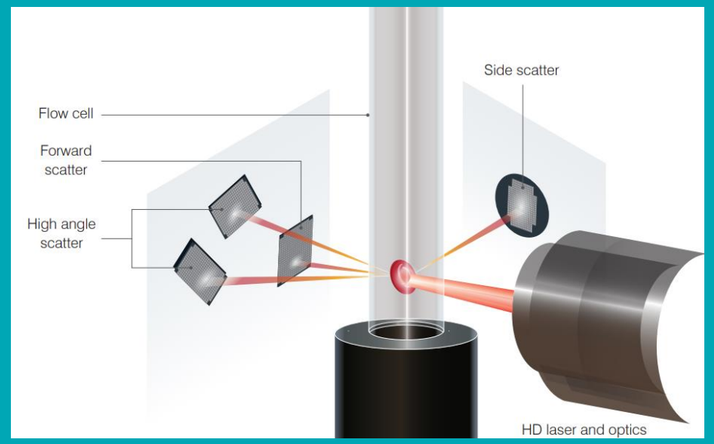
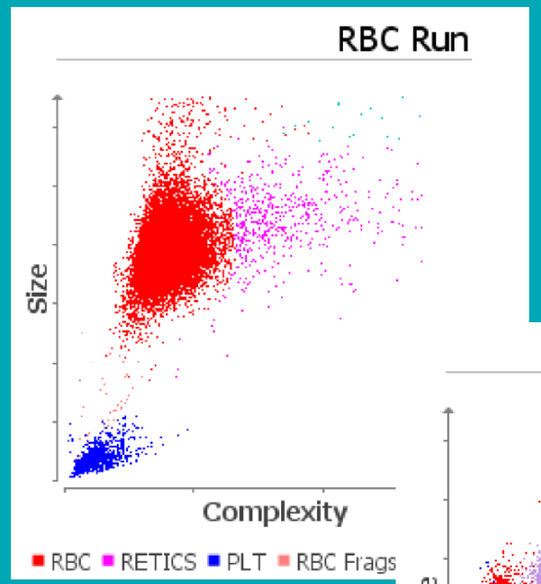
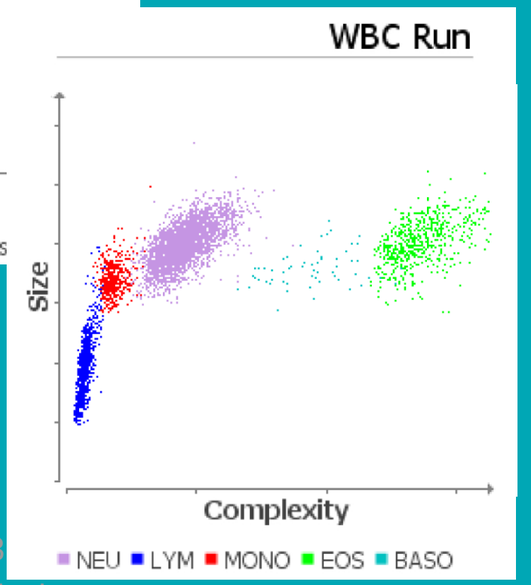
Introducing the new hematology analyzer, and discussion on the utility of reticulocyte assessment in today's practice

Dennis B. DeNicola, DVM, PhD, DACVP

IDEXX ProCyte One





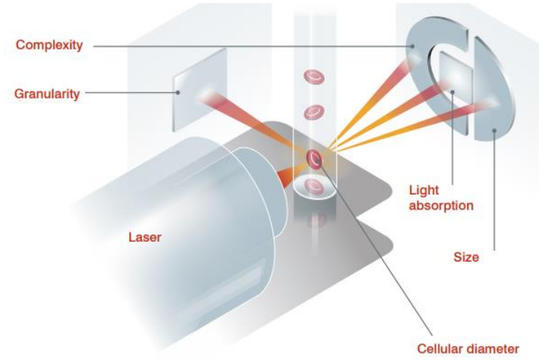


Mixture of 4.2 and 6.3

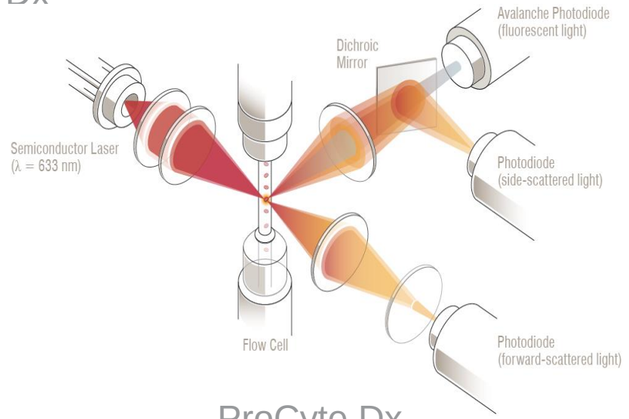
Photo credit: Dr. DeNicola

Discussion topics

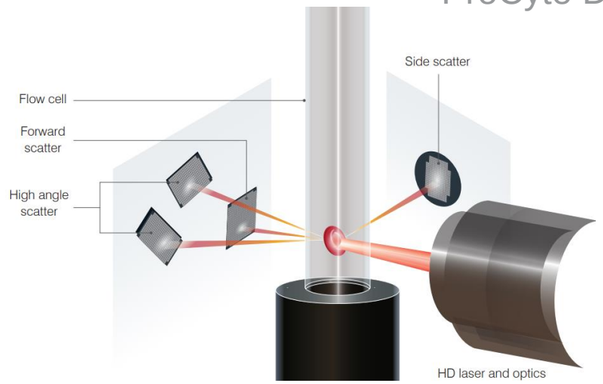
- New technology for hematology analyzer



LaserCyte Dx



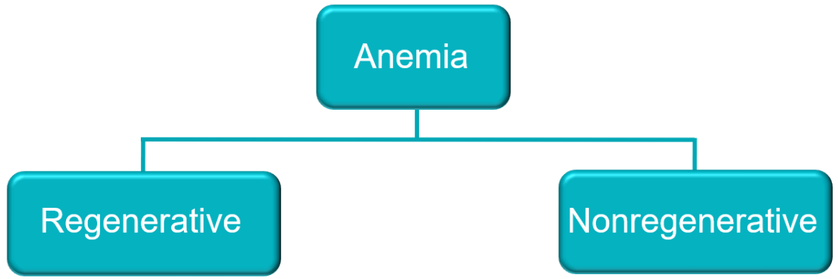
ProCyte Dx

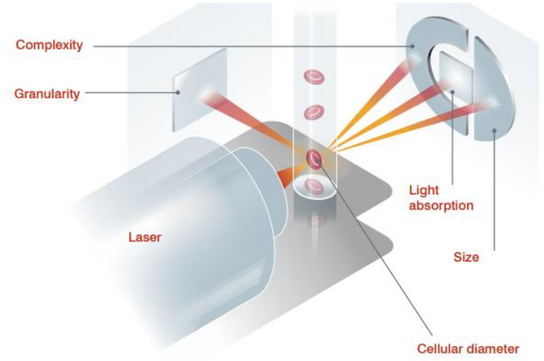


ProCyte One

Discussion topics

- New technology for hematology analyzer
- Measurement of reticulocyte and clinical application





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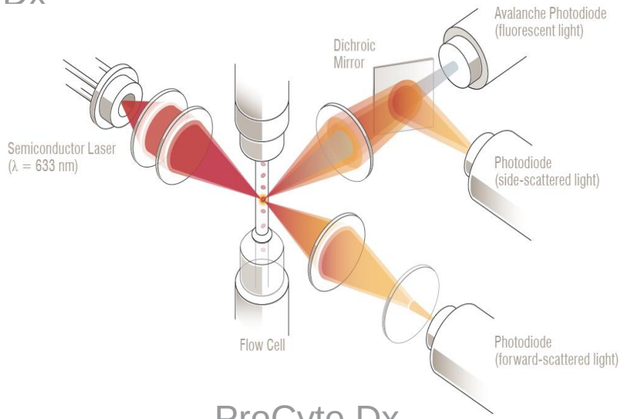

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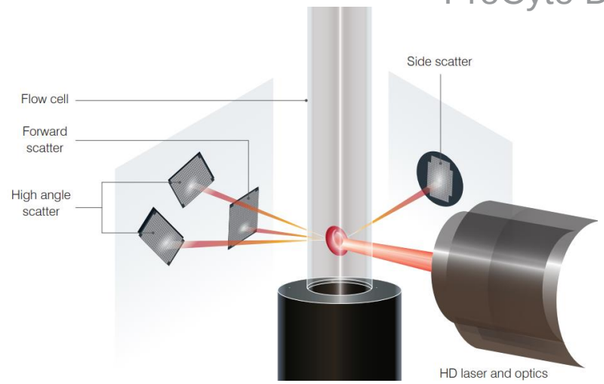
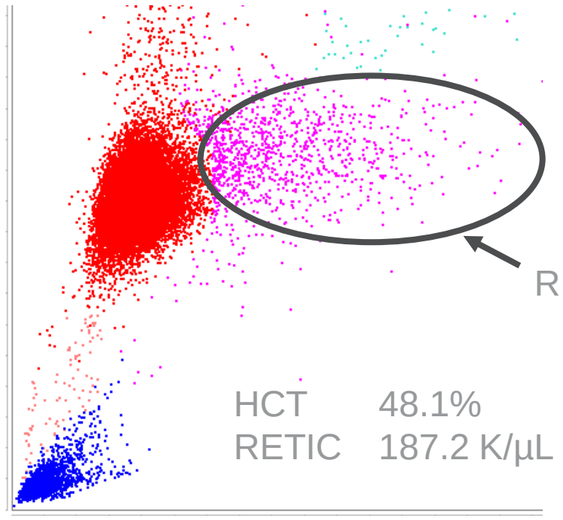
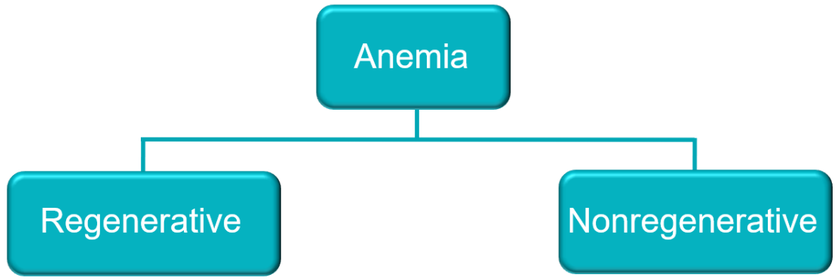


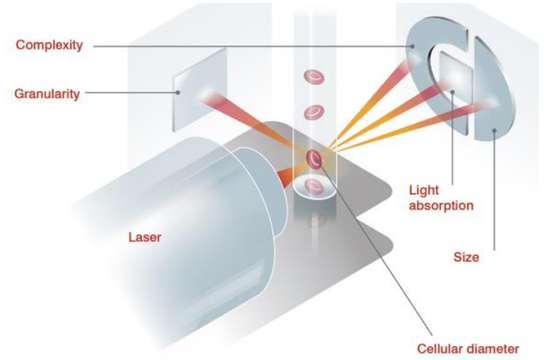
ProCyte One

Discussion topics

- New technology for hematology analyzer
- Measurement of reticulocyte and clinical application
- Value of reticulocytes in non-anemic animals







