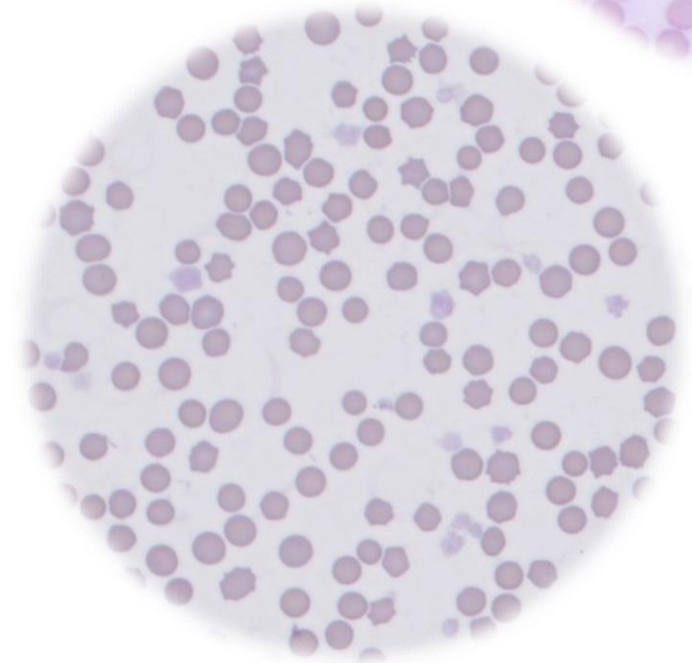
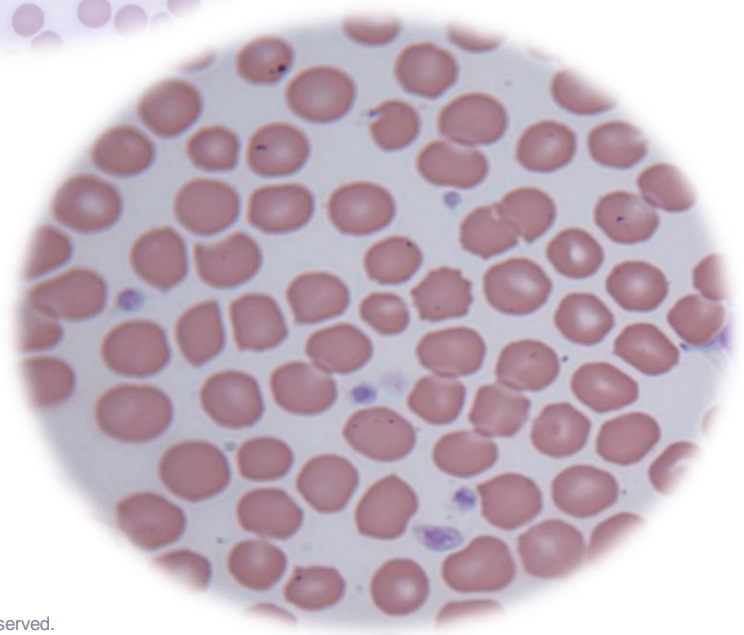
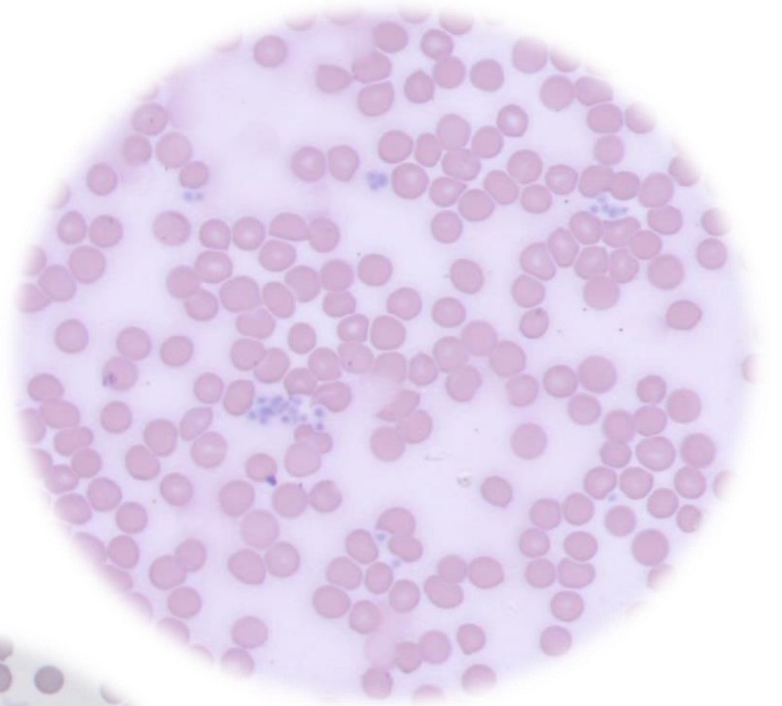
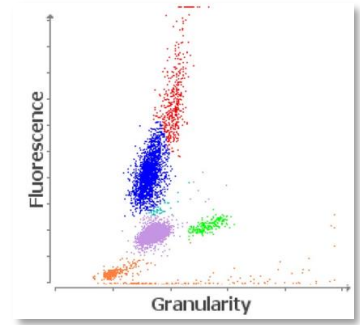
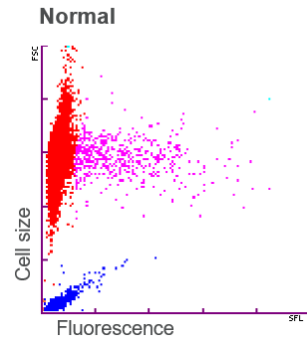
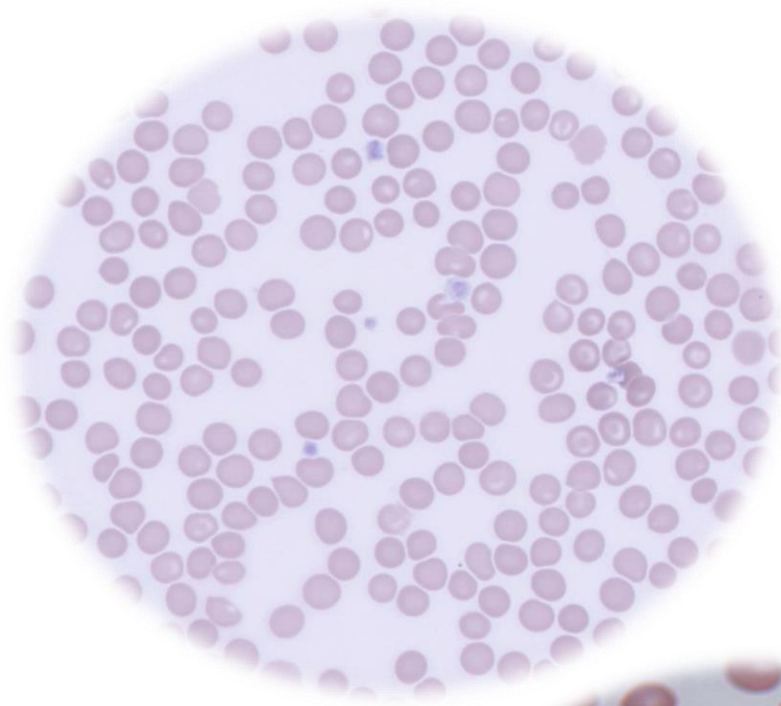
Rouleaux



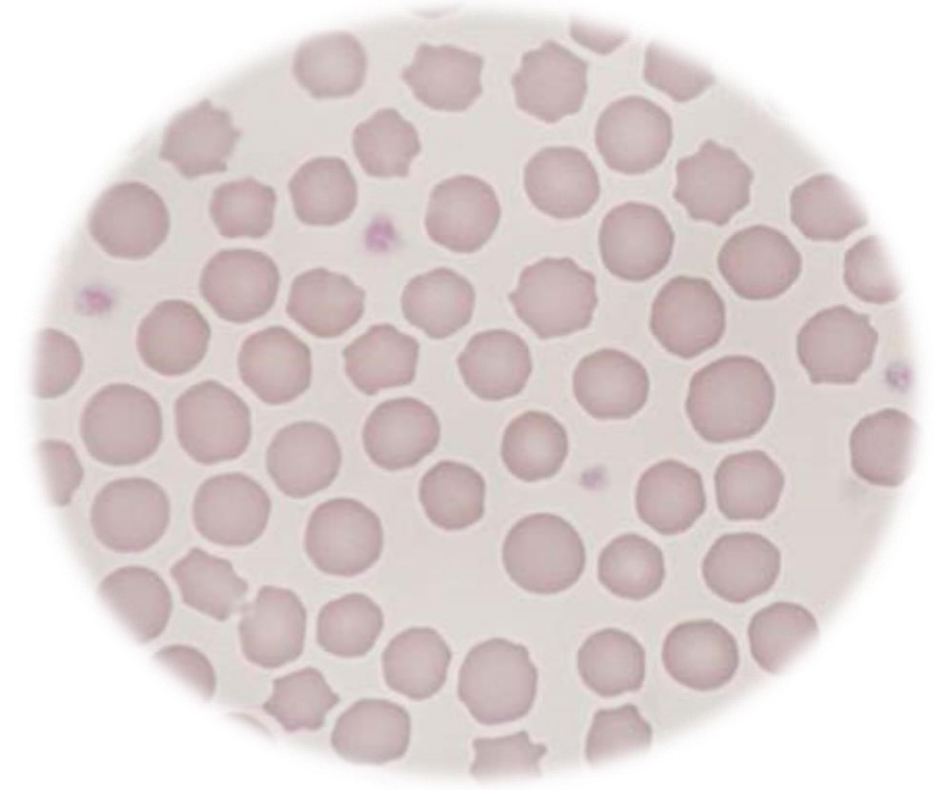
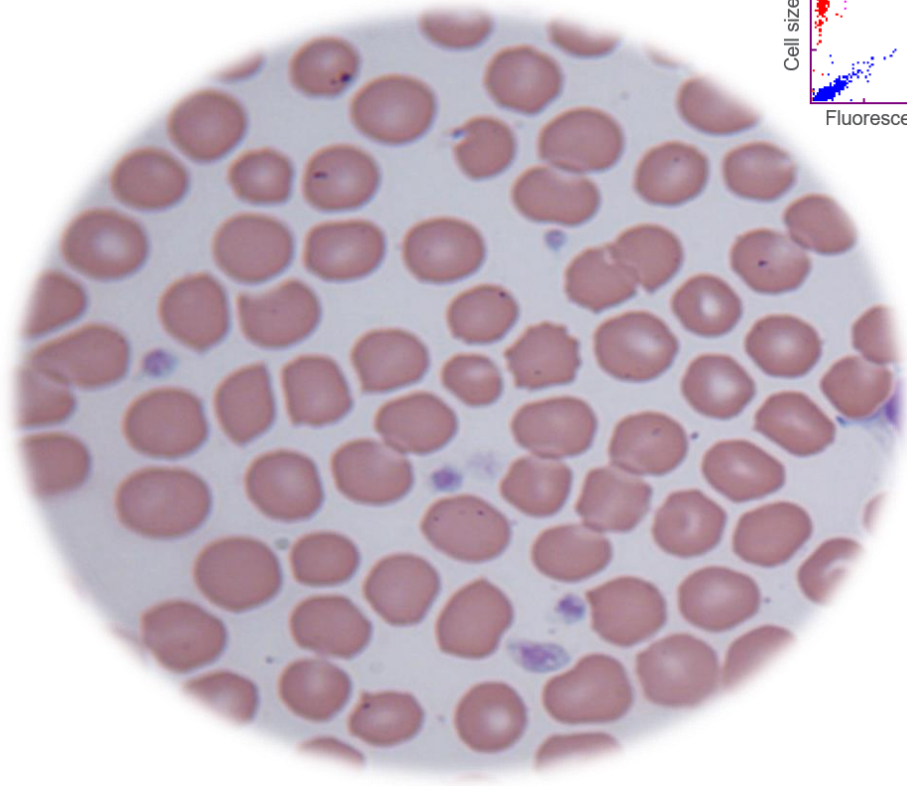
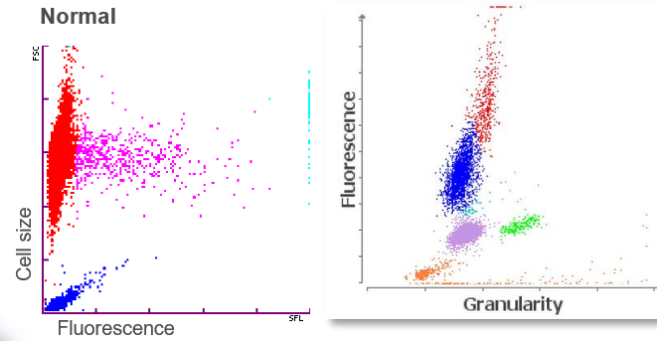
Agglutination



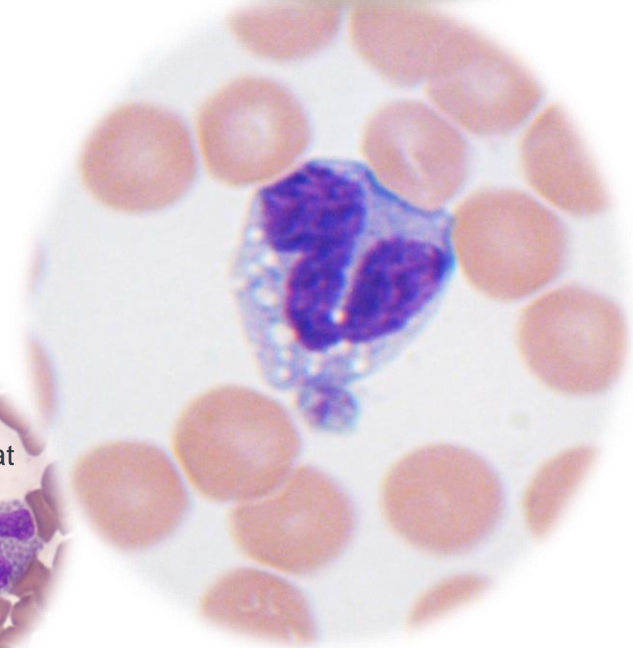
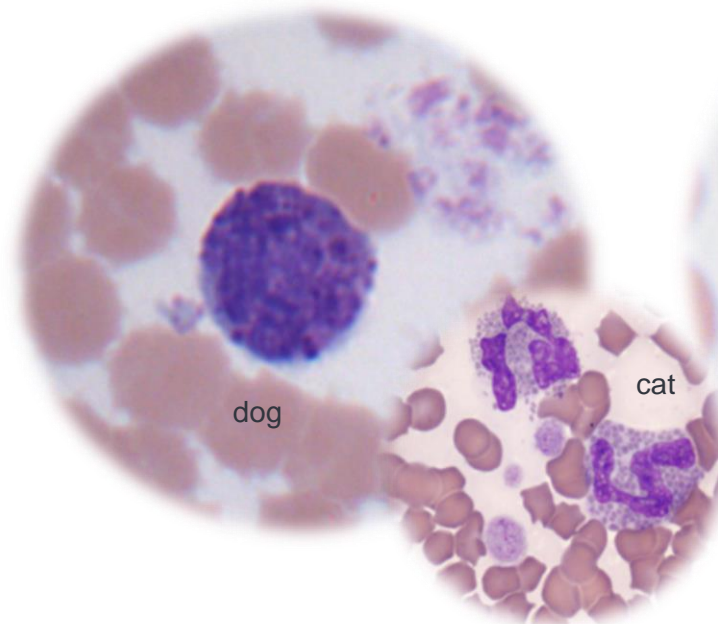
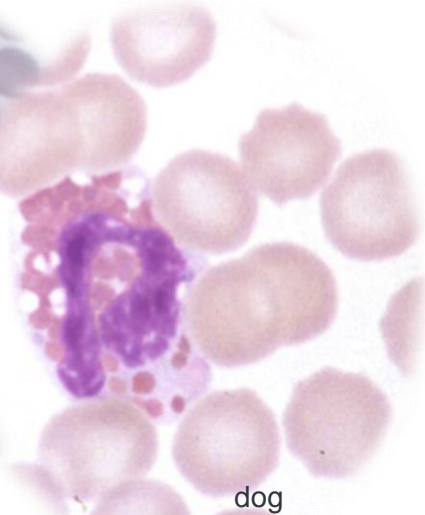
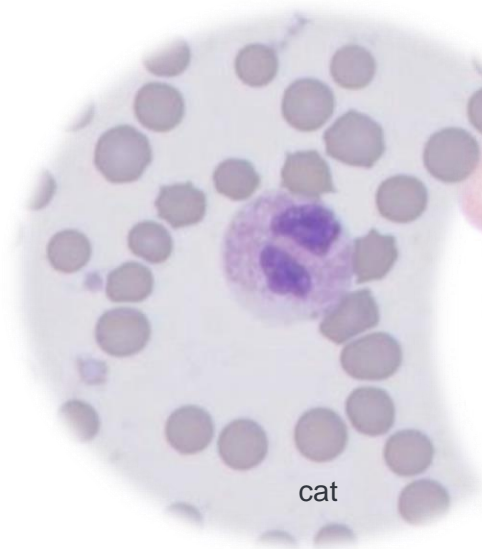
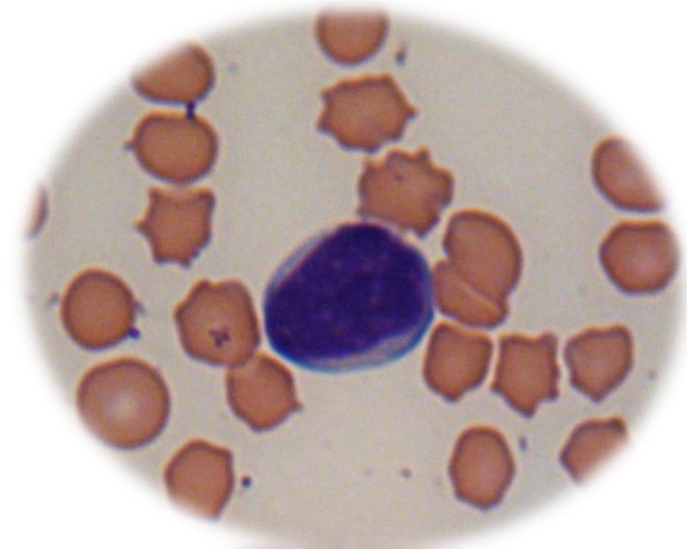
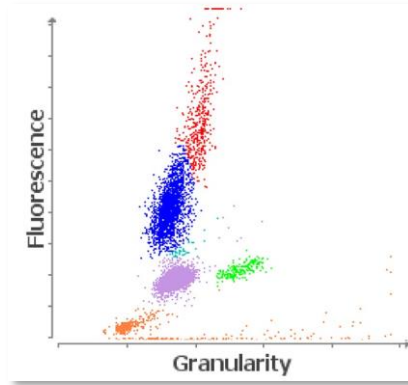
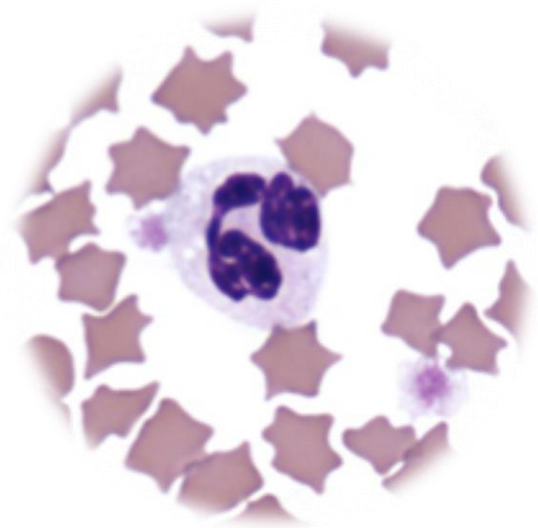
What is normal? PLT