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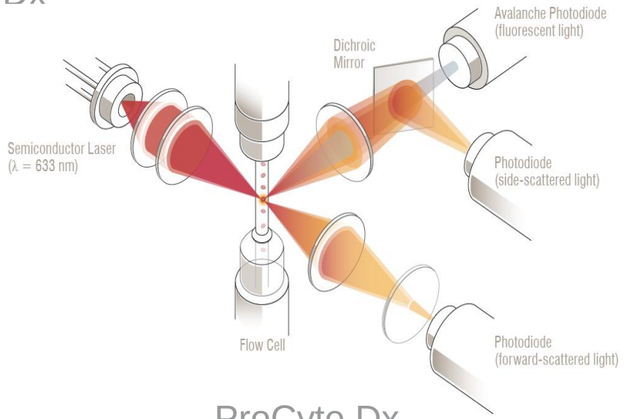

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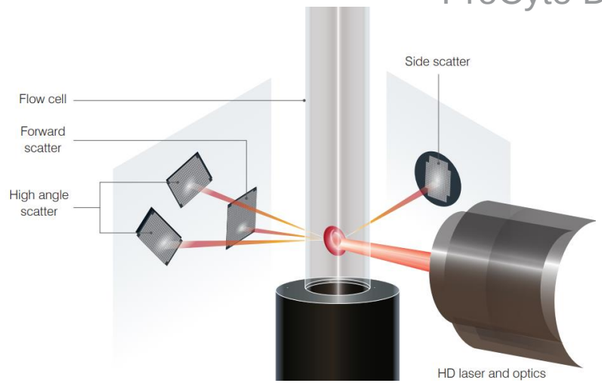


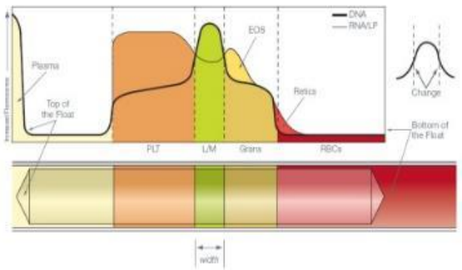
ProCyte One

Evolution of IDEXX In-House Hematology

Each step offered customers huge advancement

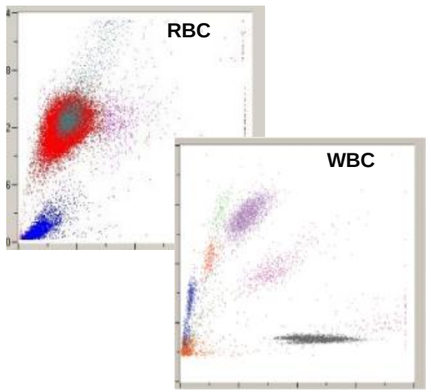
1993

VetAutoread™ Hematology Analyzer



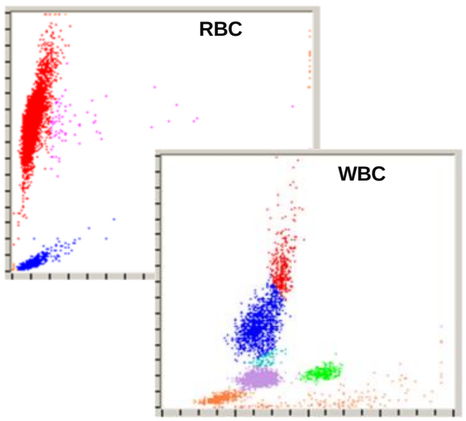
2002

LaserCyte® Dx Hematology Analyzer



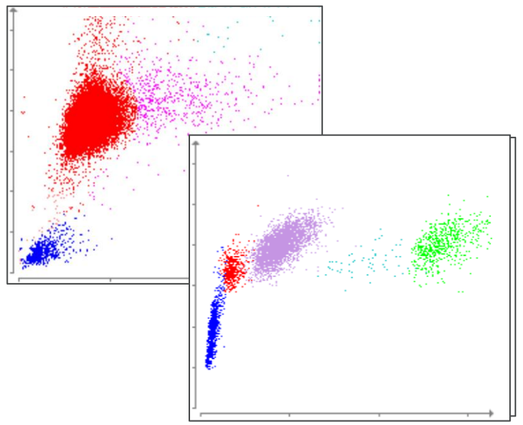
2010

ProCyte® Dx Hematology Analyzer

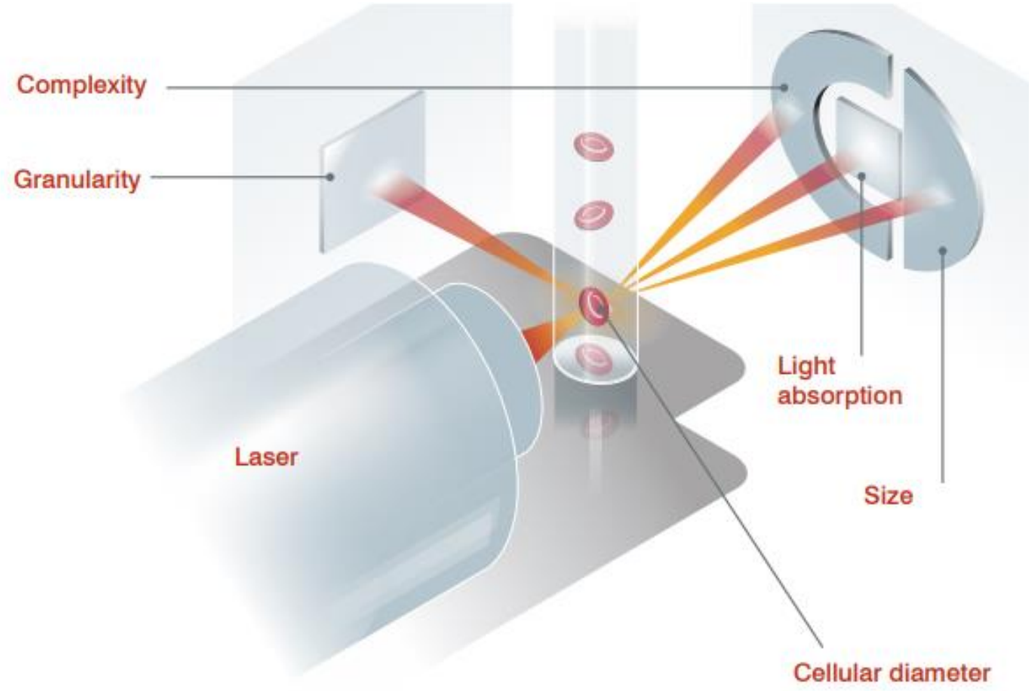


2021

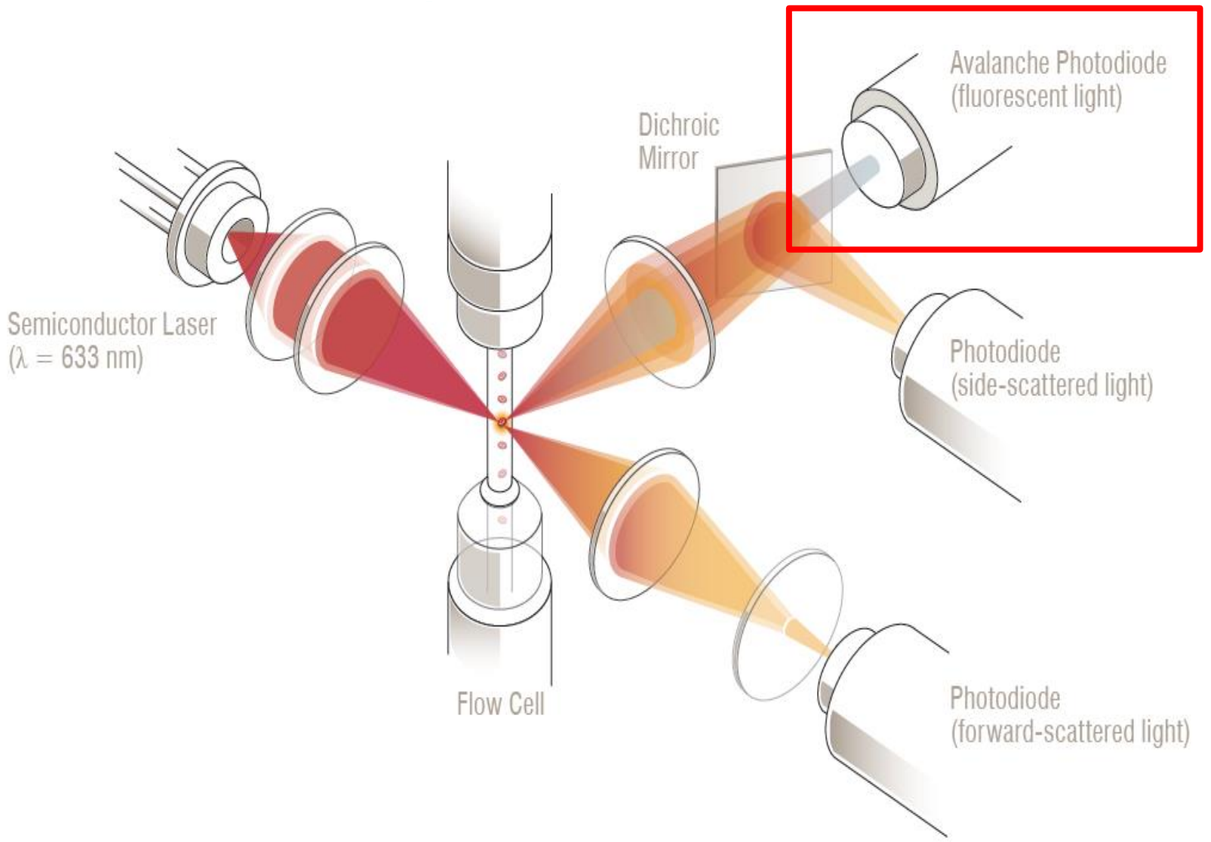
ProCyte One® Hematology Analyzer



LaserCyte Dx Technology – Flow Cytometry (FCM)
ProCyte Dx Technologies – Impedance, FCM, Optical Fluorescence



IDEXX LaserCyte Dx Hematology Analyzer



IDEXX ProCyte Dx Hematology Analyzer

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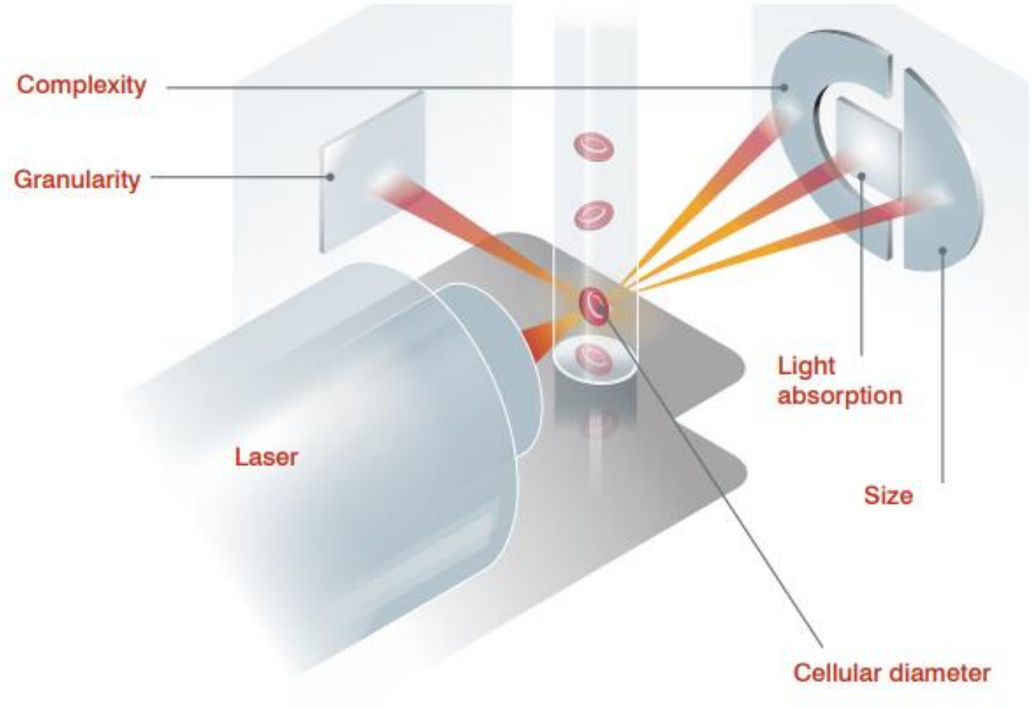
ProCyte One Technology – Flow Cytometry (FCM)



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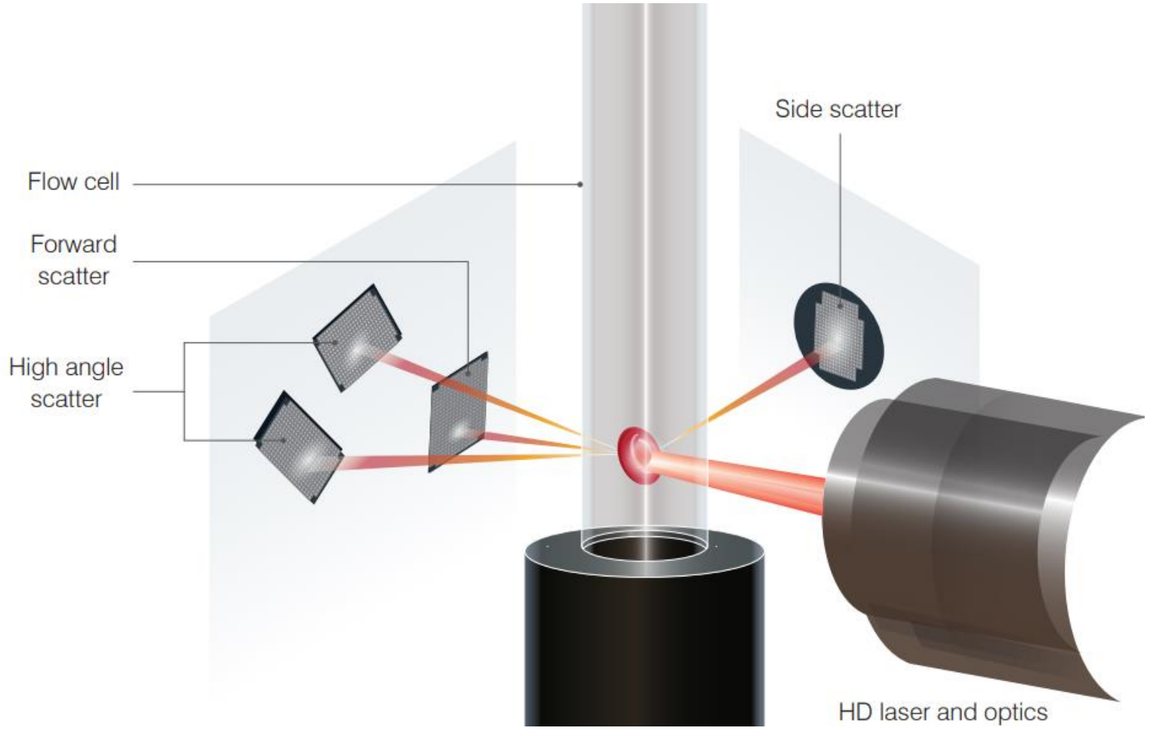

IDEXX ProCyte One Hematology Analyzer

Technology has changed over the years…cameras

1990: Basic analog film camera

2002: Advanced analog film camera

2020: Advanced digital film camera

The box may look similar, but the operation and features are *dramatically* different.

Technology has changed over the years…flow cytometers

1990: Basic research FCM

2002: LaserCyte® Dx

2020: ProCyte One™

Just as cameras have had a vast technological evolution, so has automated hematology.

ProCyte One vs LaserCyte Dx – Same Technology … Huge Difference

LaserCyte Dx

- Major Advantage over impedance
  - Flow Cytometry

Compared to ProCyte One

- Struggles at temperatures > 27^0 C (80.6^0 F)
- Precision performance just satisfies ASVCP and CLSI guideline
- Restricted light scatter angle data collection results superior to impedance but less than optimal differentiation and counting
- ‘Old’ laser technology
  - More difficult to assure stability and performance

ProCyte One

- Major Advantage over impedance
  - Flow Cytometry

Major Advantages over LaserCyte Dx

- Much wider operating temperatures
  - Up to 35^0 C (95^0 F)
- Improved precision – targeted to perform like ProCyte Dx
- Improved clustering of digitized events equals improved differentiation and counting – targeting PDx performance
- Improved laser – more consistency in results
  - Newer lasers more powerful and stable

ProCyte One key design elements

Objective: *Create the ideal, highly differentiated solution for general practice*

Economical

- Simple, elegant design
- Completely intuitive
- Reliable
- Fixed CBC price
- Pay per Run

Menu

- 5-part differentials and dot plots
- Reticulocytes
- Smart flagging
- Platelet enhancements
- Interpretive aids

Performance

- Precise and accurate
- On-board quality control
- Time to results <5 min
- Operating temp up to 35ºC
- Small footprint

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Now customers have the ability to choose which hematology instrument from the ProCyte platform fits their needs

ProCyte One

Intuitive, load-and-go workflow, requires little maintenance, frees-up time to focus on patients

+ 5 part diff / retics
+ Advanced HD laser
+ 5 minute run time
+ Automated SmartQC
+ Unprecedented Ease of Use
+ Fixed CBC Price (PPR/AR)

ProCyte Dx

Provides the most comprehensive CBC with advanced parameters in 2 minutes

+ nRBC's
+ RETIC-HGB
+ Band neutrophils
+ 2 minute run time
+ Fluids
+ 17 Species
+ Variable cost

For customers who heavily weigh the cost per test, running just 2 CBCs per day, ProCyte Dx will be more attractive on a cost per test basis than ProCyte One

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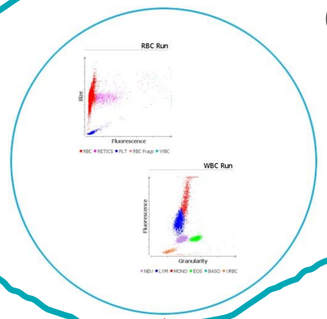
How to trust results

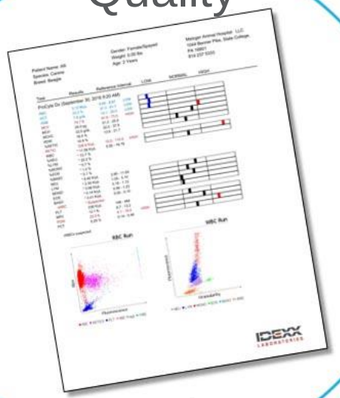
Analyzer graphics / cytograms



Dedicated personnel to operate analyzer and perform blood film review

‘Do the data match the clinical picture?’

Quality



Results

Standard Operating Protocol

External quality assurance program

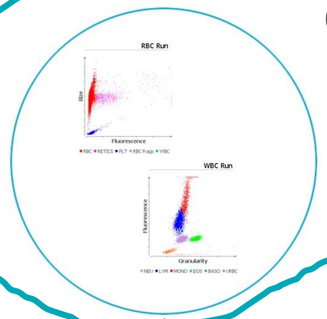
Manufacturer recommended maintenance

External quality control

How to trust results

1. Verify data in CBC
2. Identify quantitative and morphologic abnormalities

Analyzer graphics / cytograms



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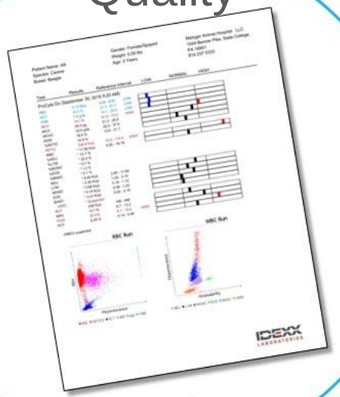

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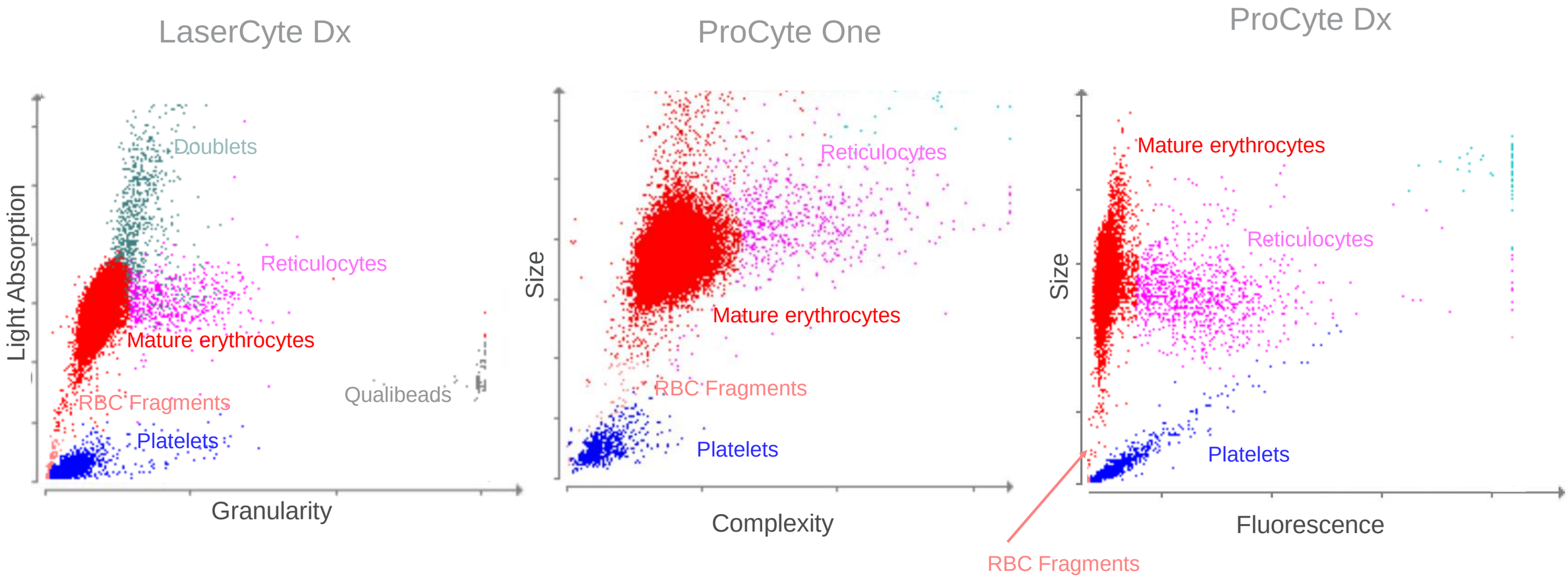
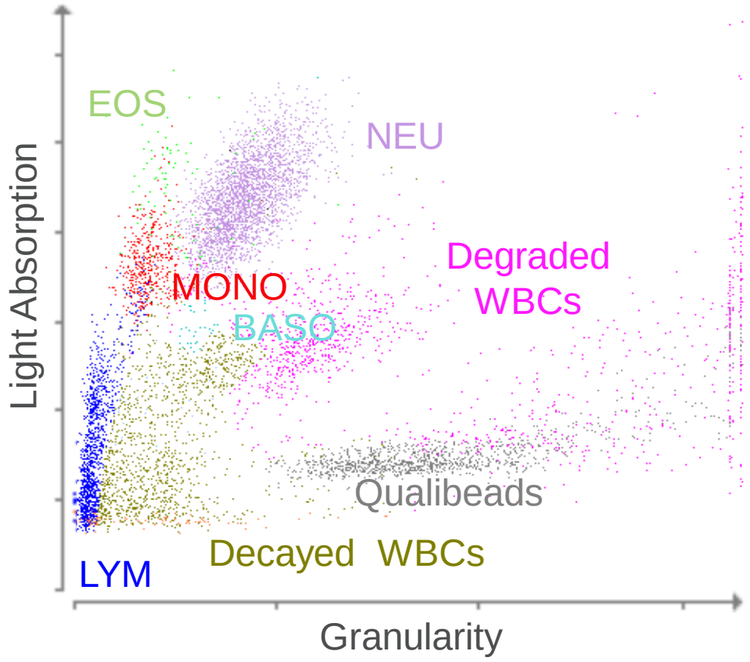
Differences between LaserCyte Dx, ProCyte One and ProCyte Dx