What is normal? RBC

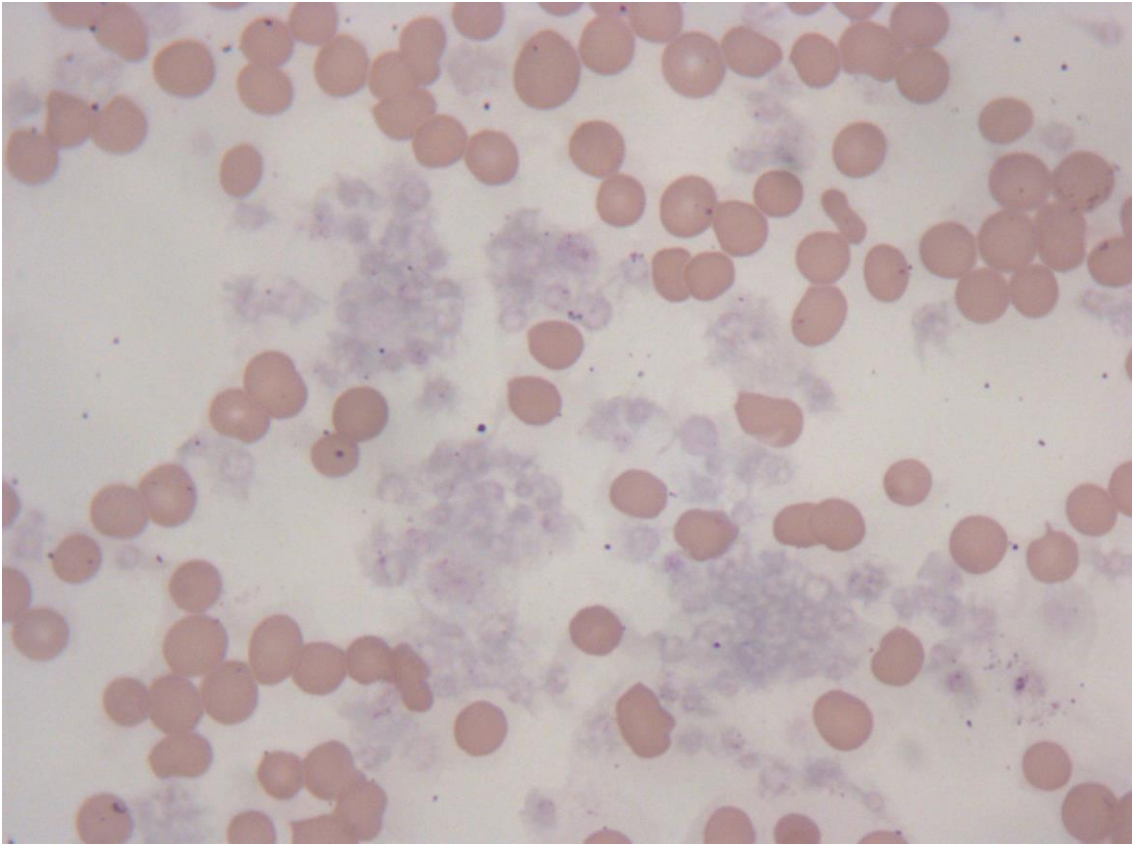


What is normal? WBC

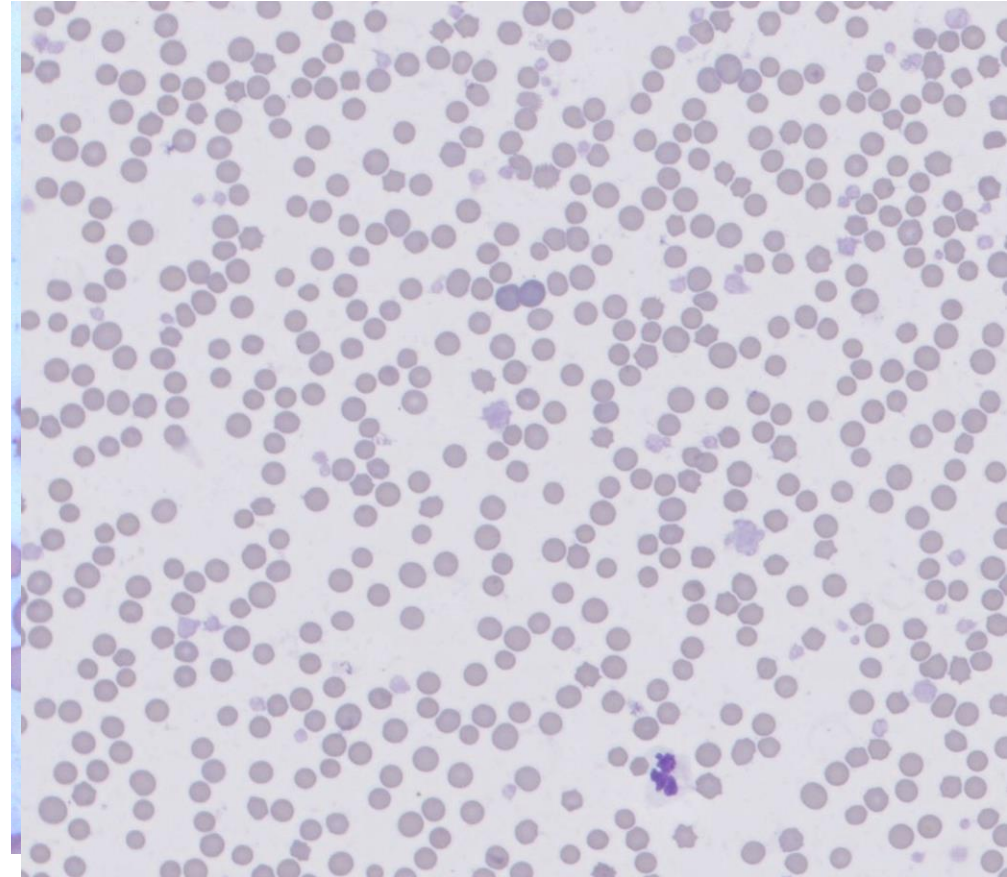


Platelets

Platelet clumps



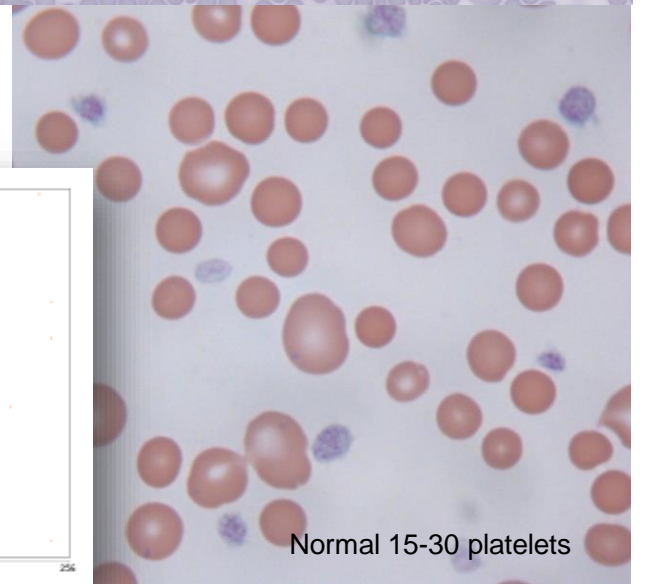
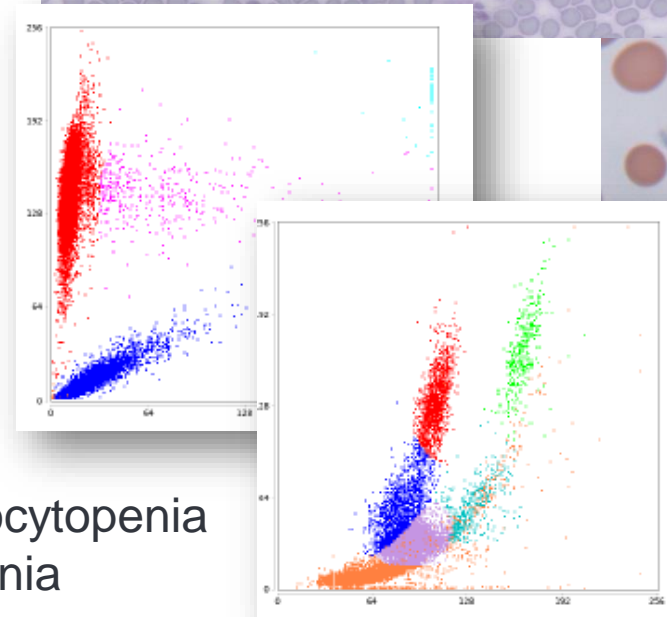
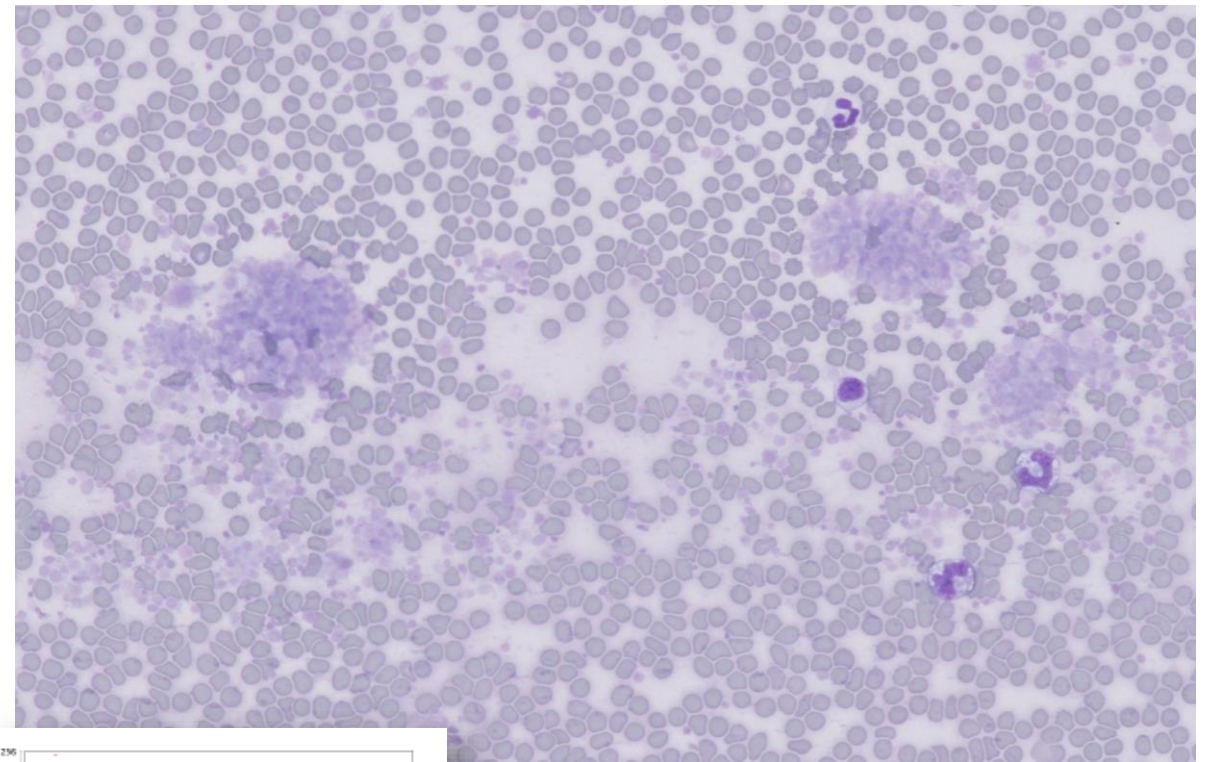
Macroplatelets



Platelet estimates

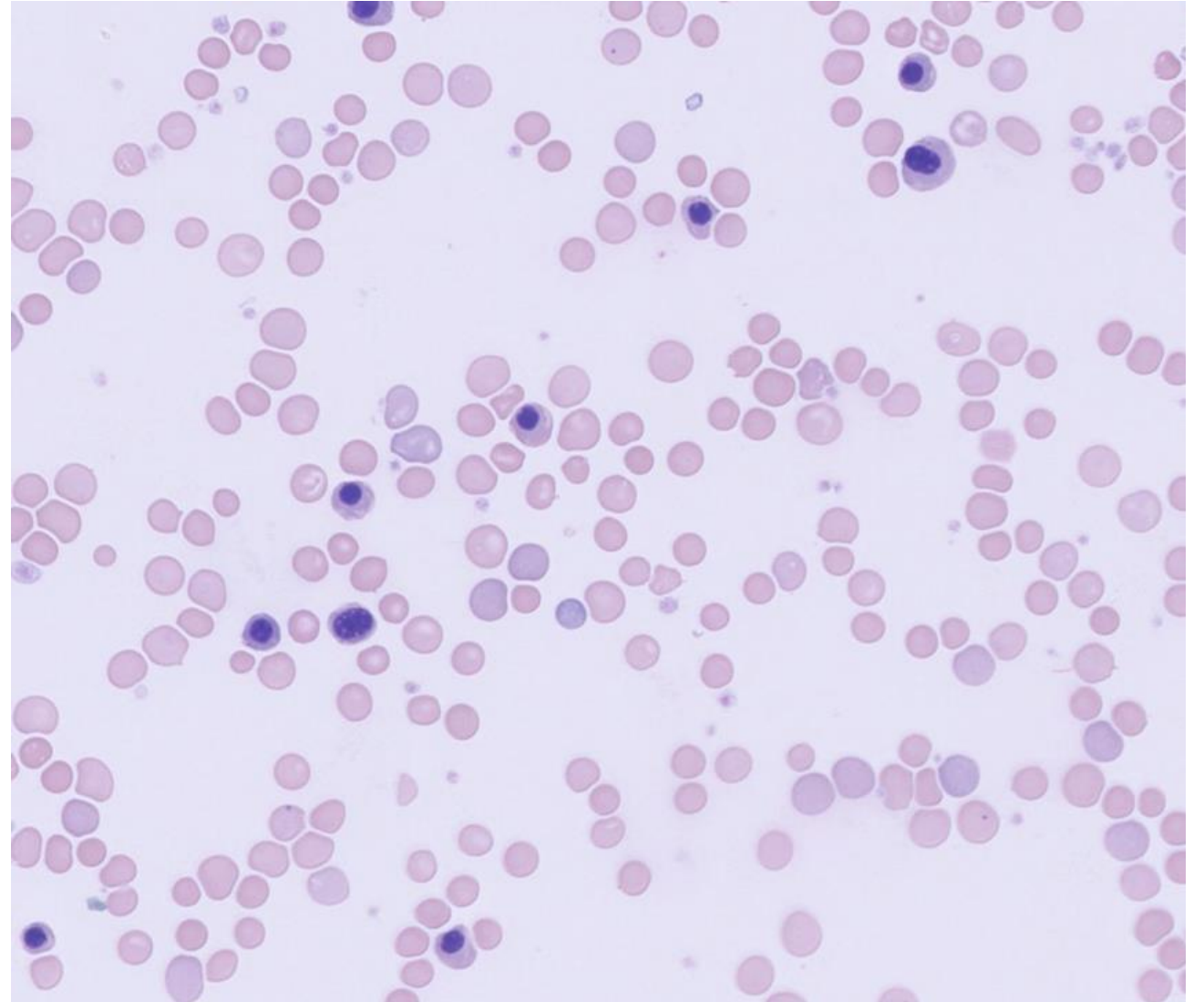
- ✓ Assuming NO PLT CLUMPS in feathered edge and NO CLOTS!
- 1. Count number of platelets in 10 fields oil immersion in monolayer
- 2. Do the average ($\Sigma / 10$)
- 3. Multiply by 15 or 20
- 4. This is the **estimated** number
($\times 10^9/L$)

>10 per HPF = no significant thrombocytopenia
<2 per HPF = marked thrombocytopenia



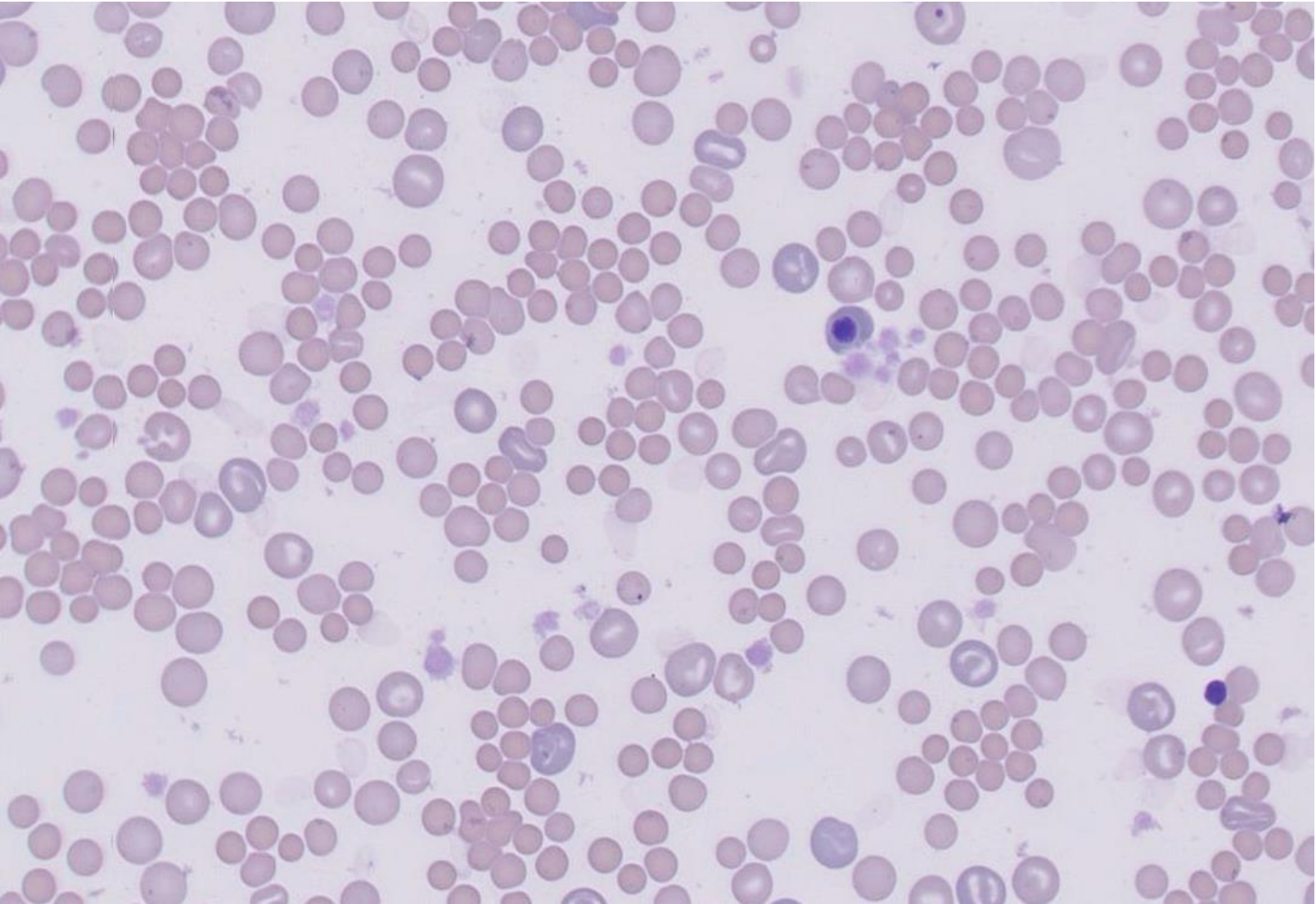
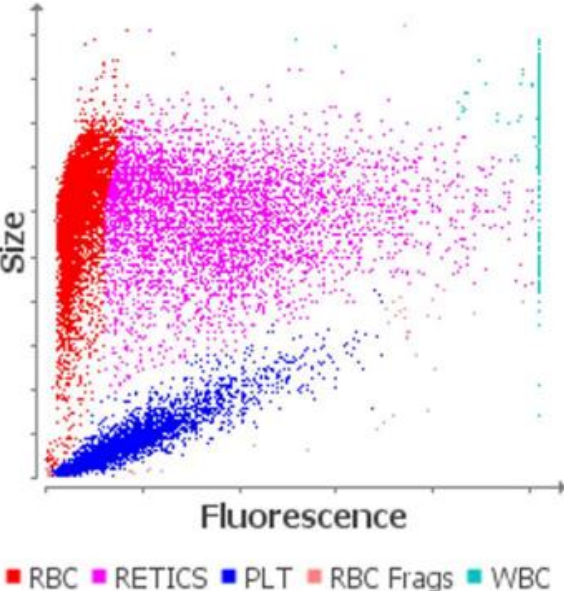
For the RBC we are evaluating 3 main things...