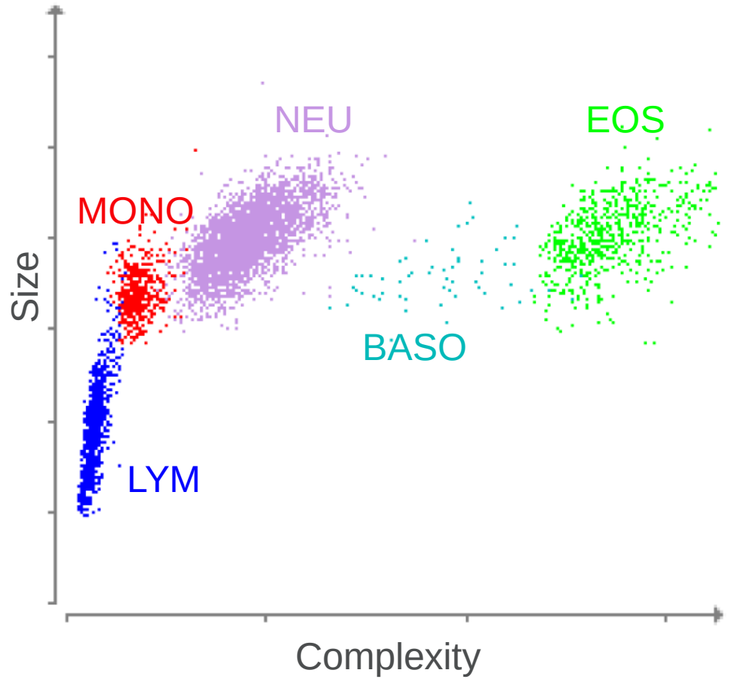


Differences between LaserCyte Dx, ProCyte One and ProCyte Dx

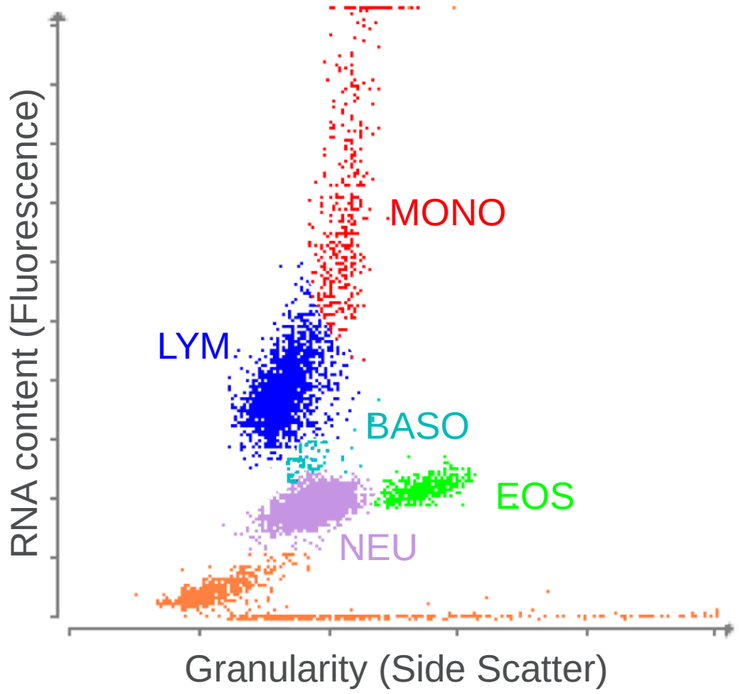
LaserCyte Dx



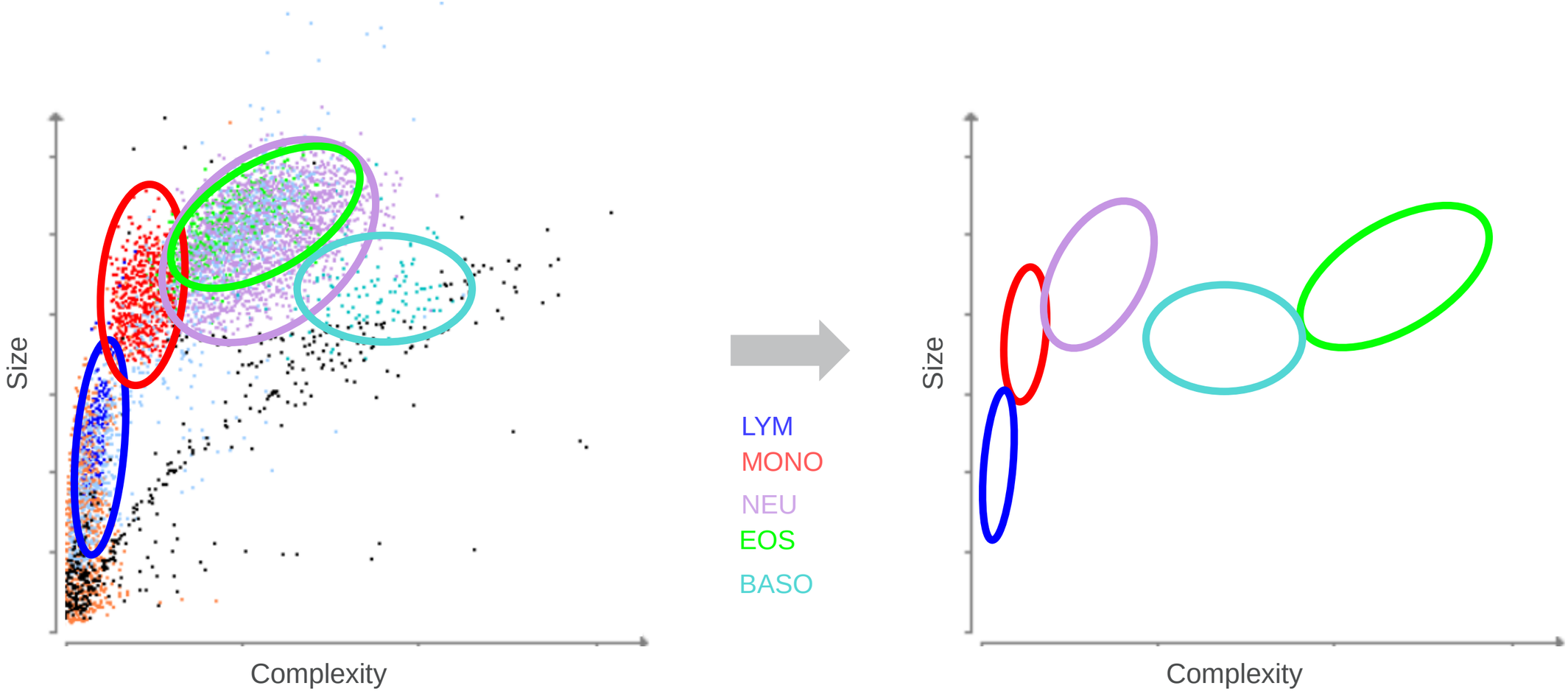
ProCyte One



ProCyte Dx



What magic is the algorithm team using?



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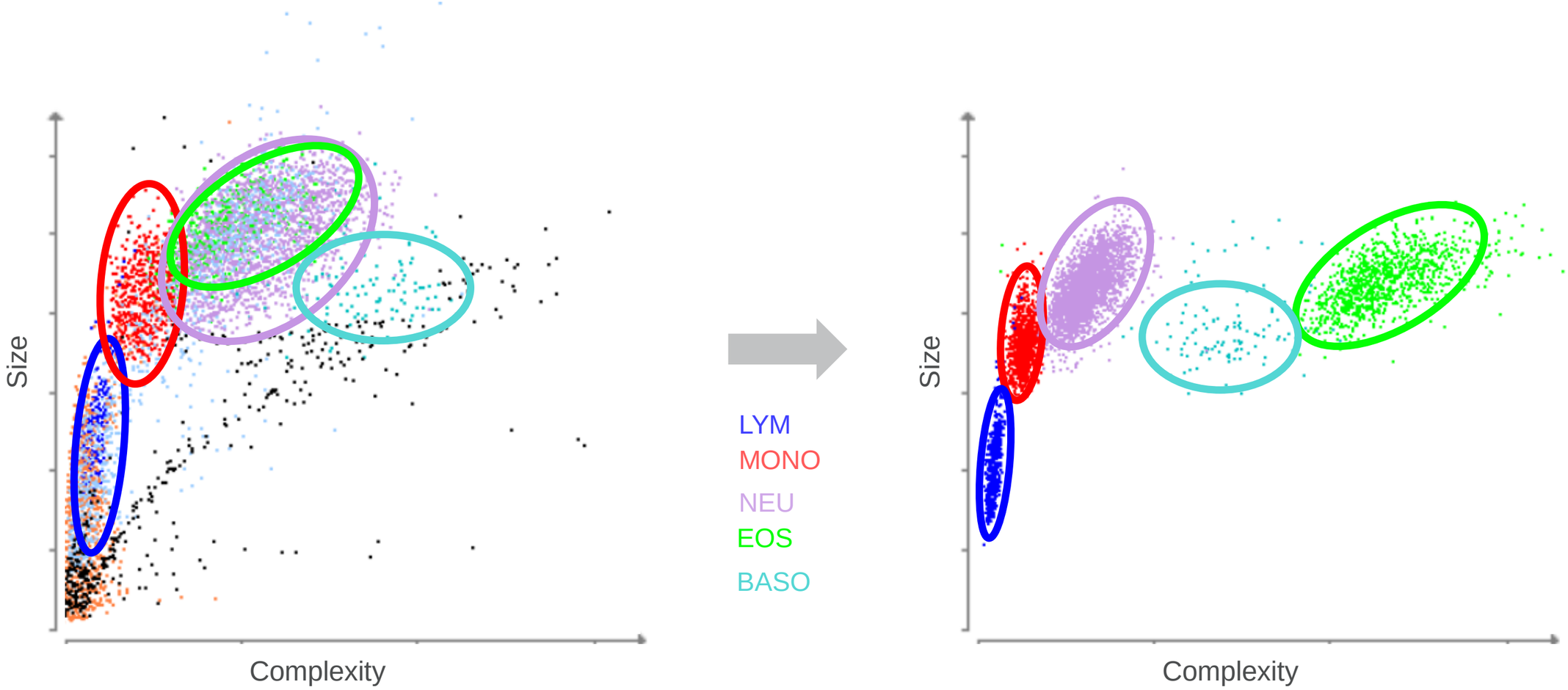

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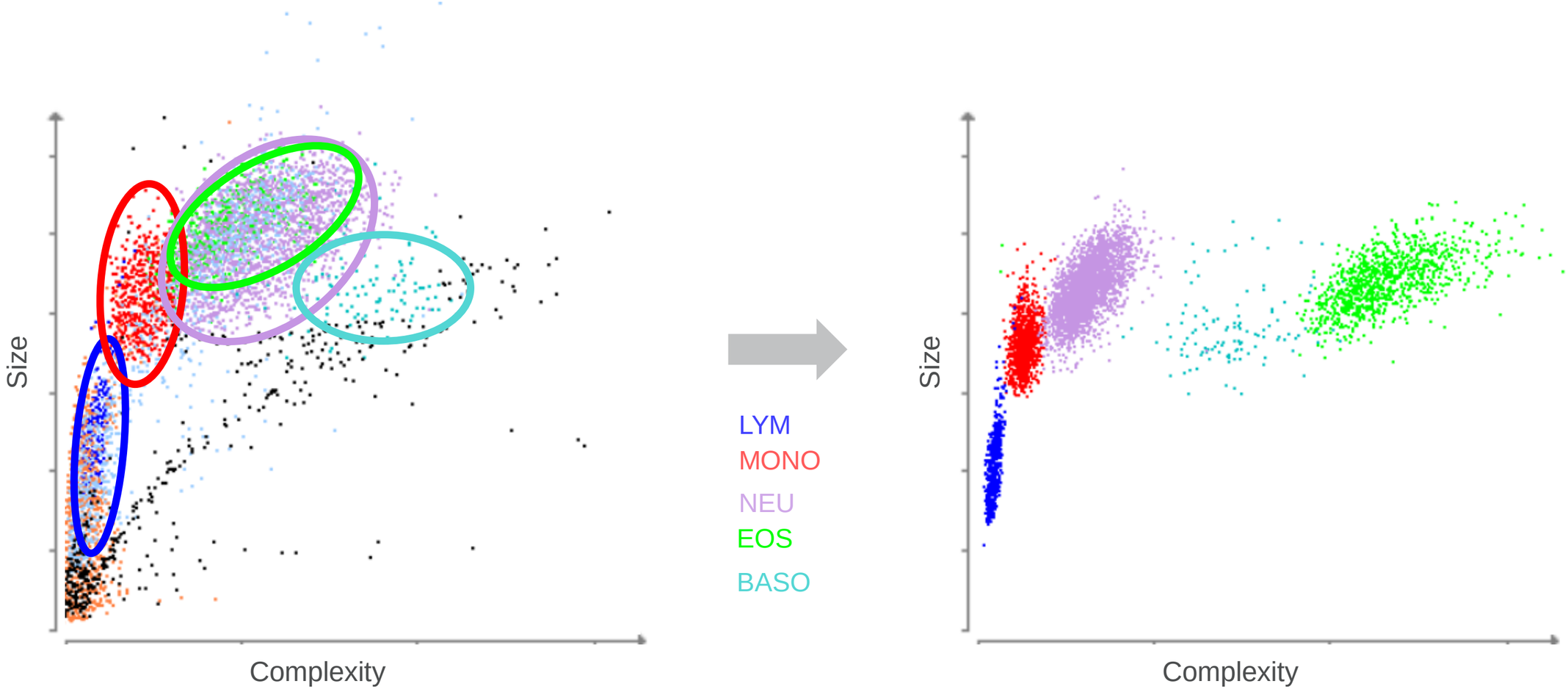
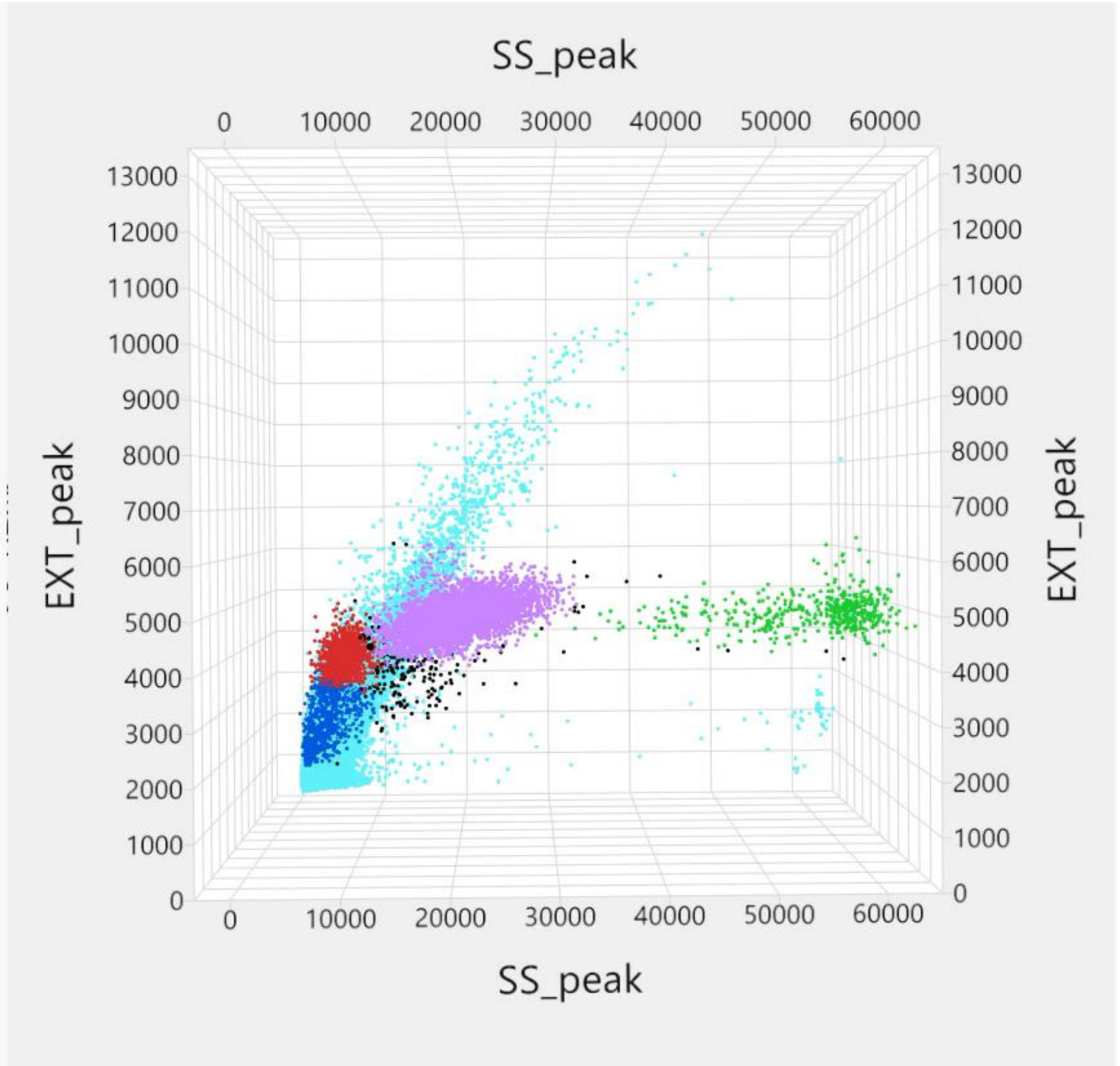
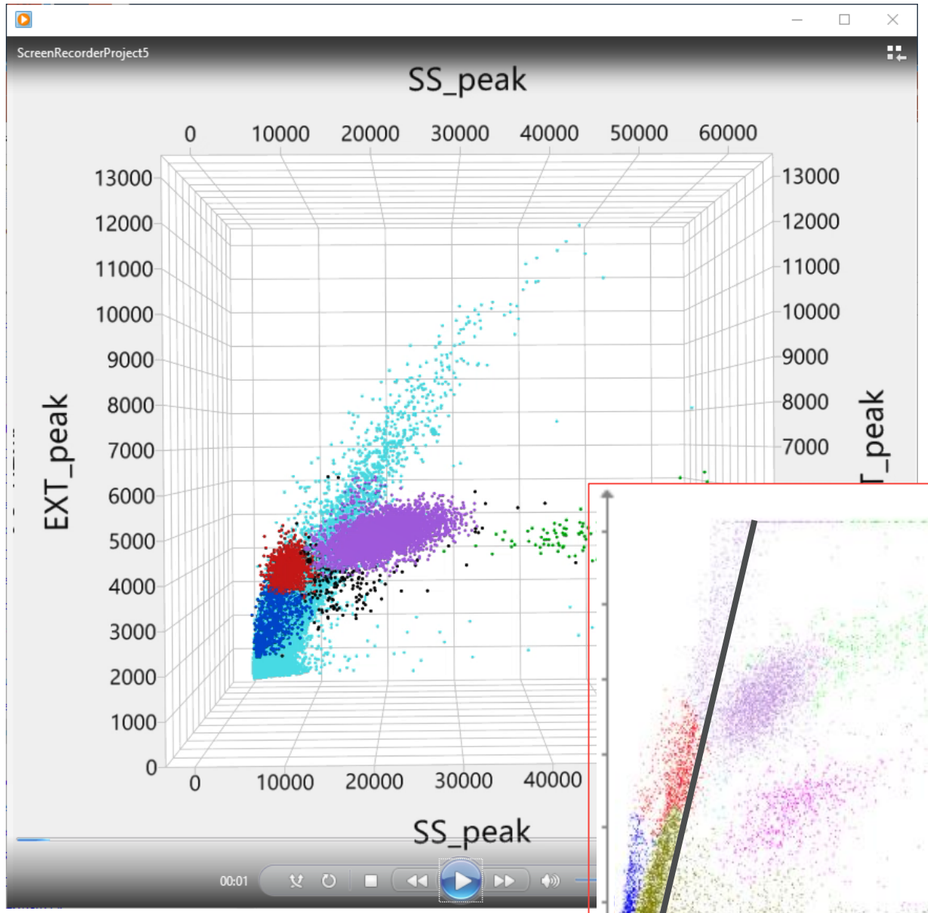


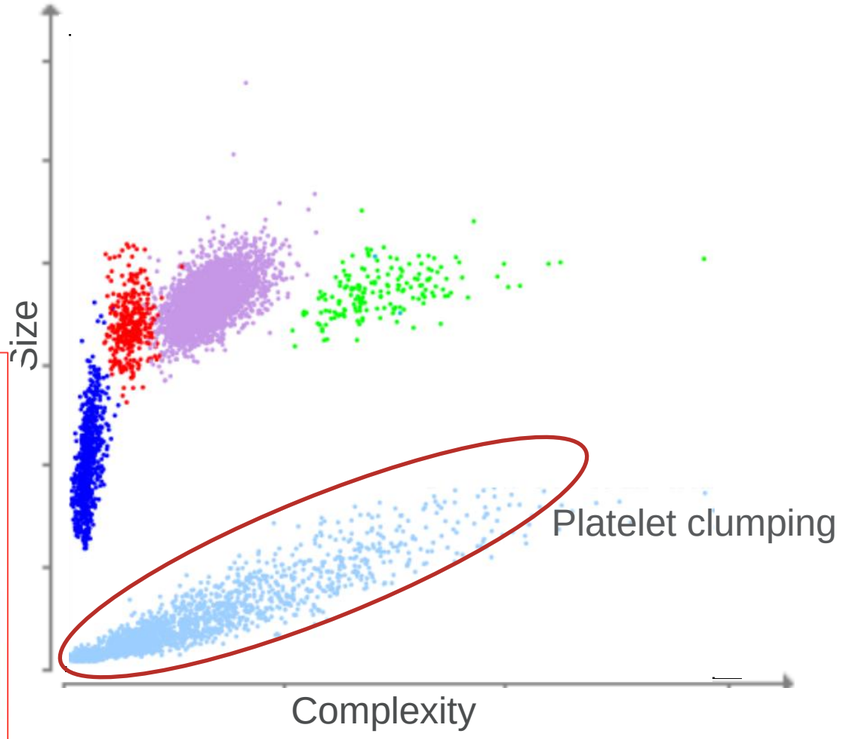
ProCyte One Cell Cluster Analysis



Magic behind the leukocyte algorithm



ProCyte One



ProCyte One Performance

- Specifications defined before construction of ProCyte One began
  - Followed recommendation by:
    - American Society for Veterinary Clinical Pathology
    - European Society of Veterinary Clinical Pathology