- + Density and spread
 - + Agglutination
- + Colour
 - + Polychromasia
 - + Hypochromasia
- + Size, shapes and inclusions
 - + nRBC
 - + Heinz bodies
 - + Spherocytes
 - + Poikilocytes



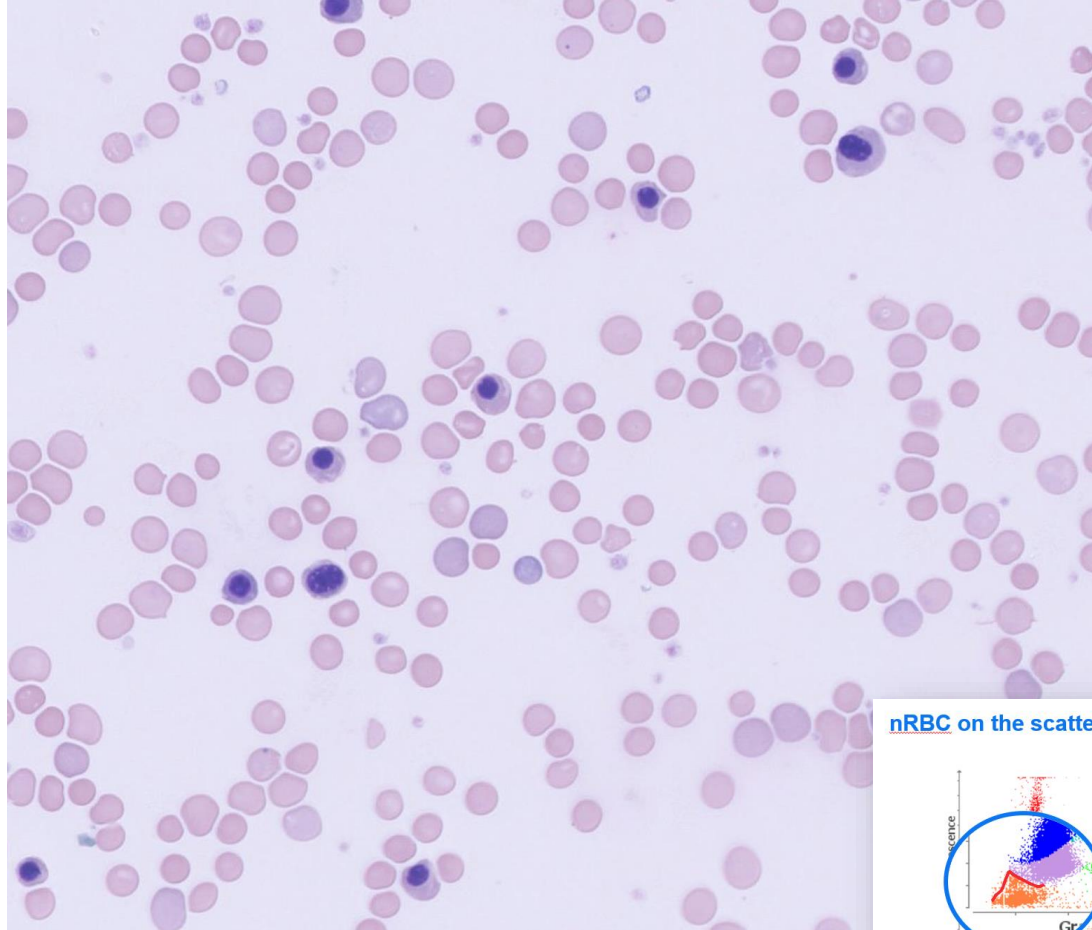
Red blood cell abnormalities

+ Polychromasia

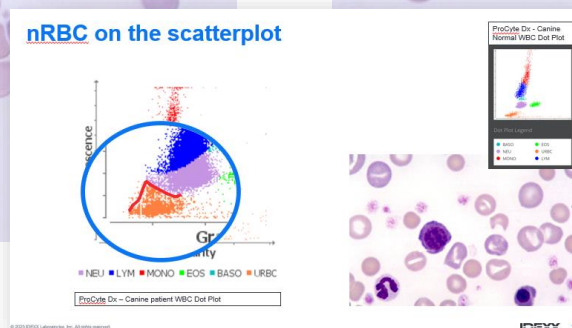


Nucleated RBC

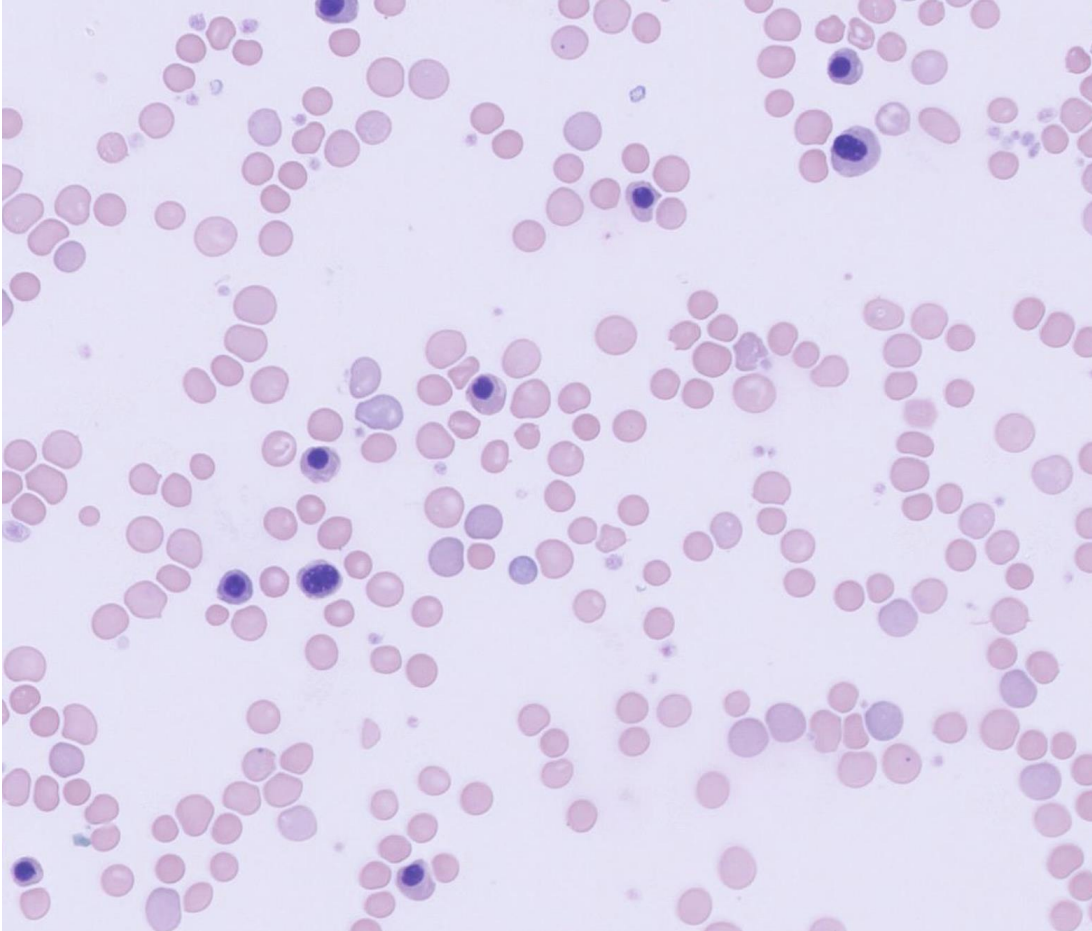
As part of regeneration



Inappropriate rubricytosis

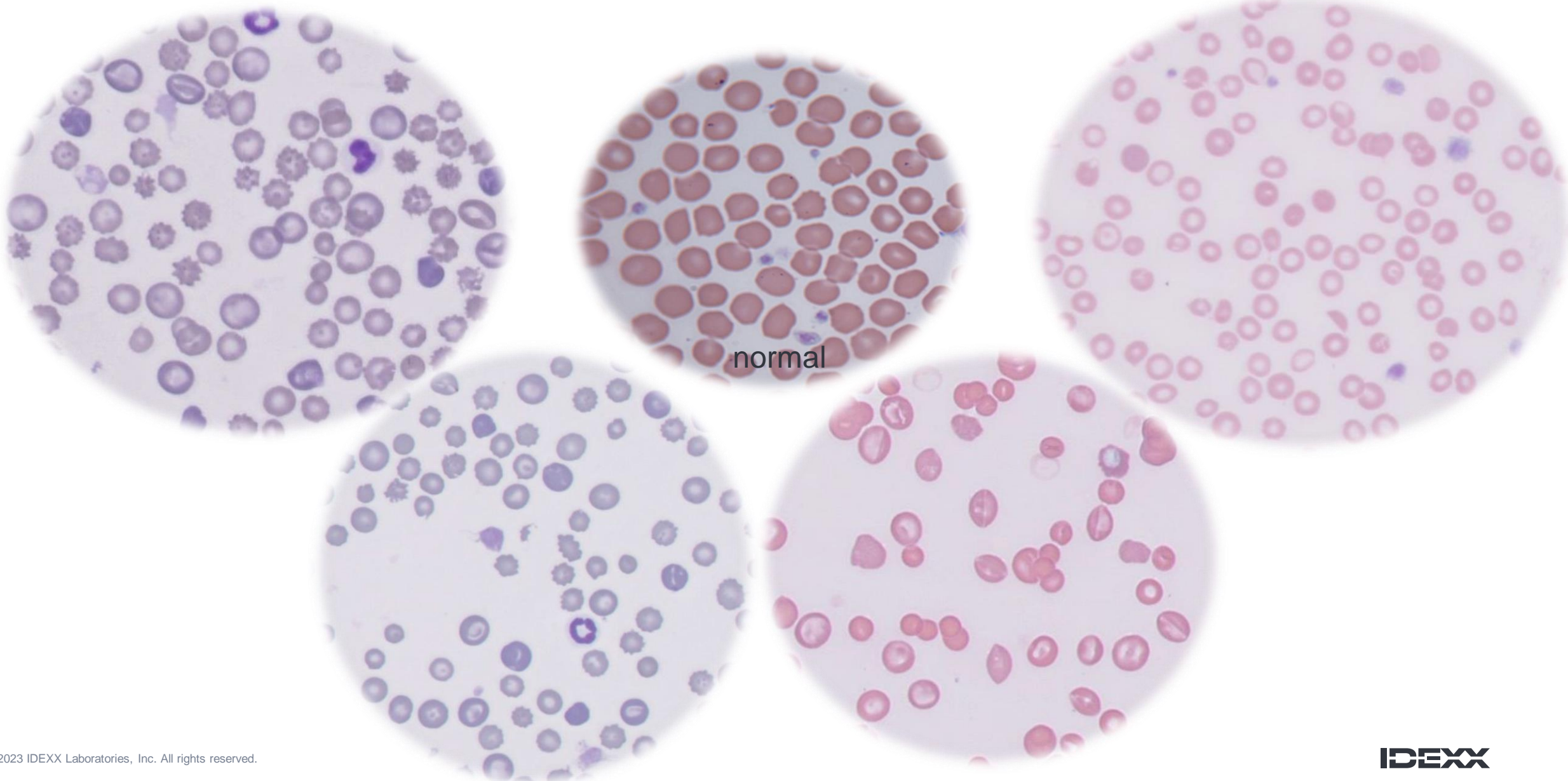


Nucleated red blood cells



- Part of regenerative response
- Number should be proportionate
- In absence of proportionate regeneration:
INAPPROPRIATE RUBRICYTOSIS
 - Bone marrow damage
 - Lead poisoning
 - Heat stroke
 - Dyserythropoiesis
 - Splenic disorder

Are there different sizes, shapes or inclusions?



Poikilocytosis (erythrocytes shape changes)

The secret coding language of haematology

- + Spherocytes
- + Ghost cells
- + Acanthocytes
- + Keratocytes
- + Schistocytes
- + Heinz bodies
- + Echinocytes (crenated RBC)
- + Torocytes
- + Codocytes/target cells
- + Eccentrocytes
- + Ovalocytes
- + Dacryocytes
- + Knizocytes
- + Leptocytes

And the list goes on...

Poikilocytosis (erythrocytes shape changes)



Two young anaemic dogs

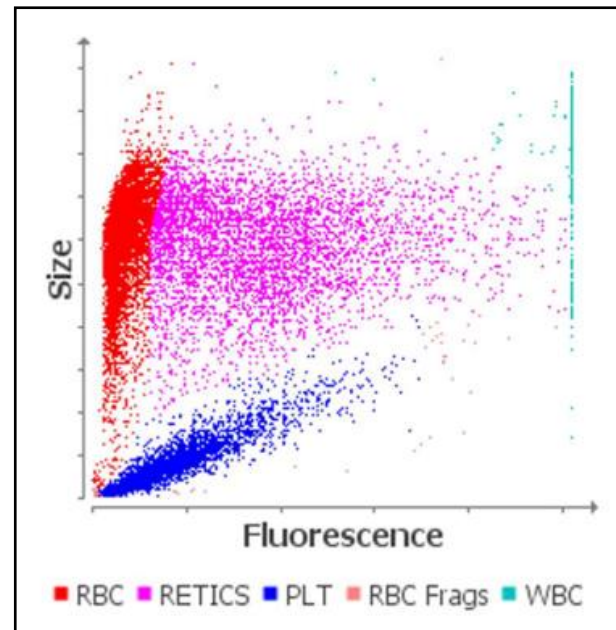
Case 1 Molly 4 yo FN Cocker Spaniel

- Lethargic for the past few days
- Off food
- Presented collapsed
- HR 140 and tachypnoea
- PCV 14.8%



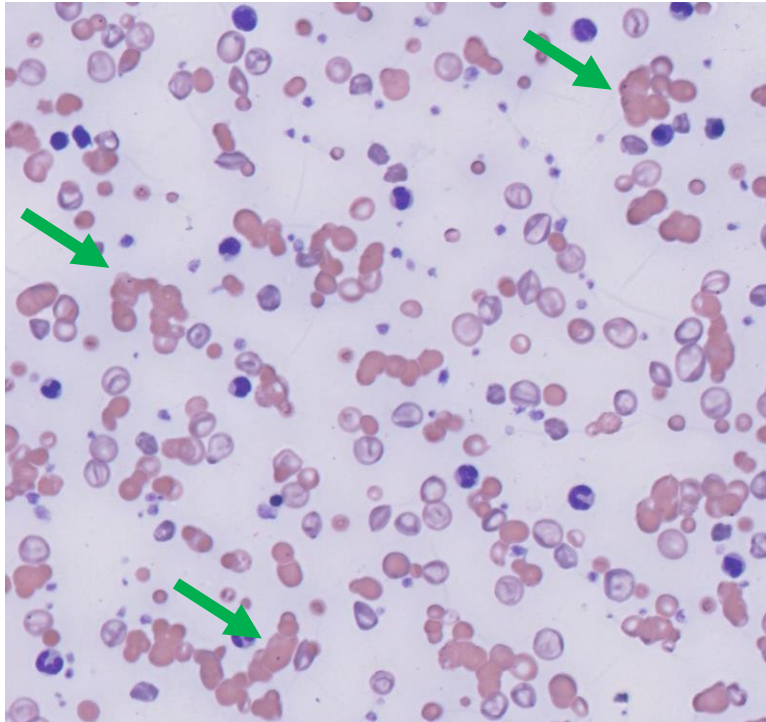
Case 2 Dodger 2 yo ME Border Collie

- Very quiet for a couple of days
- Off food
- Mucous membranes very pale
- HR 160
- PCV 20.1%

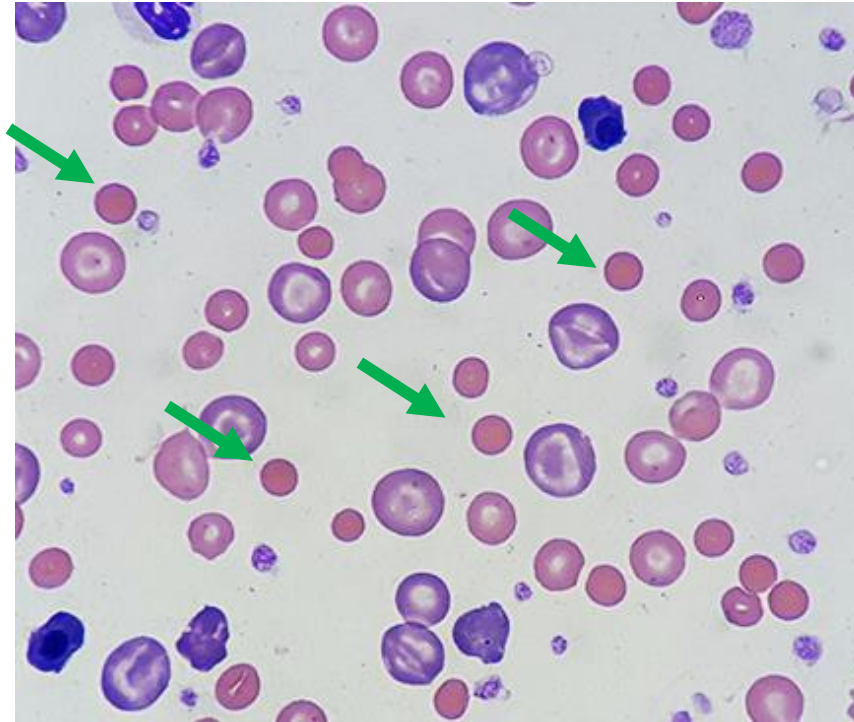


Case 1 - Molly

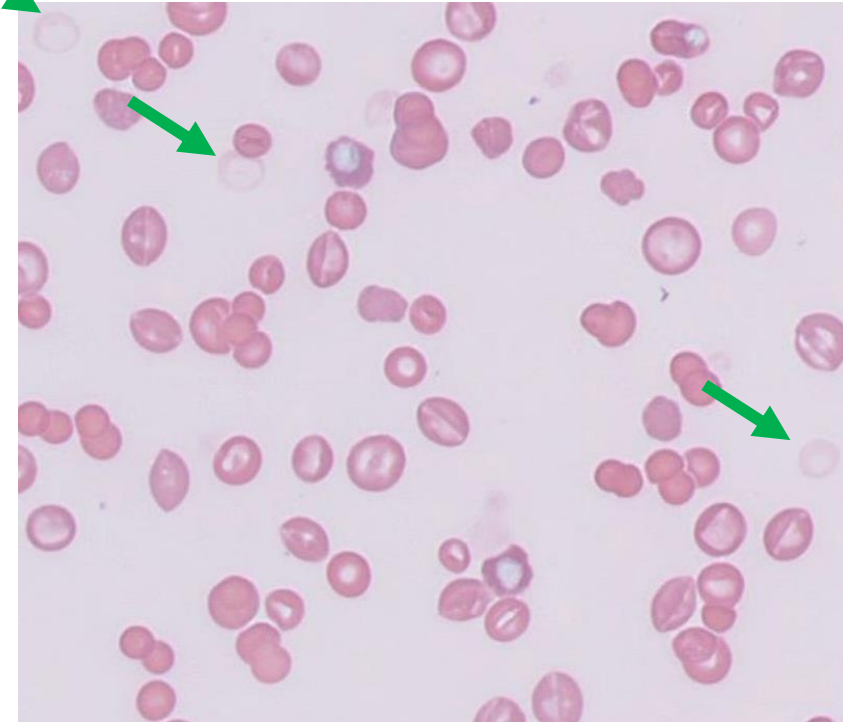
Features suggestive of immune mediated haemolytic anaemia



Agglutination
(Saline agglutination test)
(+/- Coombs test)



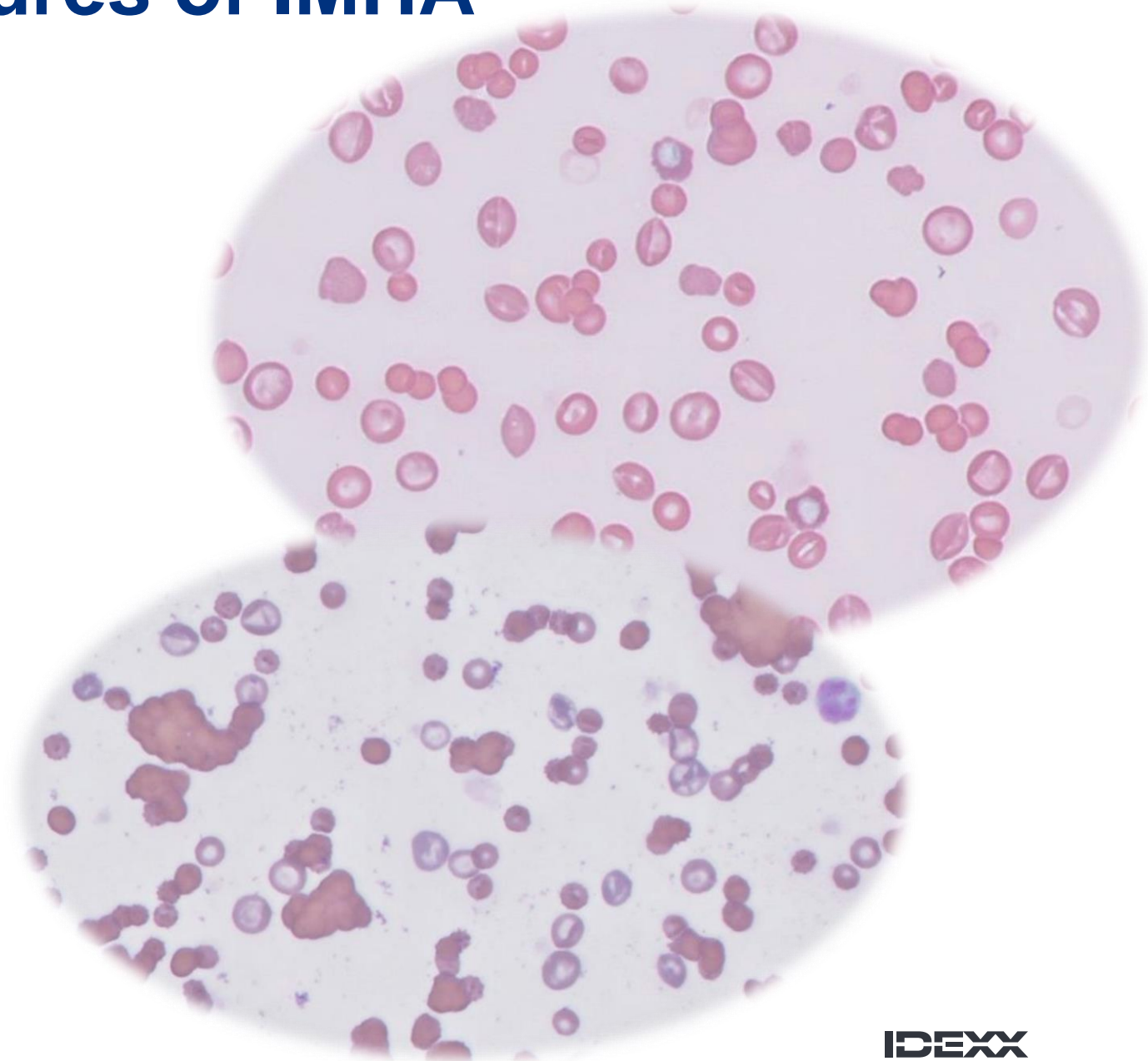
Spherocytes



Ghost cells (fresh smear)

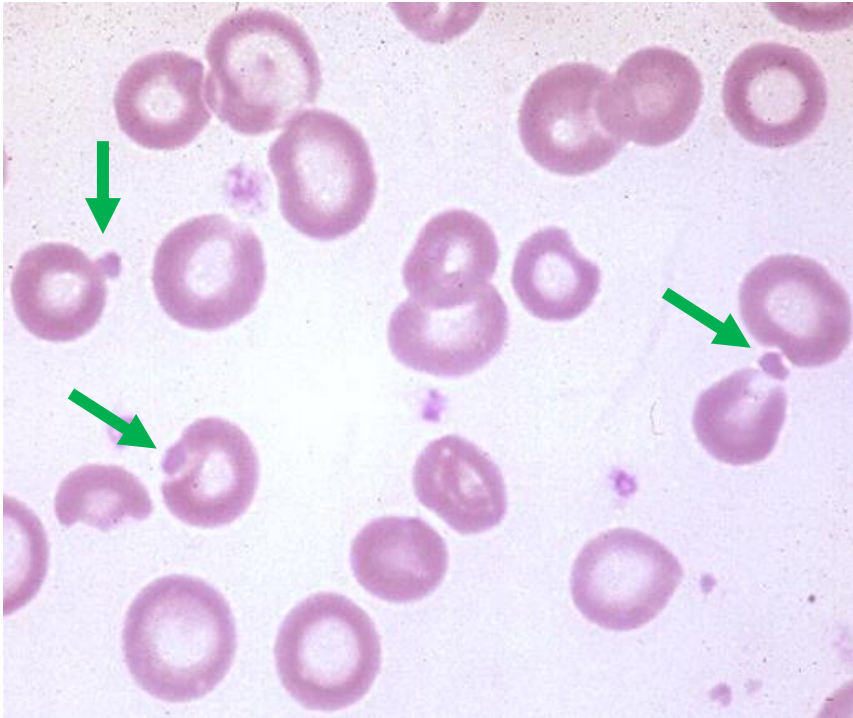
RBC morphology: Features of IMHA

- Agglutination
- Spherocytosis (Dogs)
- Ghost cells
- Ideally on a fresh smear
- Questionable results/follow up tests
 - In-saline agglutination
 - +/- Coomb's test
- Regenerative vs Non-regenerative



Case 2 - Dodger

Features suggestive of
haemolytic anaemia
due to oxidative injury



Heinz bodies

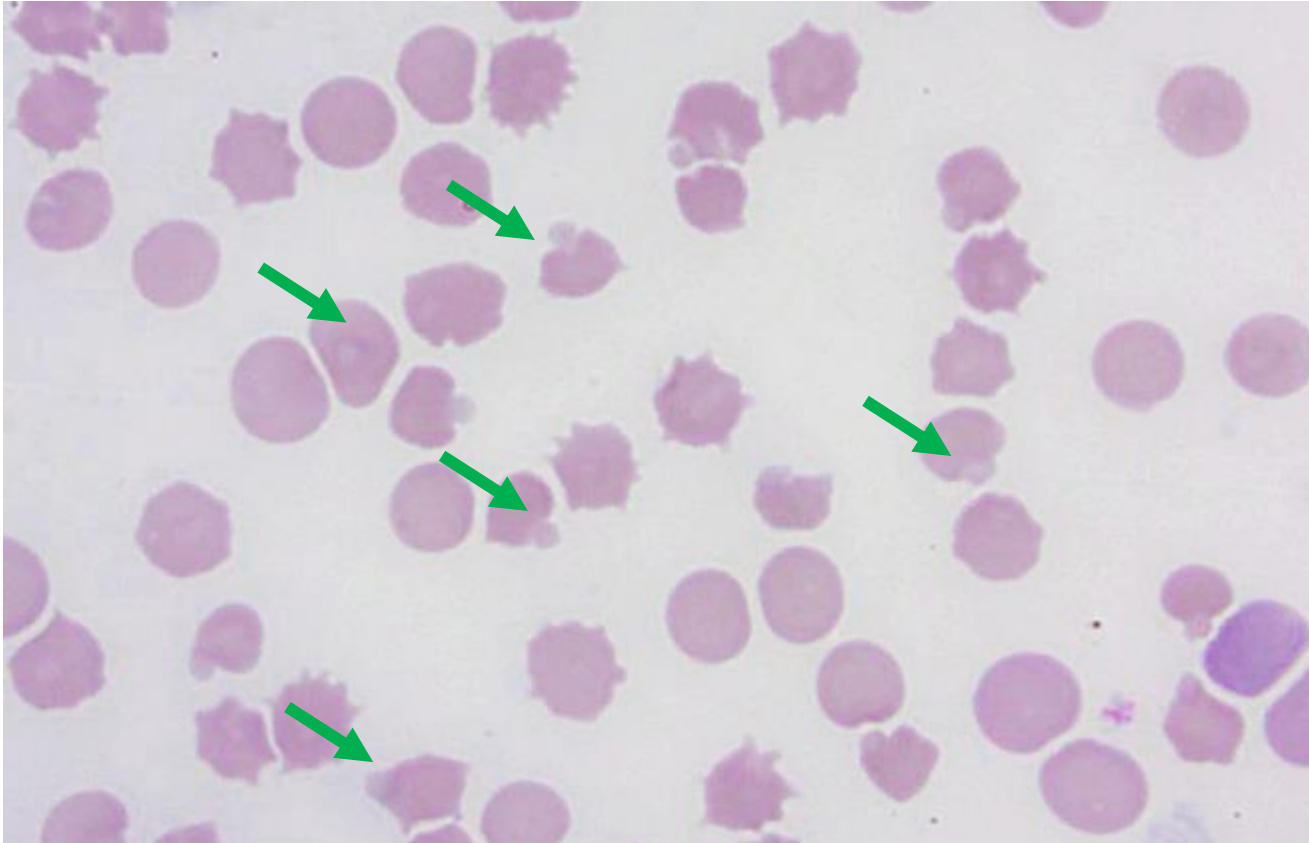


Heinz body on ghost cell

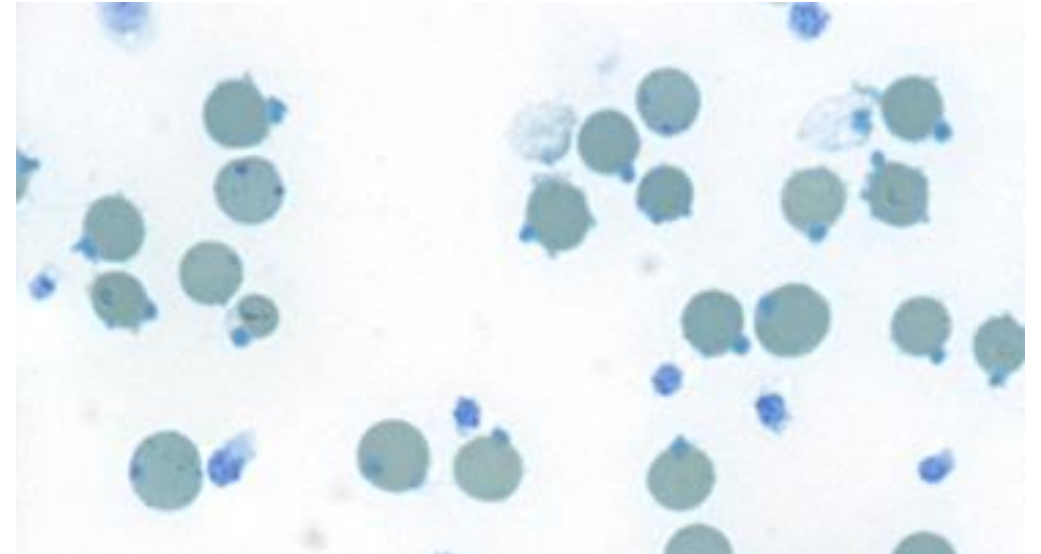


Eccentrocytes

Heinz bodies in cats



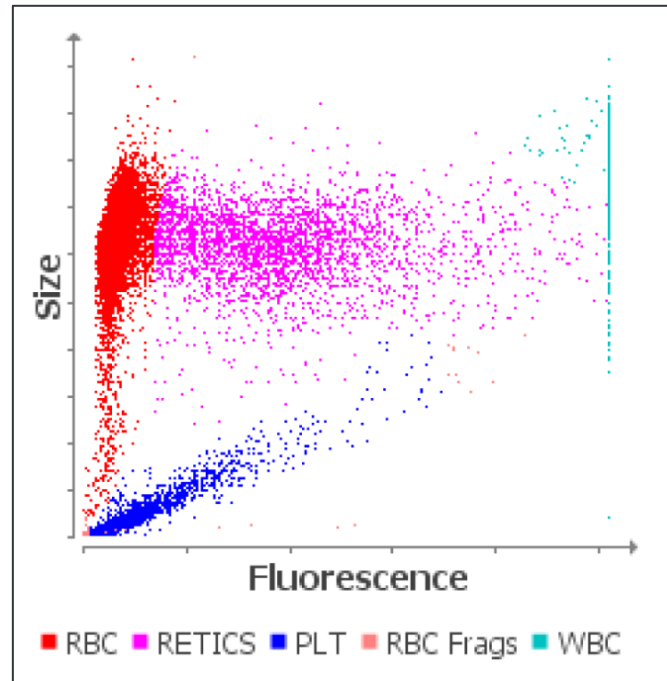
- + Small numbers normal in cats
- + When increased often due to endogenous oxidants
- + inflammation
- + diabetes mellitus (ketoacidosis)
- + hyperthyroidism
- + neoplasia (lymphoma)



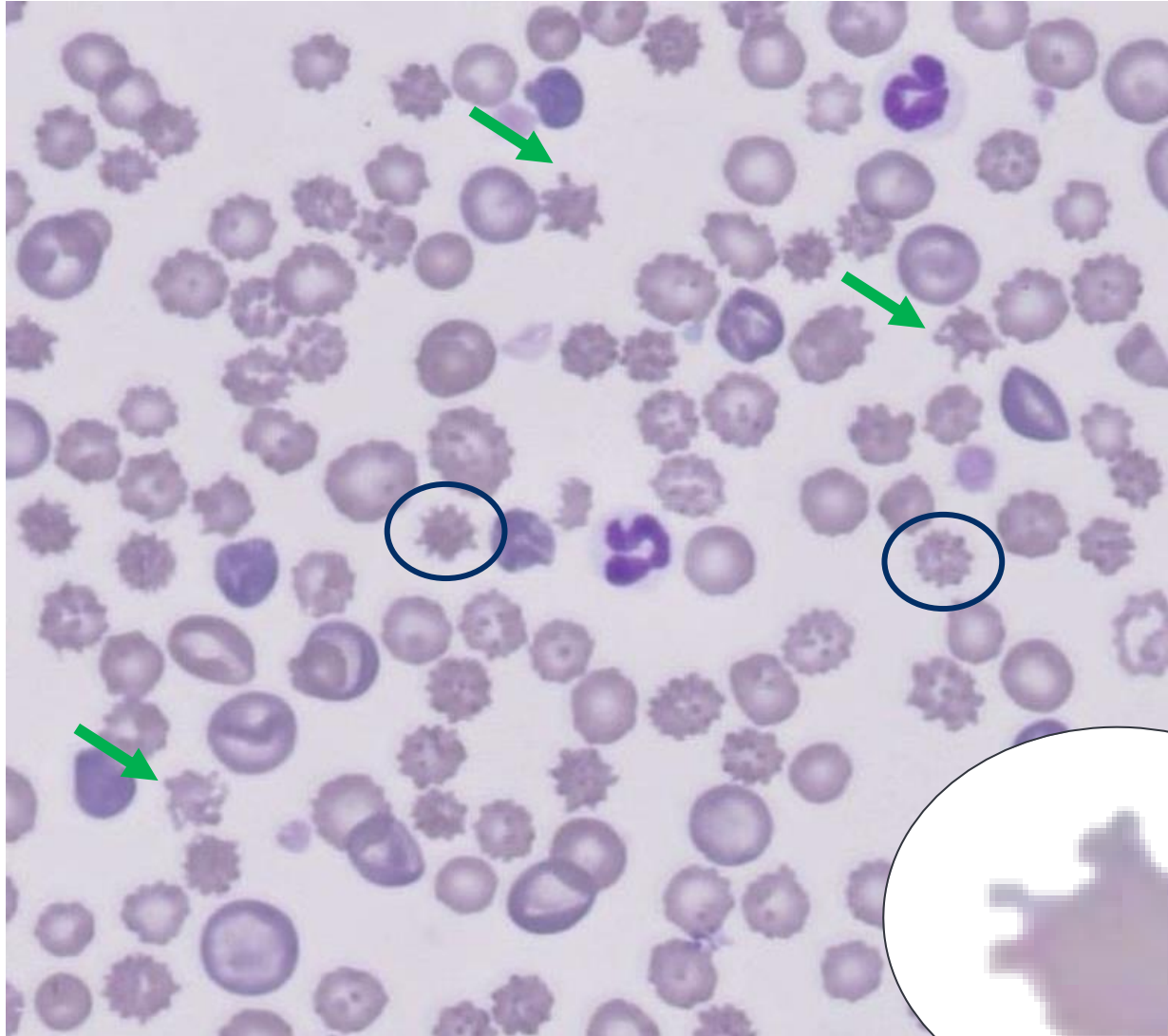
And the case of an old anaemic dog

Case 3 Buster 12 yo MN Mix breed dog

- + Occasional vomiting recently
 - + Presented collapsed
 - + Tachypnoea and tachycardia
 - + Distended abdomen
 - + Pale mucus membranes
-
- + PCV 19.4%