    - Precision (%CV)
    - Correlation (r)
    - Accuracy (compared to PDx)
    - Total allowable error (TE)

Internal data analysis – Canine only

- Erythrocytes and Platelets
  - 18 analyzers
  - 832 individual sample runs (151 Purdue runs)
    - Calibration – Westbrook R&D
    - Fresh – data collected in-clinic
    - Labs – primarily from IDEXX Oregon laboratory
  - Precision – mean of %CV of 10-canine runs from 12 analyzers / 7 analyzers had two precision runs
- Leukocytes
  - 795 individual sample runs
  - Precision – mean of %CV of 10-canine runs from 12 analyzers / 7 analyzers had two precision runs

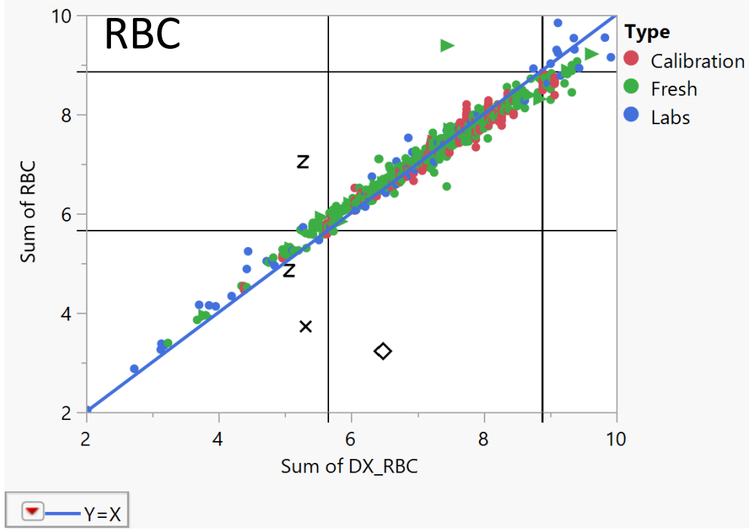
Internal data analysis – Canine only

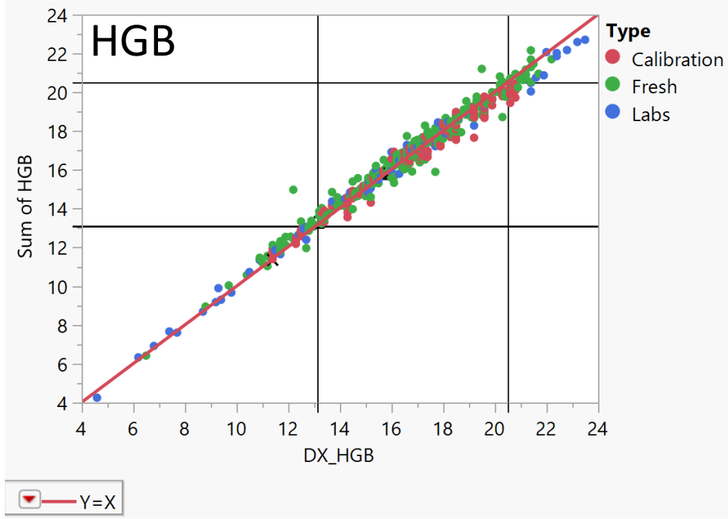
Parameter	Precision	Correlation (r)	Accuracy	Total Allowable Error
RBC	1.1% (<3%)	0.98 (>0.95)	-0.4% ±3%	2.6% (<10%)
HGB	1.3% (<3%)	0.99 (>0.90)	-0.2% (±2%)	2.8% (<10%)
HCT	1.2% (<3%)	0.96 (>0.90)	-0.2% (±4%)	2.6% (<10%)
MCV	0.5% (<1.1%)	0.91 (>0.90)	0.3% (N/A)	1.3% (<7%)
MCH	1.7% (N/A)	0.99 (N/A)	0.0% (N/A)	3.4% (N/A)
MCHC	1.8% (N/A)	0.99 (N/A)	0.0% (N/A)	3.6% (N/A)
RDW	0.5%	0.59	-3.1%	4.1%
RETIC	5% (<15%)	0.91 (>0.90)	-7 K/µL (±10 K/µL)	17% (<20%)

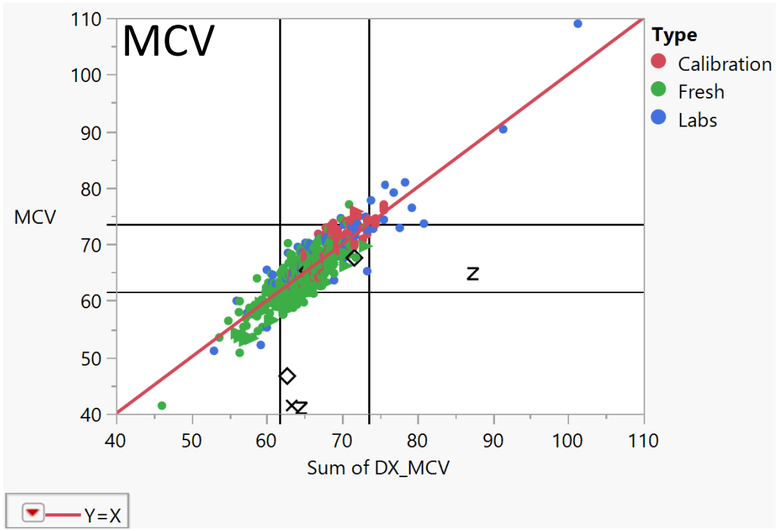
Parameter	Precision	Correlation (r)	Accuracy	Total Allowable Error
PLT	3.2% (<8%)	0.92 (>0.90)	-2.3% (±10%)	8.7% (<20%)
MPV	1.6% (N/A)	0.64 (N/A)	-0.5% (N/A)	3.7% (N/A)
PDW	4.7% (N/A)	0.89 (N/A)	1.2% (N/A)	10.6% (N/A)
PCT	3.5% (N/A)	0.87 (N/A)	-1.7% (N/A)	8.7% (N/A)