Case 3 - Buster

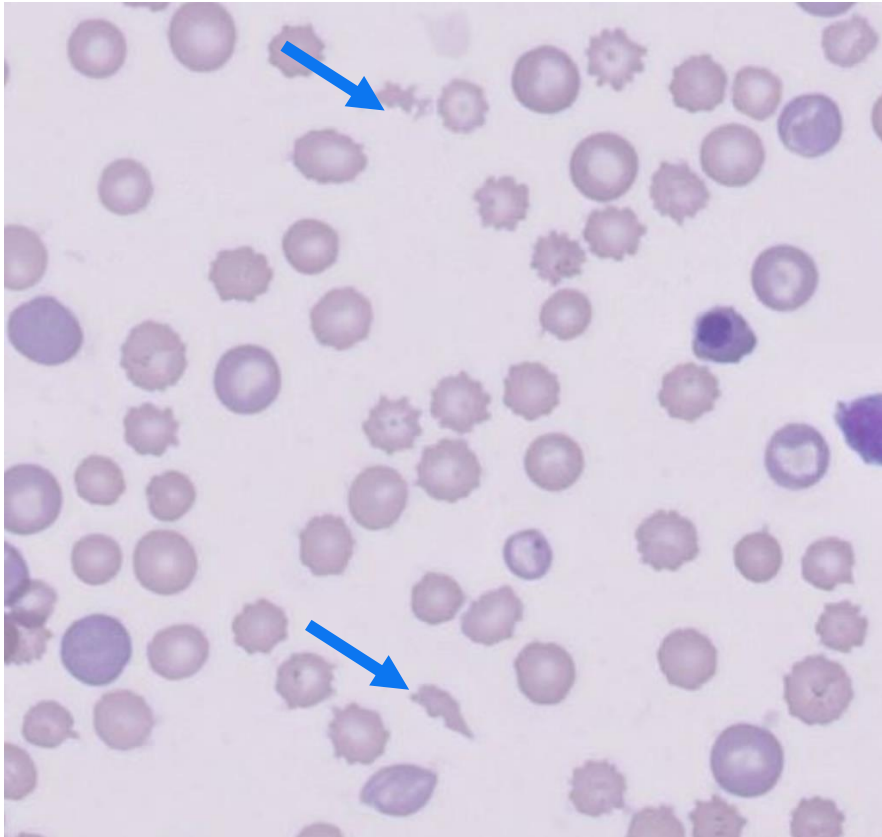


Acanthocytes

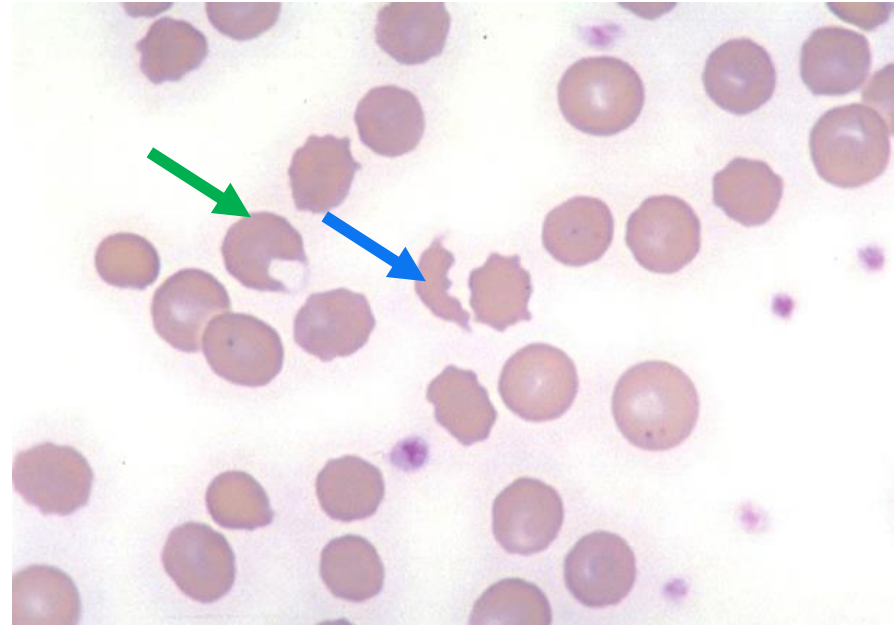
How to differentiate from echinocyte (artefact)

- + Irregular, unevenly distributed
- + Blunt-ended
- + Slender, long thread-like projections

Case 3 - Buster



Schistocytes



Keratocytes

Features suggestive of
RBC fragmentation
(microangiopathy)

Poikilocytes

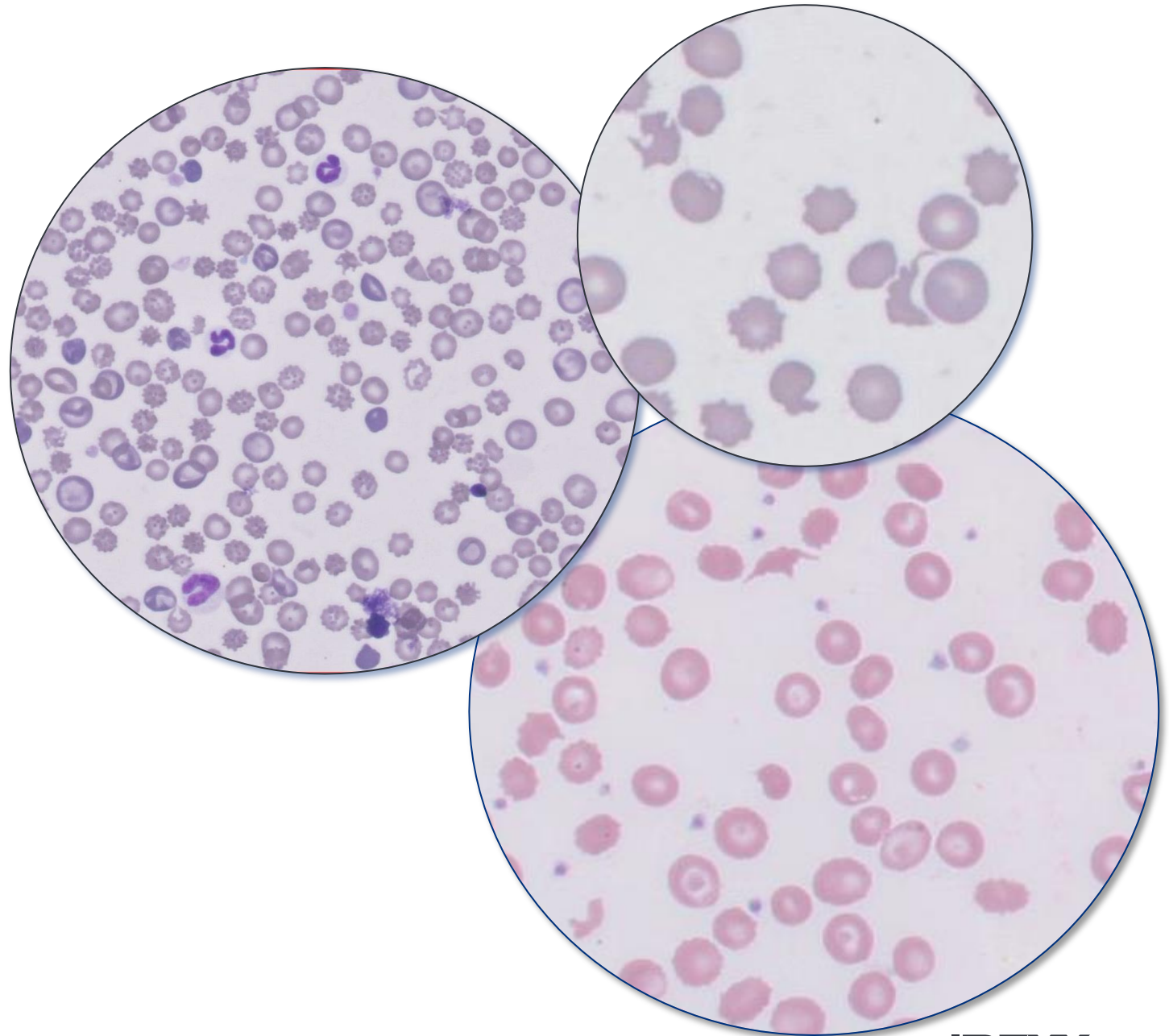
Significance?

- $>1/2$ per 100X field?
- Associated anaemia?
- Polychromasia?

Common differentials:

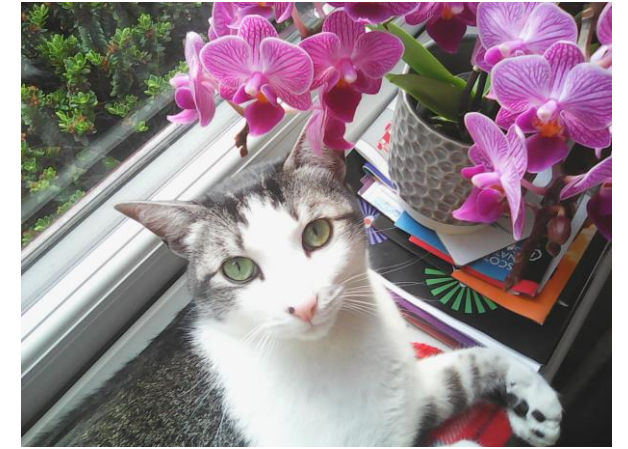
Conditions causing vascular abnormalities or turbulent blood flow, e.g.:

- Vascular tumours (haemangiosarcoma)
- Splenic/liver disease
- DIC
- Vasculitis
- Glomerulonephritis





















White blood cell abnormalities

When the numbers don't tell everything

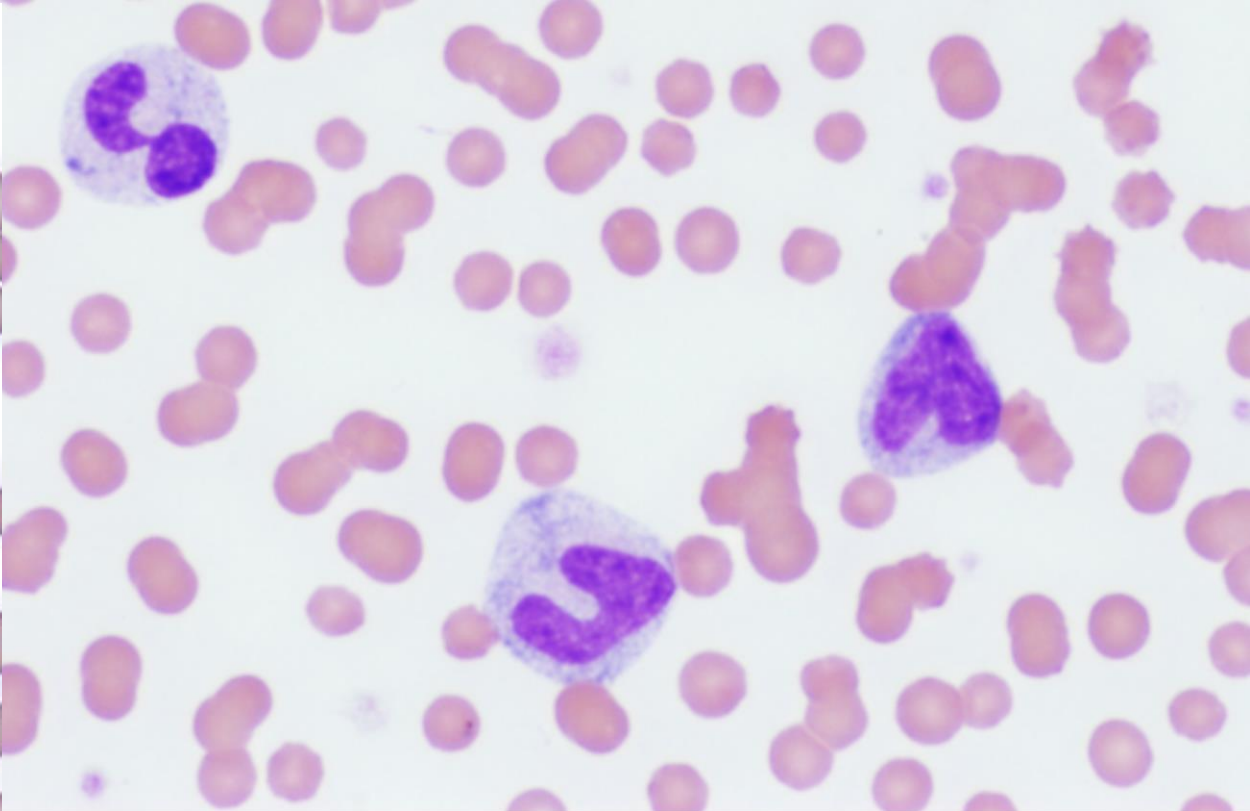
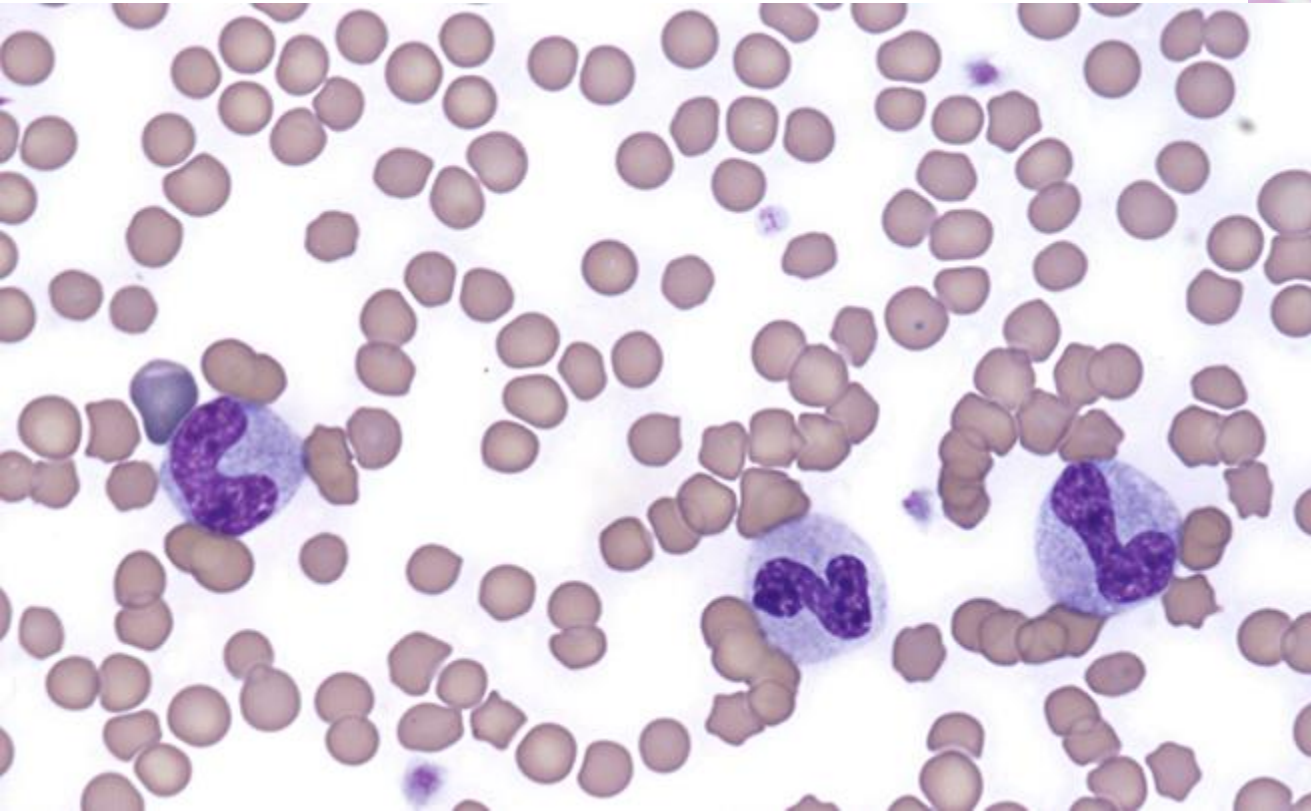


Case 4 Bella 8yo FN Domestic Shorthair

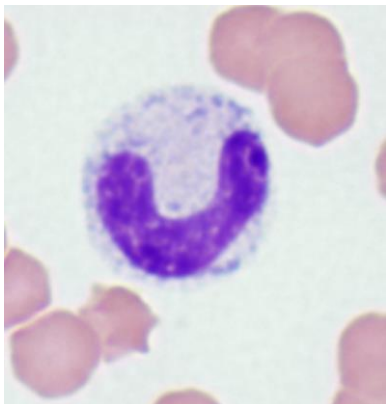
- + Lethargic
- + Anorexia
- + Occasional vomiting

  WBC	6.26	2.87 - 17.02 x10 ⁹ /L	
  Neutrophils	4.05	2.30 - 10.29 x10 ⁹ /L	
  Lymphocytes	1.42	0.92 - 6.88 x10 ⁹ /L	
  Monocytes	0.24	0.05 - 0.67 x10 ⁹ /L	
  Eosinophils	0.46	0.17 - 1.57 x10 ⁹ /L	
  Basophils	0.09	0.01 - 0.26 x10 ⁹ /L	

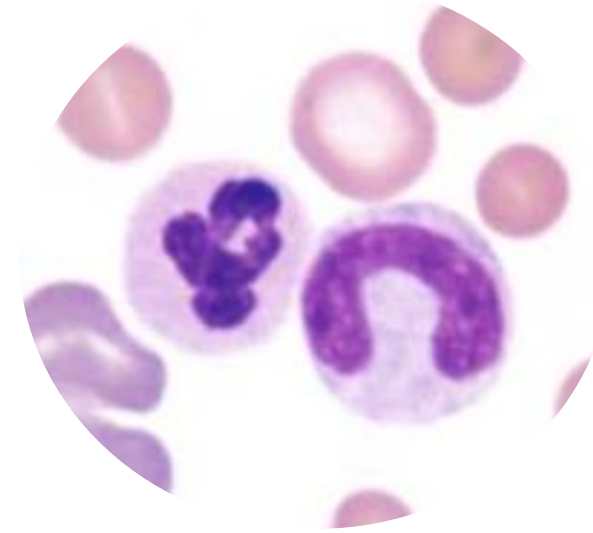
Case 4 - Bella



Case 4 - Bella

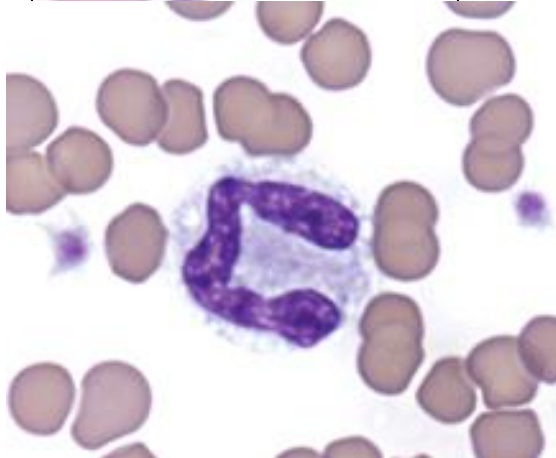
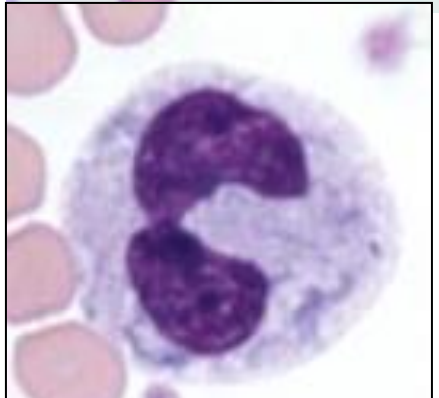
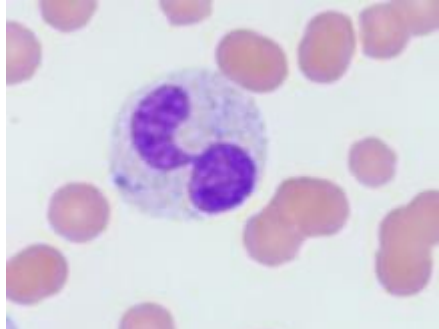


+ Left shift



■ ■	% Neutrophils	76.0	%
■ ■	% Bands	12.0	%
■ ■	% Lymphocytes	4.0	%
■ ■	% Monocytes	7.0	%
■ ■	% Eosinophils	1.0	%
■ ■	% Basophils	0.0	%

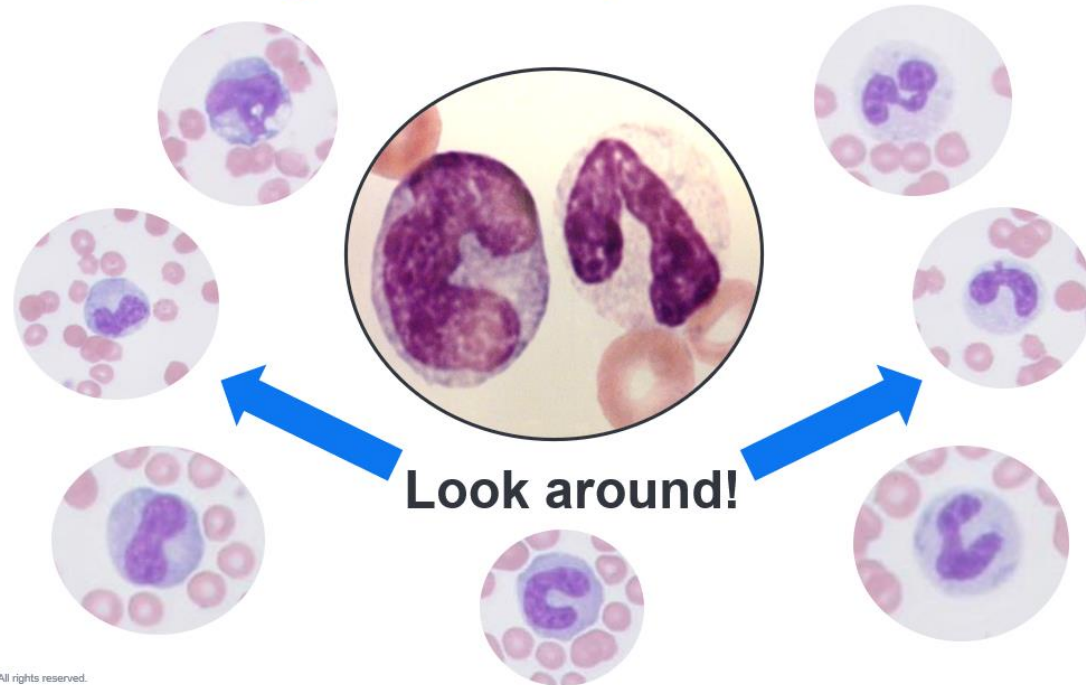
Case 4 - Bella



+ Toxic changes

- + Dohle bodies (*cats)
- + Cytoplasmic basophilia
- + Foamy cytoplasm

Differentiating the monocyte from the toxic band



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Case 4 - Bella

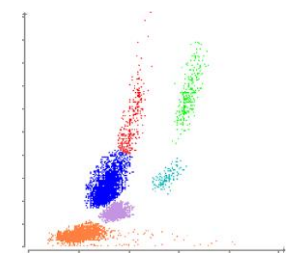
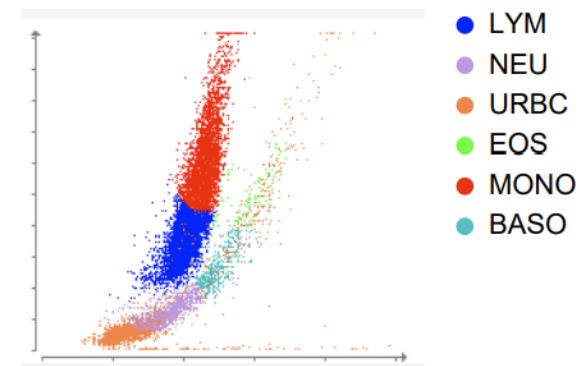
On further investigations, Bella was diagnosed with a GI foreign body (hairball) with secondary peritonitis



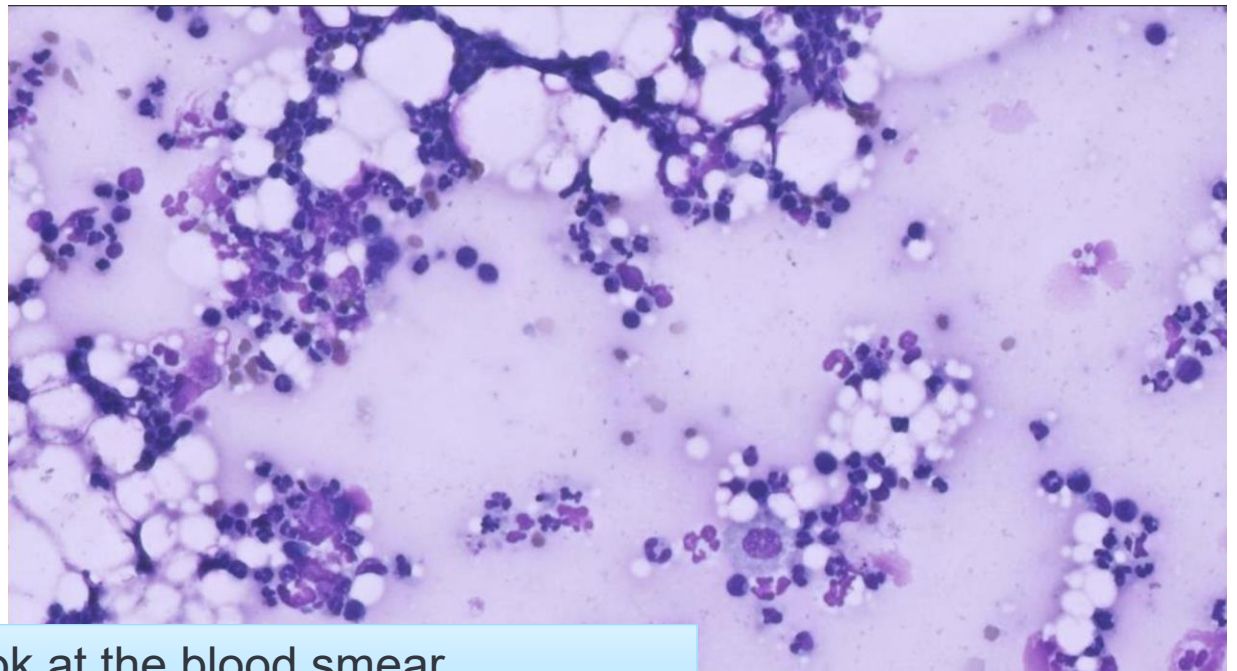
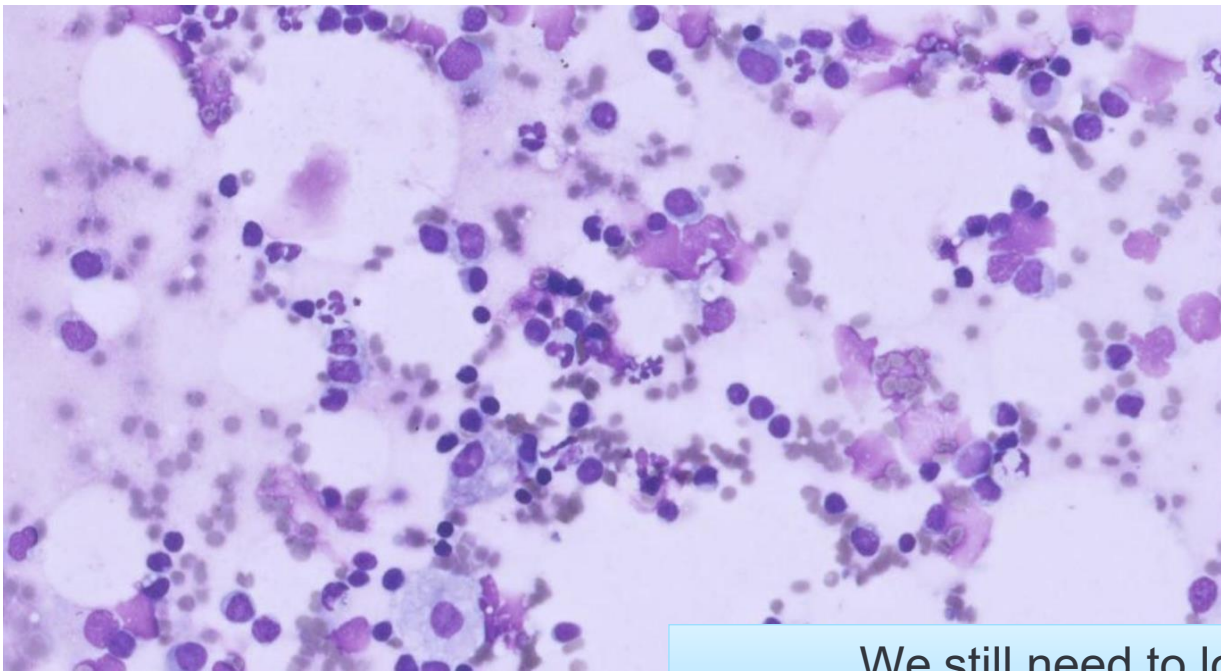
Case 5 - Nefeli

- 6Y FN
- History of lethargy, anorexia, ascites, jaundice/48 hours.
- Abdominal ultrasound - moderate amount of free fluid (chylous?), large mass in mid/caudal abdomen consistent with mesenteric lymph nodes, liver diffusely enlarged and hyperechoic.
- Ascitic fluid submitted for analysis.
- 1st site - liver, 2nd site - abdominal mass (lymph node)

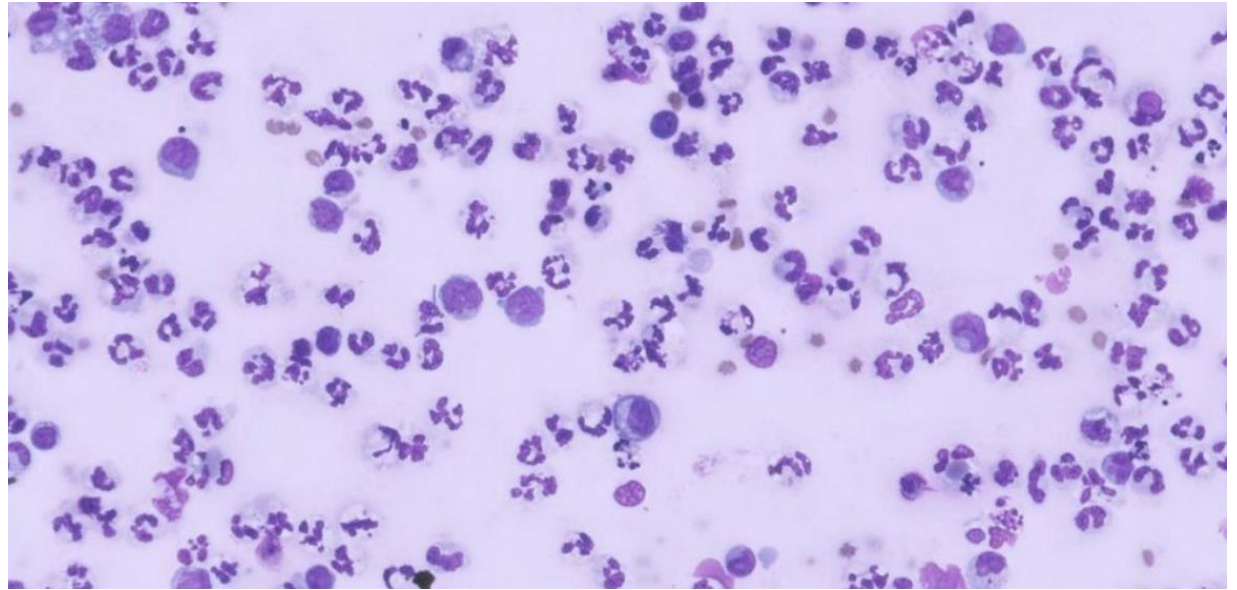
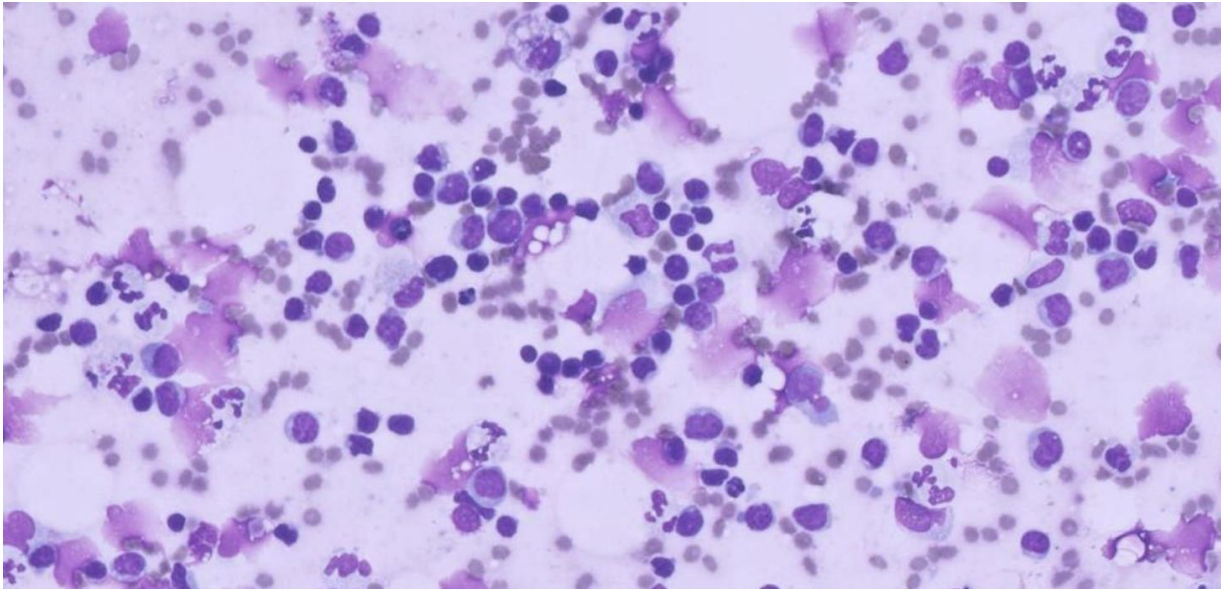
■	WBC	*17.78	2.87 - 17.02 x10 ⁹ /L	
■	% Neutrophils	*8.3	%	
■	% Lymphocytes	*46.2	%	
■	% Monocytes	*42.7	%	
■	% Eosinophils	*0.7	%	
■	% Basophils	-	---	%
■	Neutrophils	*1.47	2.30 - 10.29 x10 ⁹ /L	
■	Bands	*Suspected		
■	Lymphocytes	*8.21	0.92 - 6.88 x10 ⁹ /L	
■	Monocytes	*7.60	0.05 - 0.67 x10 ⁹ /L	
■	Eosinophils	*0.12	0.17 - 1.57 x10 ⁹ /L	
■	Basophils	-	---	0.01 - 0.26 x10 ⁹ /L



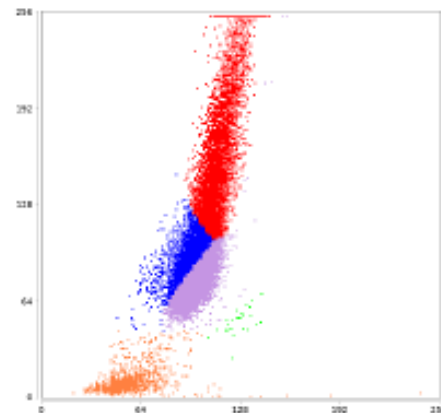
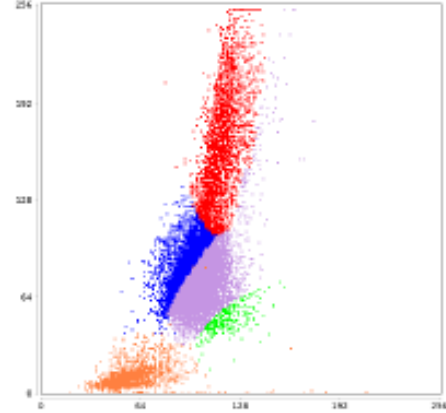
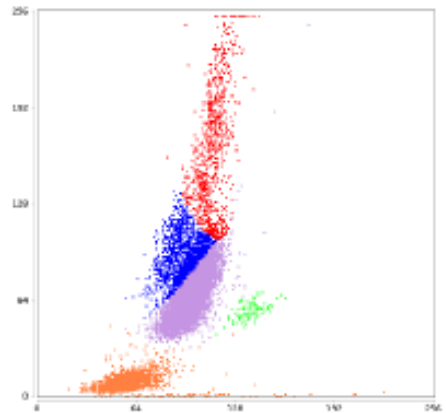
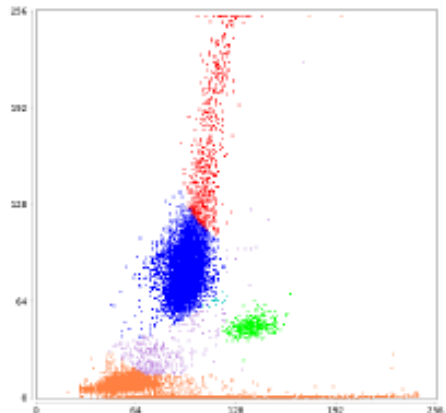
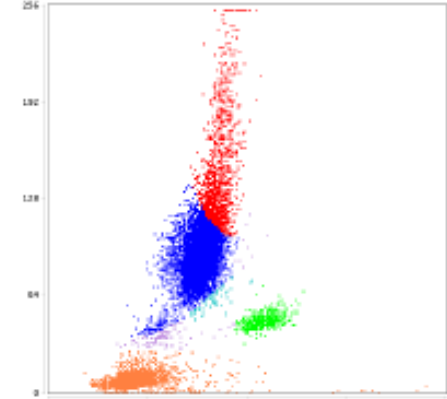
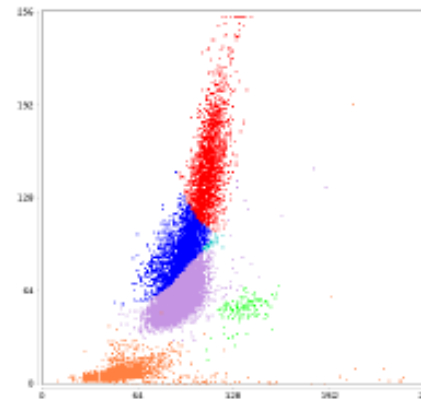
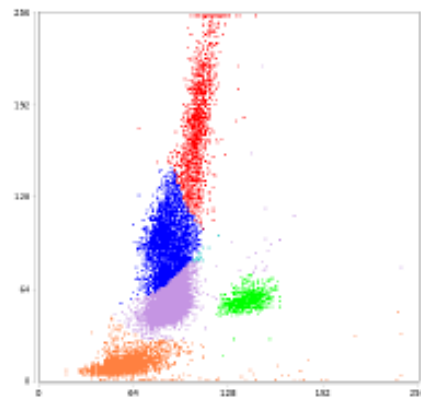
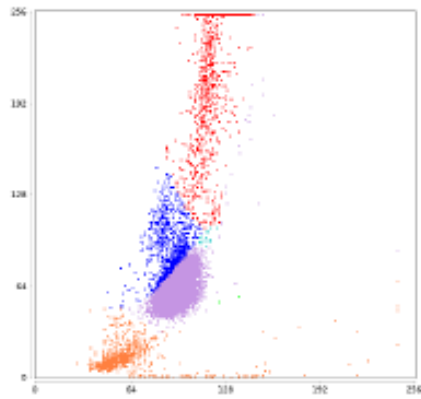
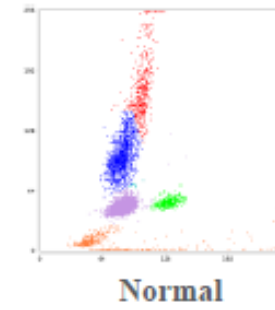
ProCyte Dx – Feline
Normal WBC Dot Plot