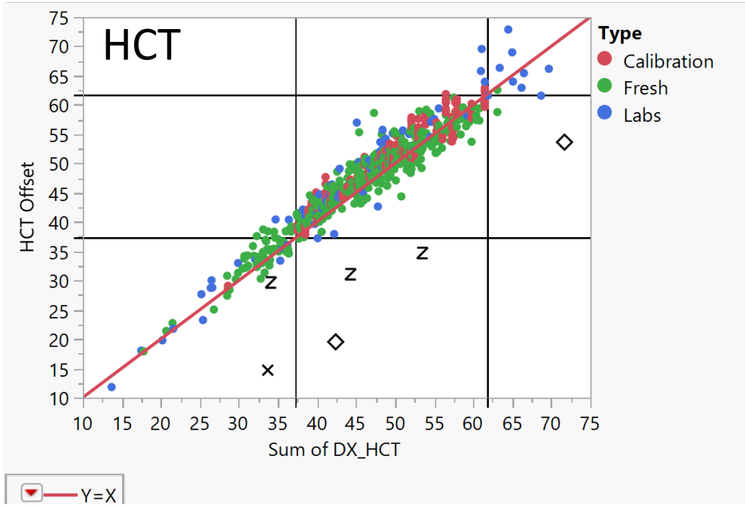
() – ASVCP guidelines

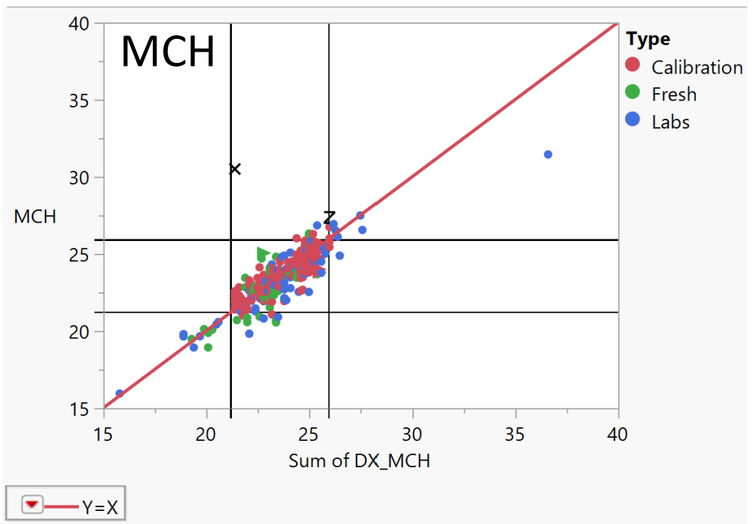
Correlations – RBC parameters

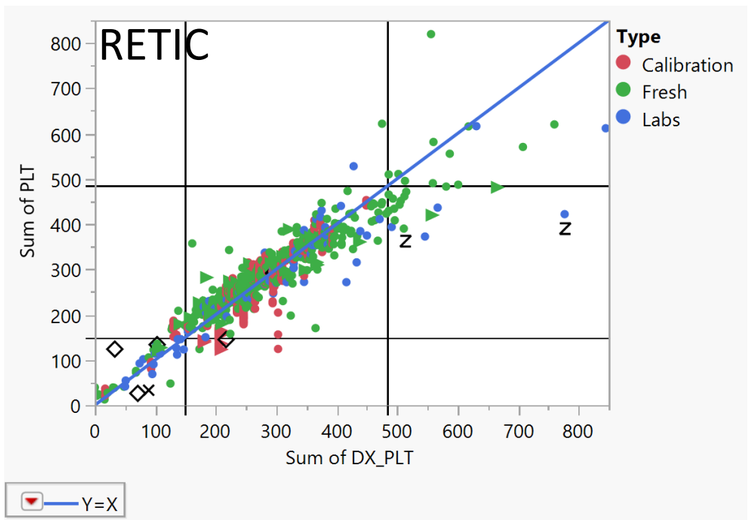




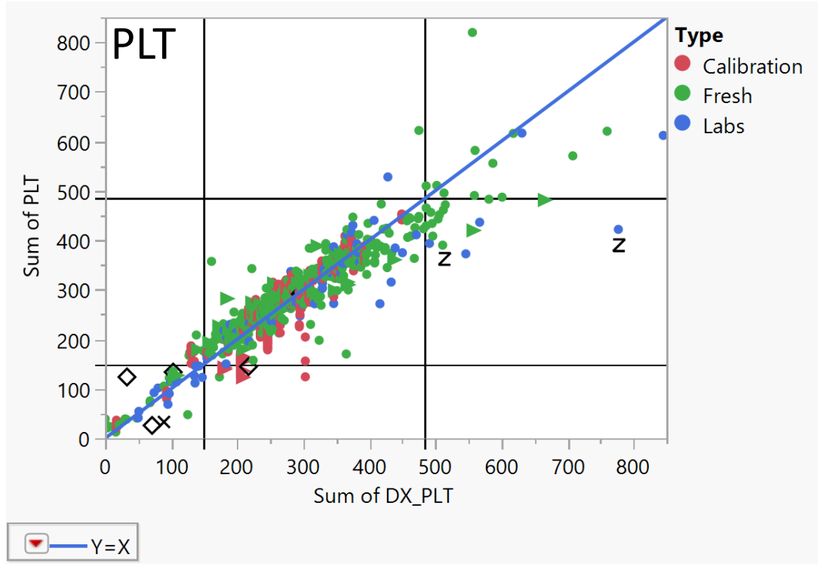


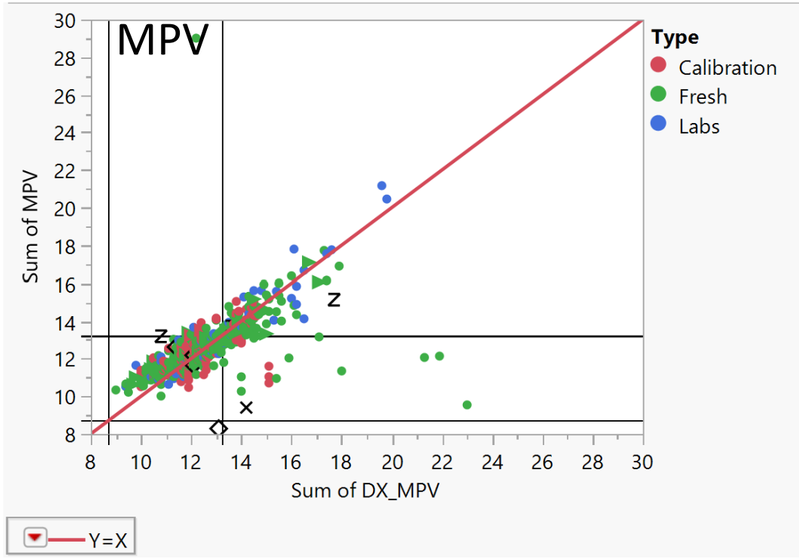


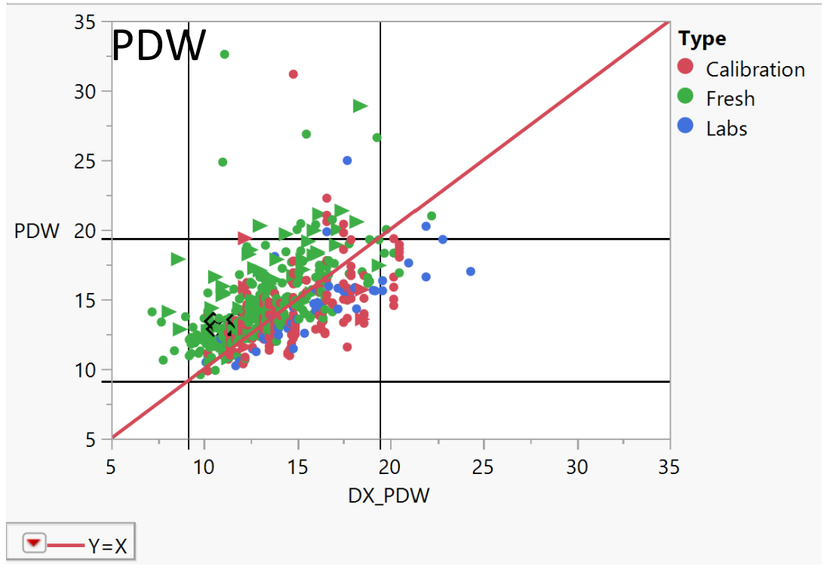


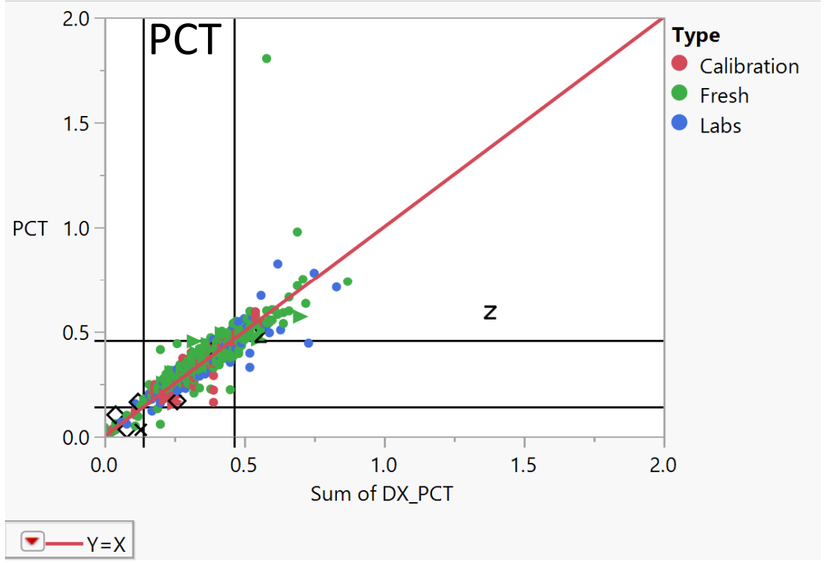


Correlations – PLT parameters









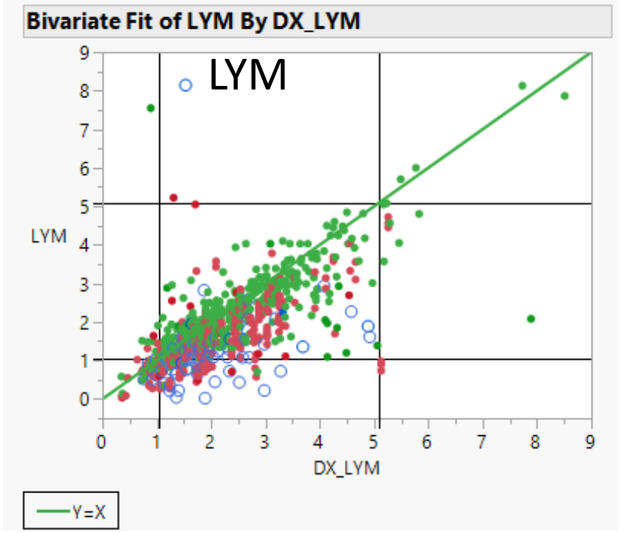
Internal data analysis – Canine only

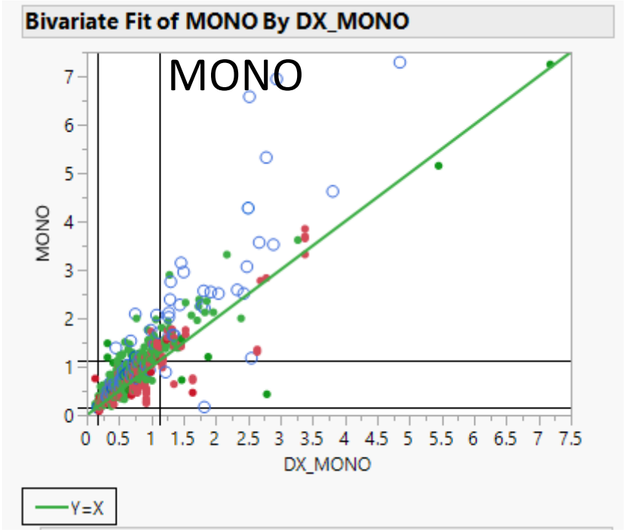
Parameter	Precision	Correlation (r)	Accuracy	Total Allowable Error
WBC	3.4% (<6%)	0.97 (>0.9)	3.2% ±5%	9.96% (<15%)
NEU	3.8% (N/A)	0.98 (>0.90)	-.14% (±2%)	9.3% (<15%)
LYM	9% (N/A)	0.70 (>0.60)	-0.38% (N/A)	18.4% (<15%)
MONO	10.9% (N/A)	0.87 (>0.60)	-.15% (N/A)	21.9% (<60%)
EOS	7.2% (N/A)	0.97 (>0.7)	- (N/A)	14.4% (<50%)
BASO	- (N/A)	- (>0.45)	- (N/A)	- (N/A)

() – ASVCP guidelines

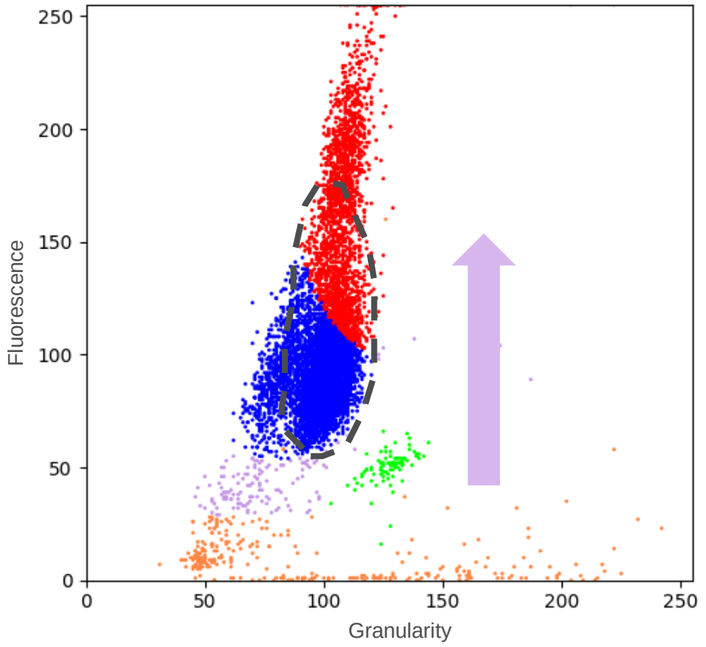
Reflection of PDx automated differential

WBC/LYM Outlier High (Oregon)