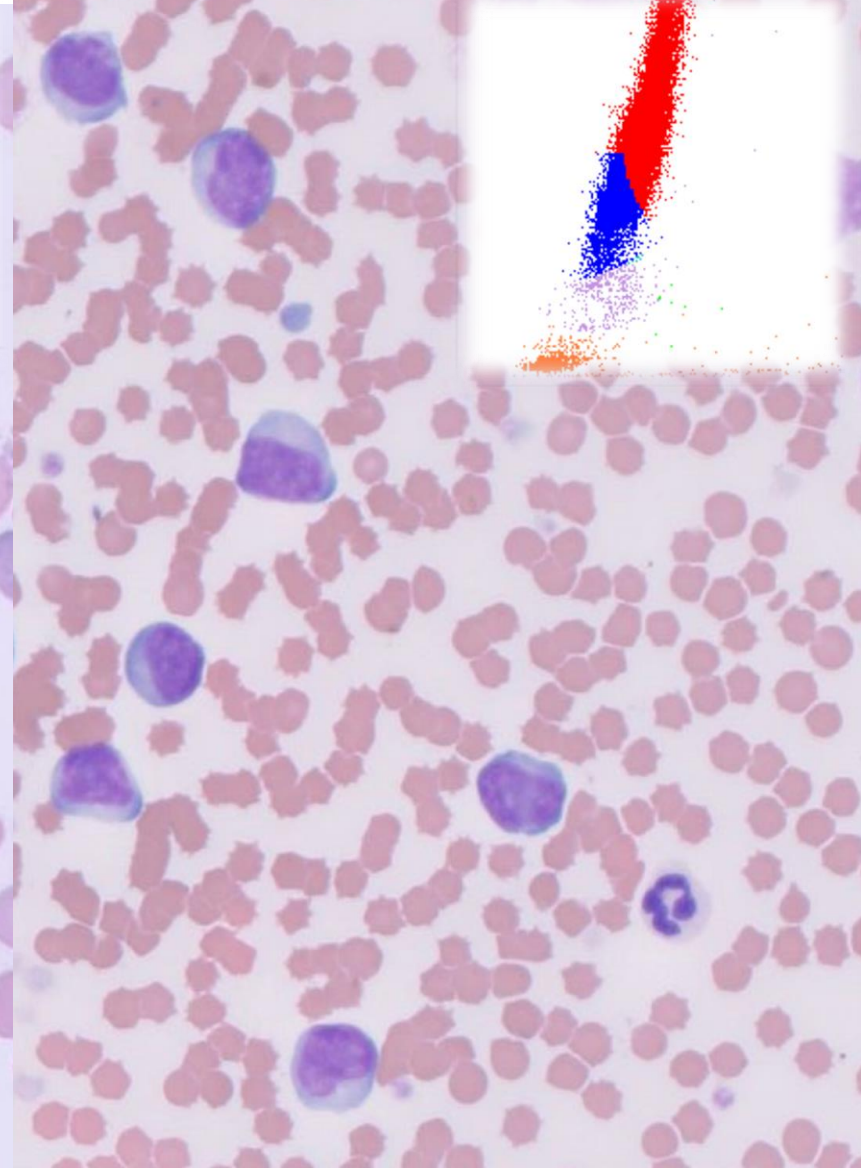
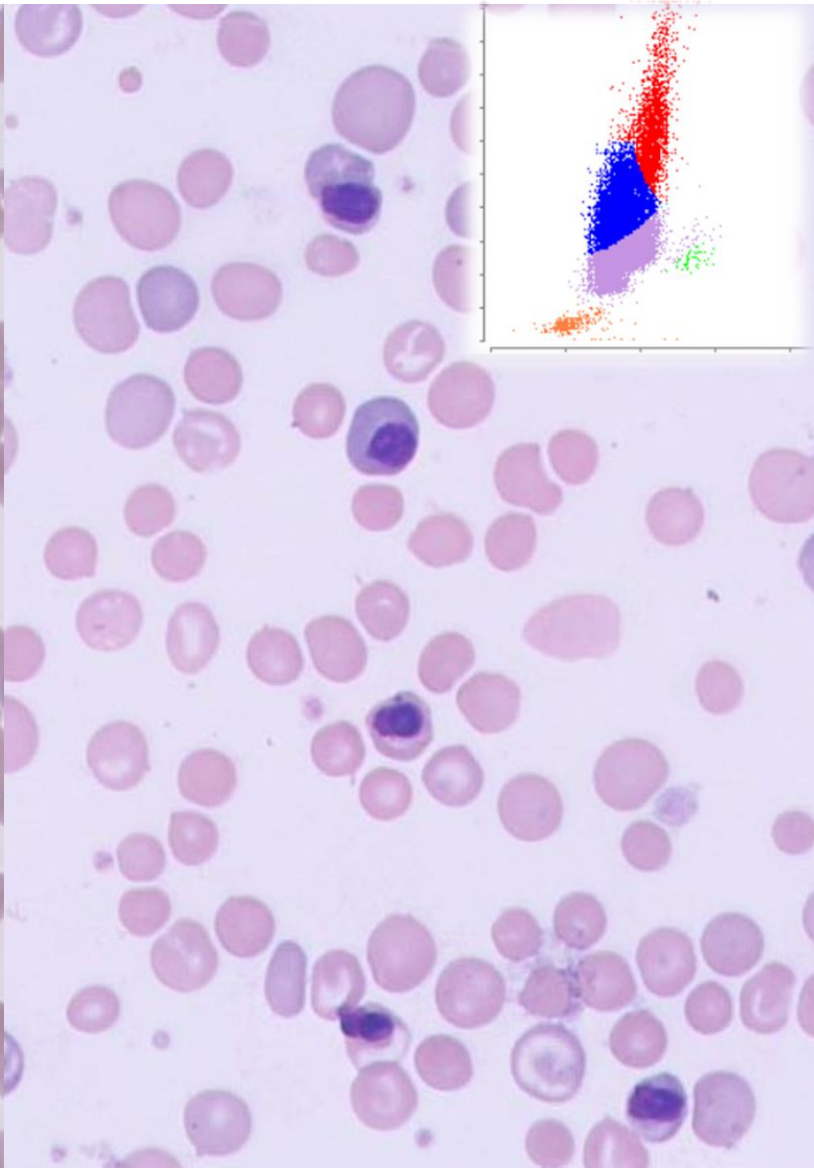
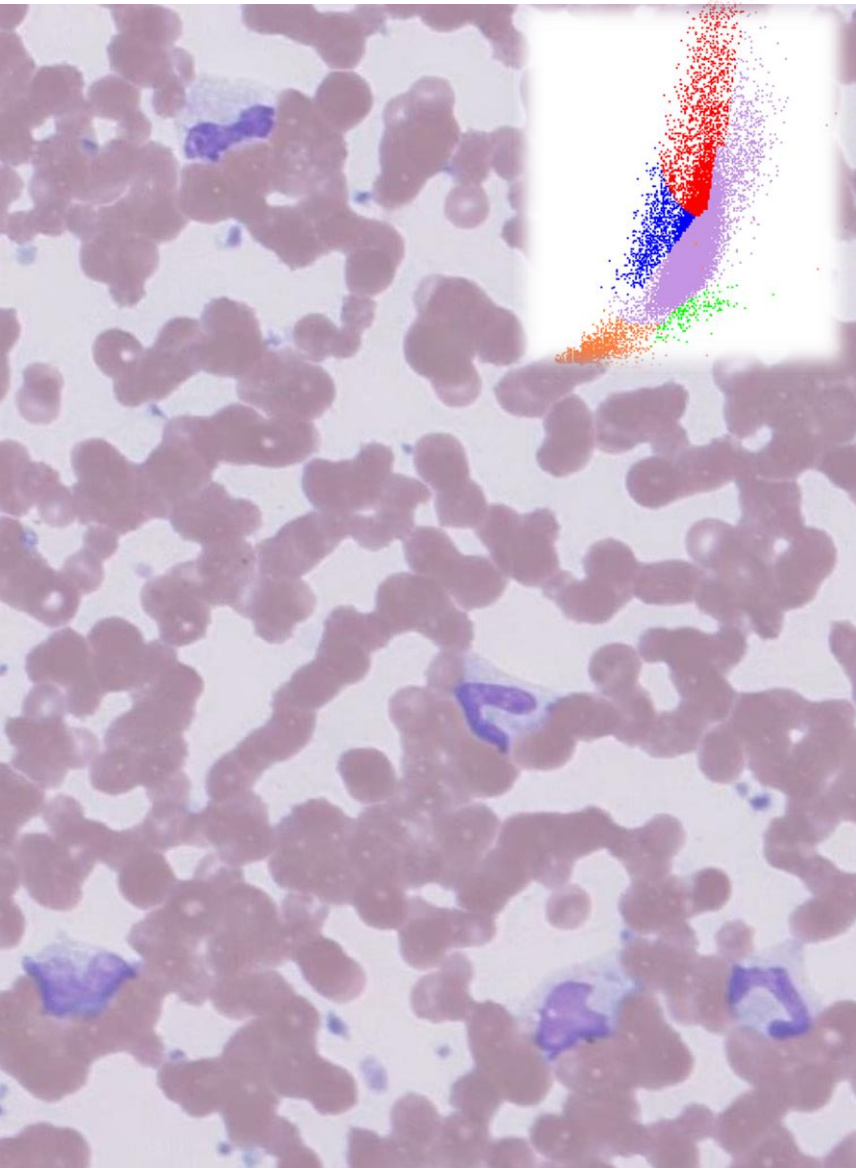
We still need to look at the blood smear....



ProCyte DX – examples of left shift



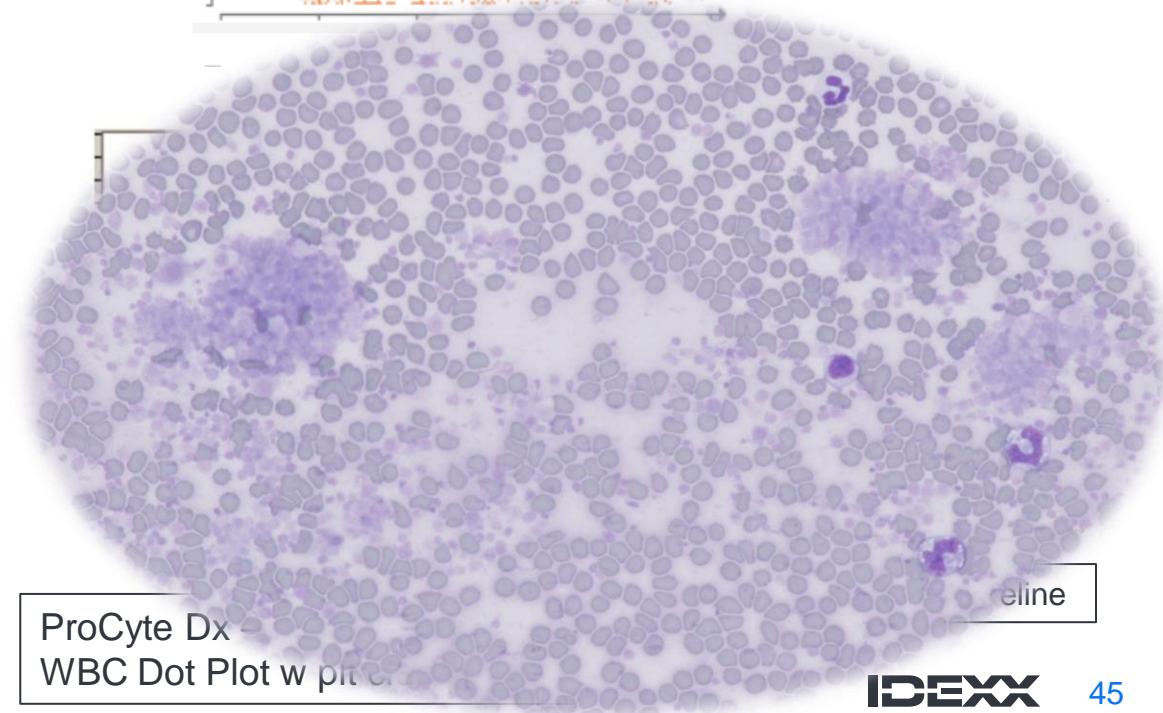
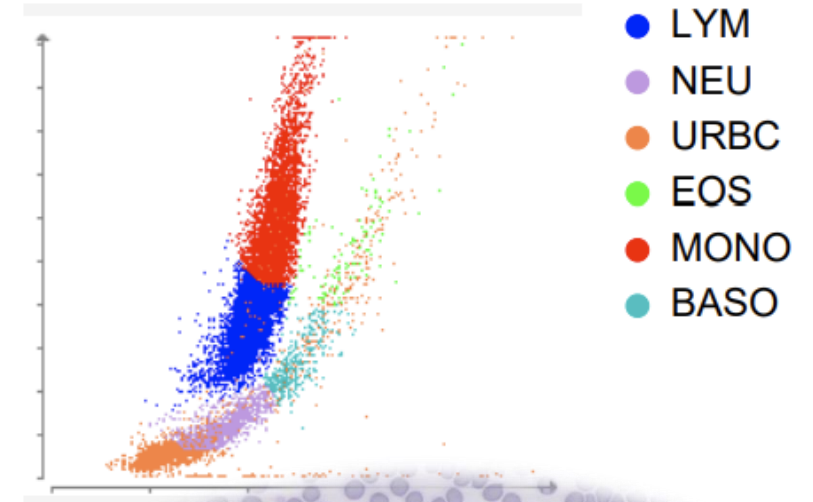
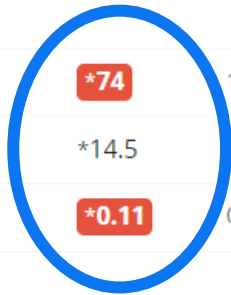
White blood cell abnormalities... When the dot plots don't help



ProCyte Dx – Canine Patient WBC Dot Plots and respective blood smears

Case 5 – Nefeli – What else may be happening ...

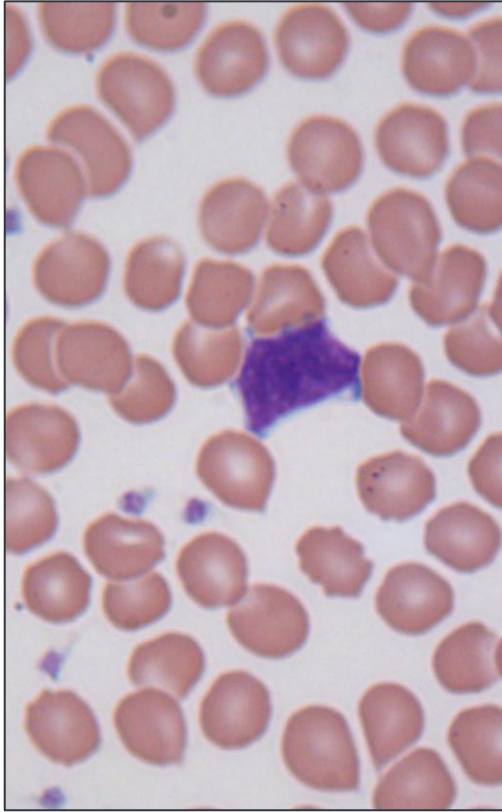
WBC	*17.78	2.87 - 17.02 x10 ⁹ /L	
% Neutrophils	*8.3	%	
% Lymphocytes	*46.2	%	
% Monocytes	*42.7	%	
% Eosinophils	*0.7	%	
% Basophils	-	---	%
Neutrophils	*1.47	2.30 - 10.29 x10 ⁹ /L	
Bands	*Suspected		
Lymphocytes	*8.21	0.92 - 6.88 x10 ⁹ /L	
Monocytes	*7.60	0.05 - 0.67 x10 ⁹ /L	
Eosinophils	*0.12	0.17 - 1.57 x10 ⁹ /L	
Basophils	-	---	0.01 - 0.26 x10 ⁹ /L
Platelets	*74	151 - 600 x10 ⁹ /L	
MPV	*14.5	11.4 - 21.6 fL	
Plateletcrit	*0.11	0.17 - 0.86 %	



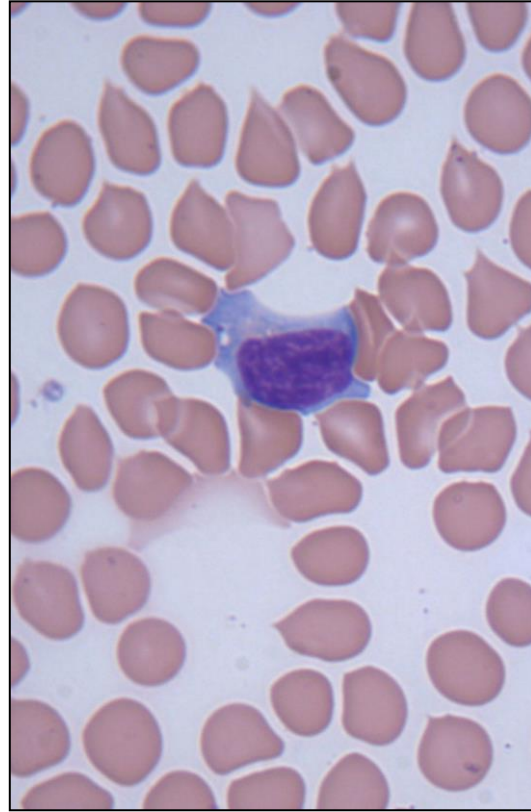
ProCyte Dx – WBC Dot Plot w platelets

Lymphocytes morphological assessment

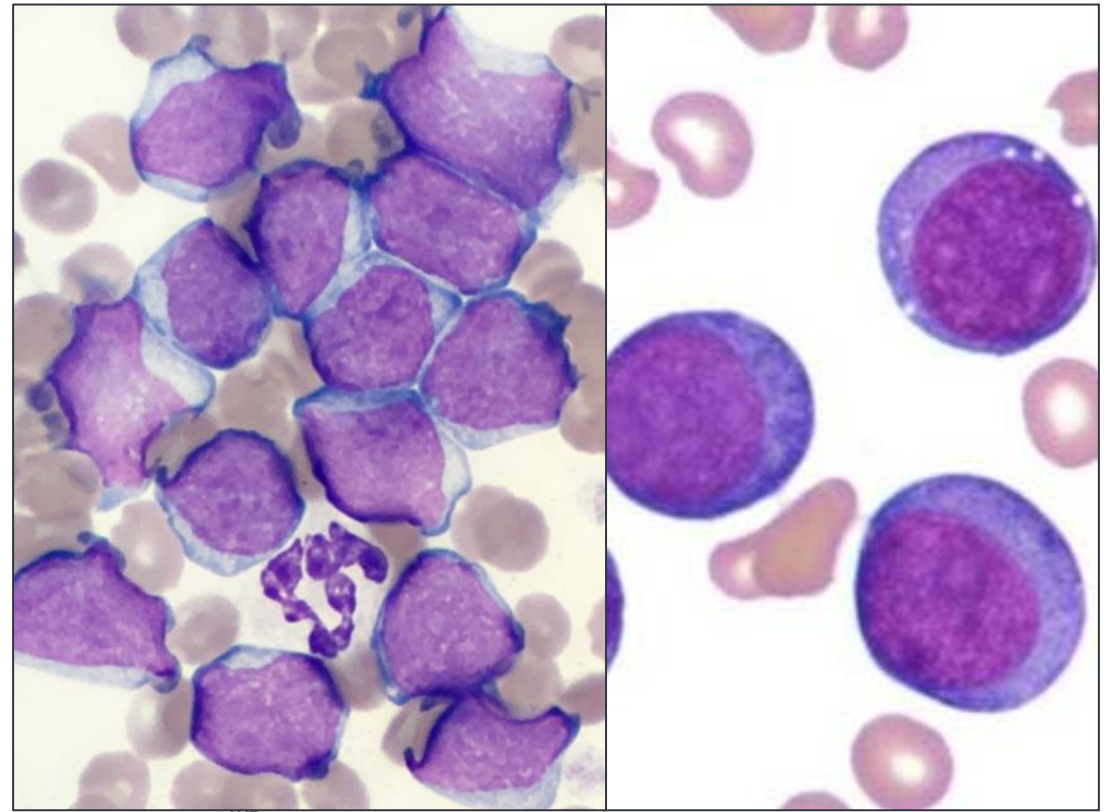
Normal Lymphocyte



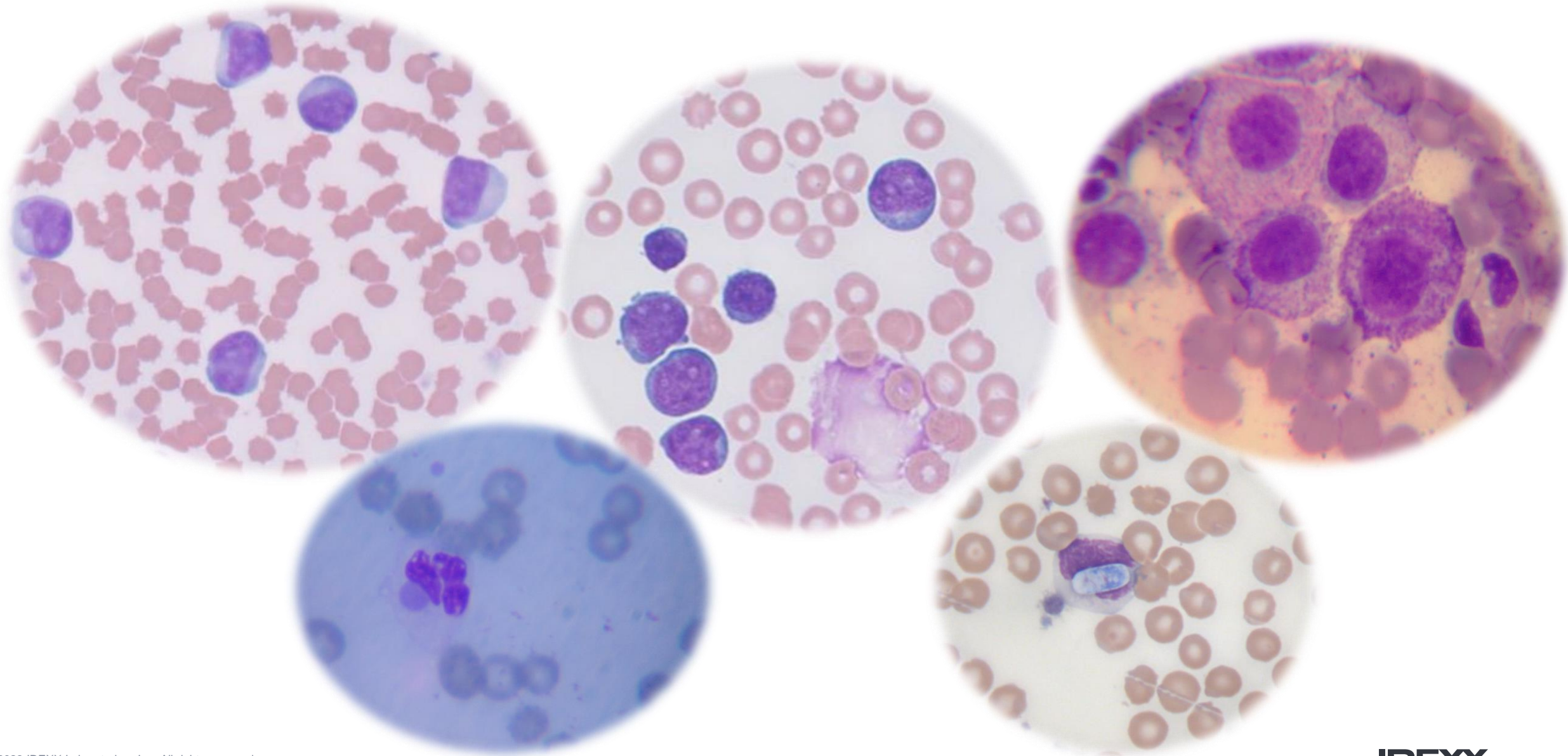
Reactive Lymphocyte



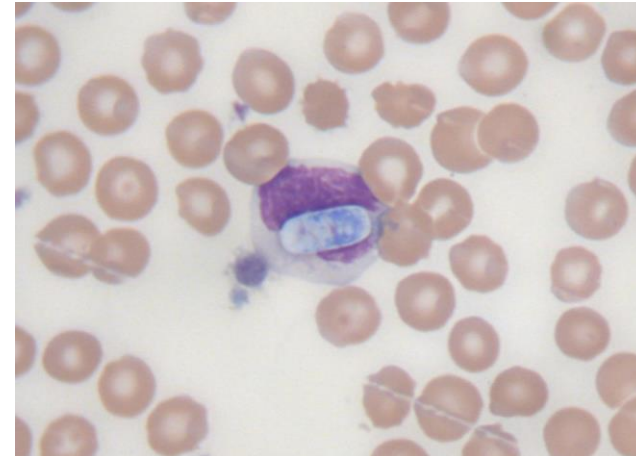
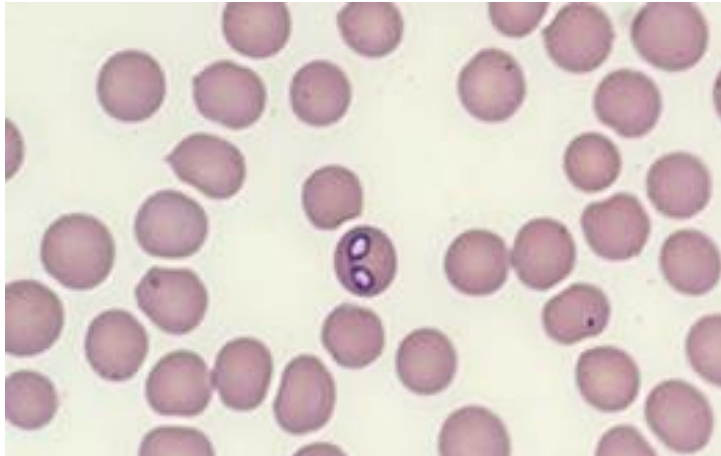
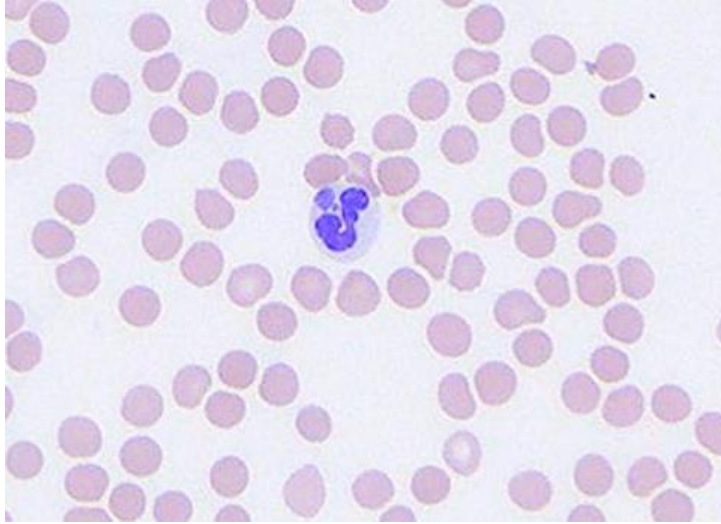
Atypical cells/blasts

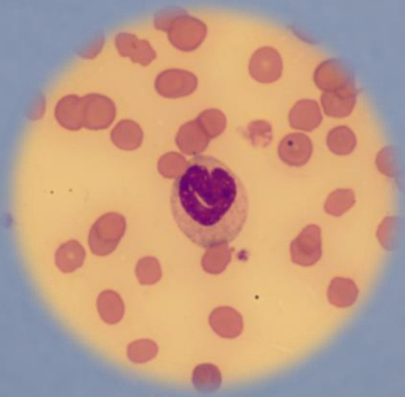


Inclusions, atypical cells and blasts



Infectious agents

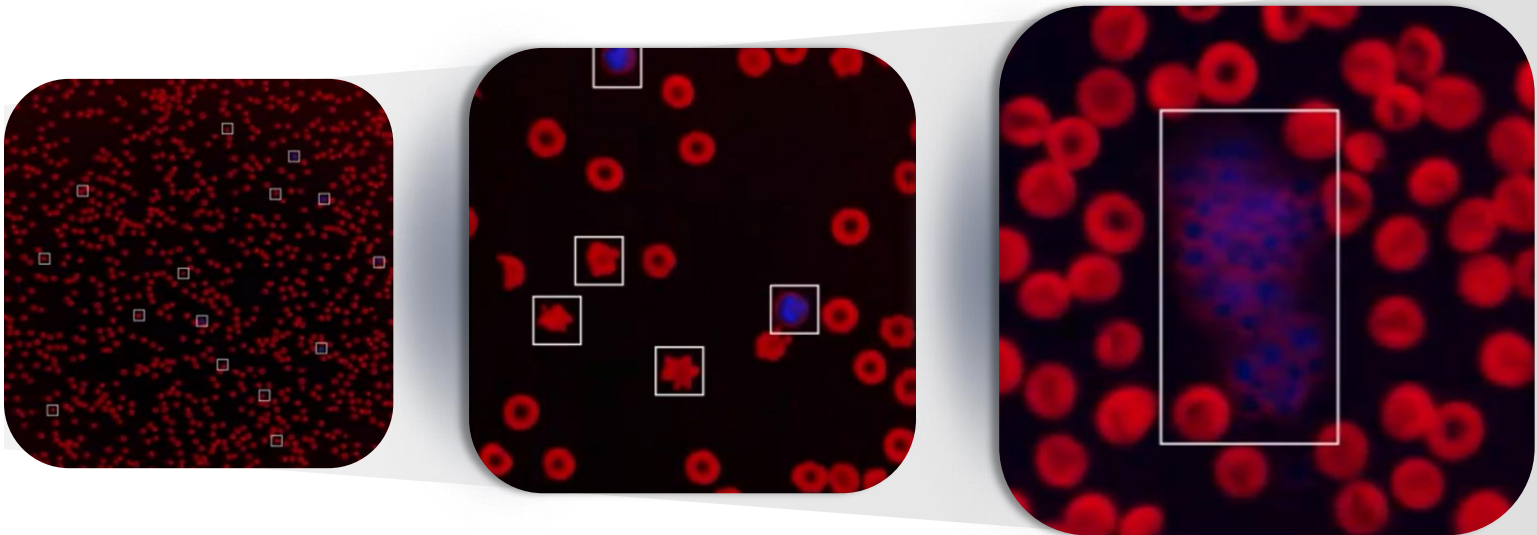




Take home MSG

- Even with best analyzers
Blood smear exam allows you to get more out of your CBC results
- Start with a good quality smear
- Have a systematic approach
- Cross check findings with analyzer and history
- If in doubt... refer...get us to help out!
- **A different workflow to blood morphology evaluation is in the cards**

IDEXX inVue Dx™ analyzer: automated quantification, classification, and interpretation of blood morphology



IDEXX VetConnect PLUS Home Directory of Services Imaging Telemedicine

BREE BENSON 123456 Patient Management
Canine | Anatolian Shepherd | Female | 9y

2023 **Oct 19**

Result Details Add to Order

Blood Morphology 10/19/23 9:43 AM

RBC	3.69	5.65 - 8.87 M/uL	
Acanthocytes	0.5% Mild		
HCT	23.9	37.3 - 61.7 %	
Reticulocytes	124.4	10.0 - 110.0 K/uL	
WBC	12.00	5.05 - 16.76 K/uL	
Neutrophils	8.93	2.95 - 11.64 K/uL	
Lymphocytes	1.94	1.05 - 5.10 K/uL	
Monocytes	0.96	0.16 - 1.12 K/uL	
Eosinophils	0.13	0.06 - 1.23 K/uL	
Basophils	0.04	0.00 - 0.10 K/uL	
Platelets	Adequate		
Platelet Clumps	Present		

Comment: Results imported from ProCyte and updated when indicated based on cytologic evaluation

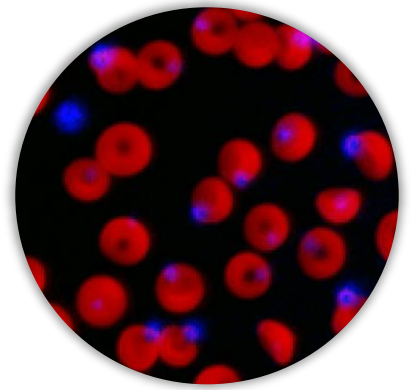
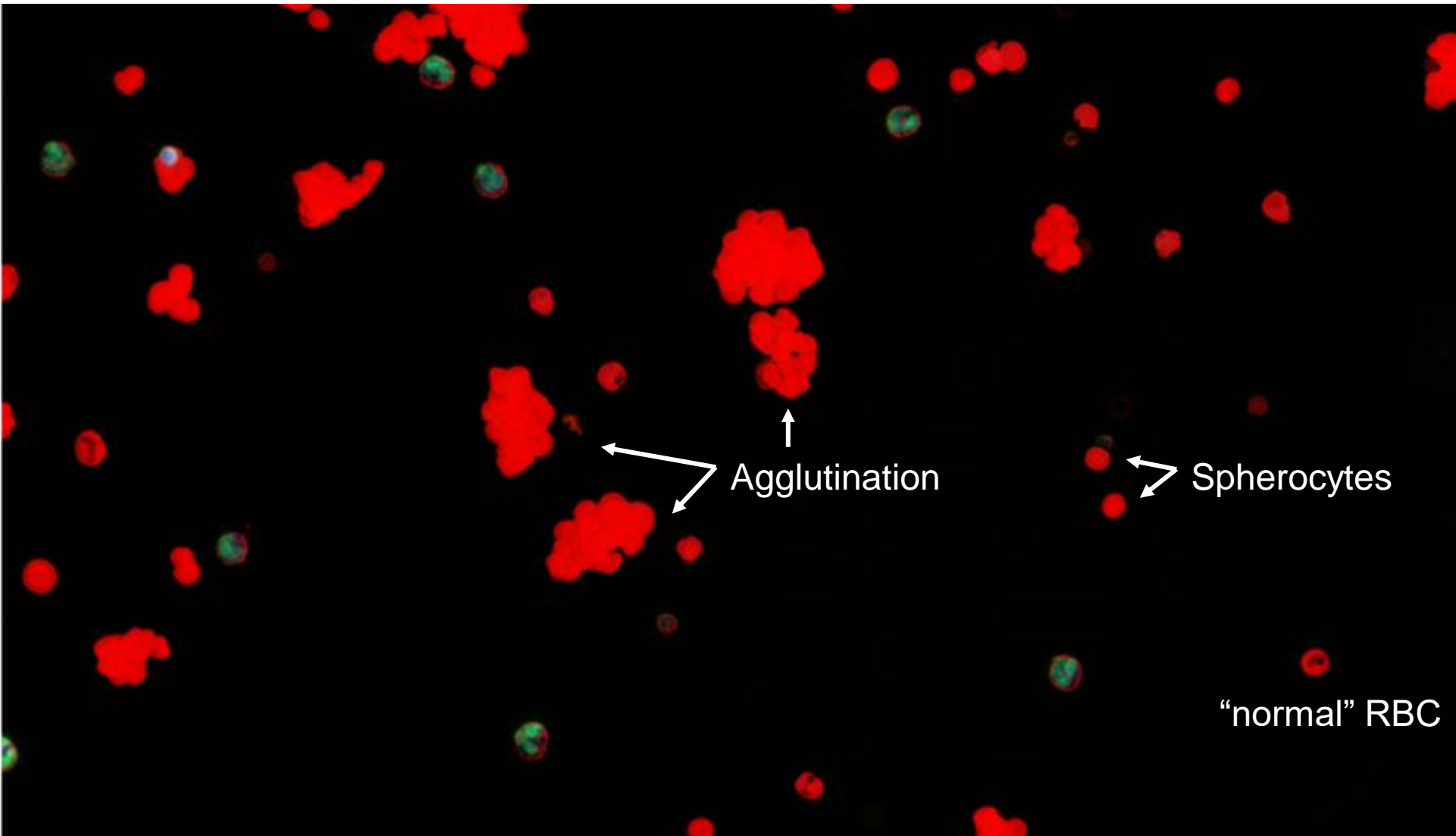
Diagnostic Considerations: Acanthocytes are abnormally shaped RBC which can be observed in dogs with liver disease or glomerulonephritis and with conditions such as DIC, hemangiosarcoma and iron deficiency anemia.

Images:



Results
in **10 minutes**

IDEXX inVue Dx™ analyzer: blood morphology image



IDEXX inVue Dx™ analyzer: Integrated report



+ + +



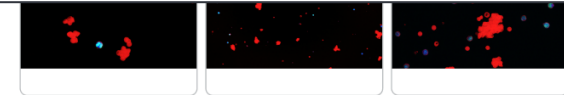
RBC		a. 1.09 M/μL	5.65 - 8.87 M/μL	<input type="text"/>
Hematocrit		a. 9.8%	37.3 - 61.7 %	<input type="text"/>
Spherocytes		60% (Marked)		
Agglutination		Present		
Reticulocytes		184.8 K/μL	10.0 - 110.0 K/μL	<input type="text"/>
WBC		a, b. 43.20 K/μL	5.05 - 16.76 K/μL	<input type="text"/>

% Immature Neutrophils	18.5 %	<input type="text"/>
% Lymphocytes	1.9 %	<input type="text"/>

Neutrophils	30.02 K/μL	2.95 - 11.64 K/μL	<input type="text"/>
Immature Neutrophils	7.99 K/μL		<input type="text"/>
Lymphocytes	0.84 K/μL	1.05 - 5.10 K/μL	<input type="text"/>
Monocytes	4.20 K/μL	0.16 - 1.12 K/μL	<input type="text"/>
Eosinophils	0.09 K/μL	0.06 - 1.23 K/μL	<input type="text"/>
Basophils	0.03 K/μL	0.00 - 0.10 K/μL	<input type="text"/>
Toxic Change	Mild to moderate		
Platelet Estimate	Decreased		
Platelet Clumping	Absent		

Diagnostic Considerations

- Regenerative anemia, marked spherocytosis, and RBC agglutination are supportive of immune-mediated hemolytic anemia (IMHA).
- Left shift and toxic change confirm inflammatory leukogram.
- Platelets appear decreased based on morphologic assessment.



a. Results imported from ProCyte.
b. The white blood cell differential has been updated based on cytologic evaluation.



Thank you!
Any questions?

IDEXX

References:

- + J. Harvey. Veterinary Hematology: A Diagnostic Guide and Color Atlas. Elsevier, 2012
- + Stockham, Steven L., and Michael A. Scott. Fundamentals of veterinary clinical pathology. 2nd ed, Blackwell, 2008
- + Douglas J. Weiss, K. Jane Wardrop; Schalm's Veterinary Hematology, 6th ed, Wiley, 2010
- + American Society for Veterinary Clinical Pathology (ASVCP). Quality Assurance for Point-of-Care Testing in Veterinary Medicine. Available at <http://www.asvcp.org/pubs/qas/index.cfm>. Accessed June 2024.
- + Cornell University College of Veterinary Medicine <https://eclinpath.com/> Accessed June 2024.