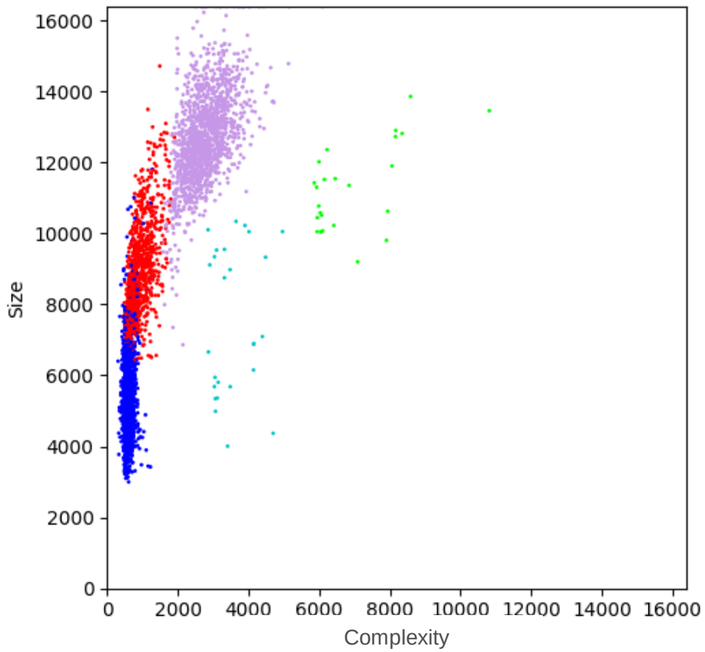




ProCyte Dx



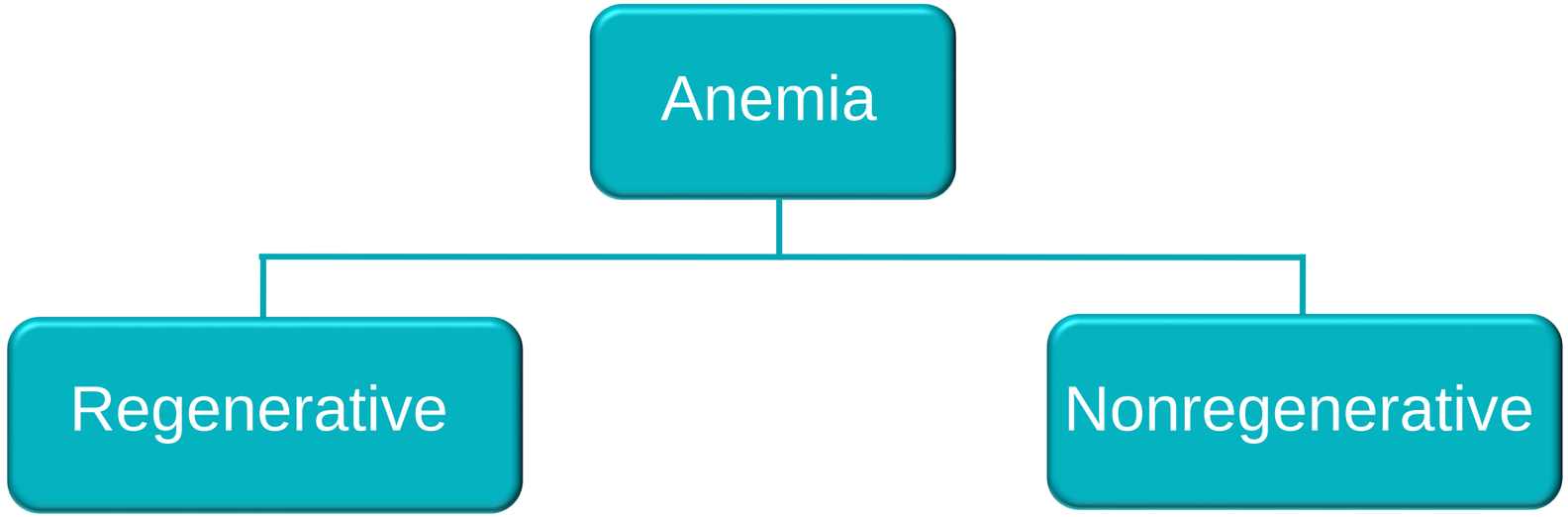
ProCyte One



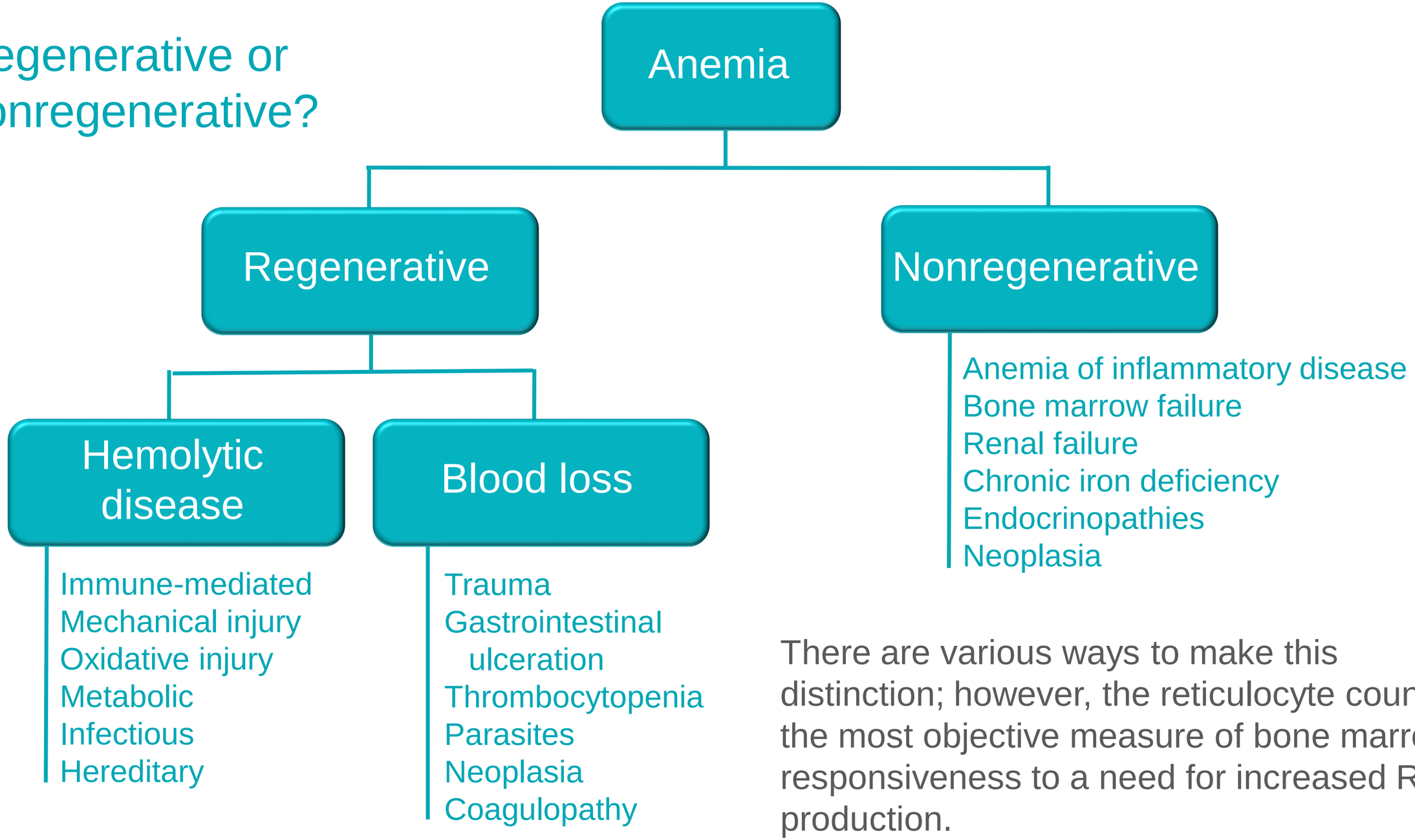
Value of Reticulocytes in the Anemic Patient

The value of reticulocyte counts with the anemic patient

- First question to ask with an anemic patient:
  - ‘Is the anemia regenerative or nonregenerative?’



Regenerative or nonregenerative?



There are various ways to make this distinction; however, the reticulocyte count is the most objective measure of bone marrow responsiveness to a need for increased RBC production.

What is the prevalence of anemia

- Two different studies
  - Random data collection from global fleet of ProCyte Dx Analyzers in 2017 (one year)
    - 1,000,000 Canine CBCs
    - 1,000,000 Feline CBCs

What is the prevalence of anemia

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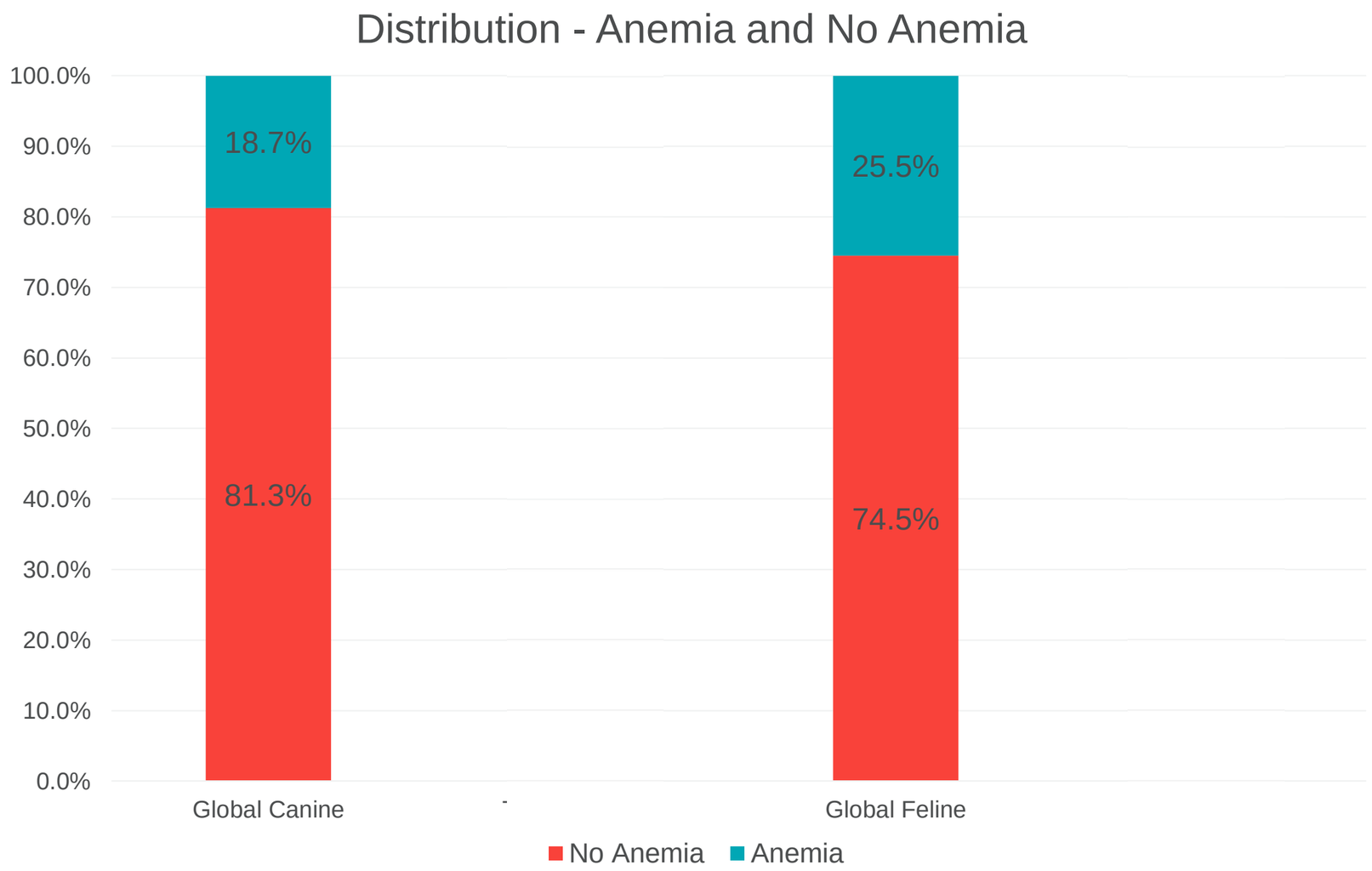
    - 1,000,000 Canine CBCs
    - 1,000,000 Feline CBCs
  - Taiwan ProCyte Dx Analyzers – 2018-12-1 to 2020-12-31
    - 149,076 Canine CBCs
    - 116,951 Feline CBCs

Breed	N	%
Other	96,555	64.8
Poodle Standard	12,329	8.3
Maltese	8,822	5.9
Dachshund	5,319	3.6
Shiba Inu	4,014	2.7
Chihuahua	3,303	2.2
Pomeranian	2,558	1.7
French Bulldog	2,122	1.4
Yorkshire Terrier	2,025	1.4
Golden Retriever	1,393	0.9
Shih Tzu	1,308	0.9

What is the prevalence of anemia



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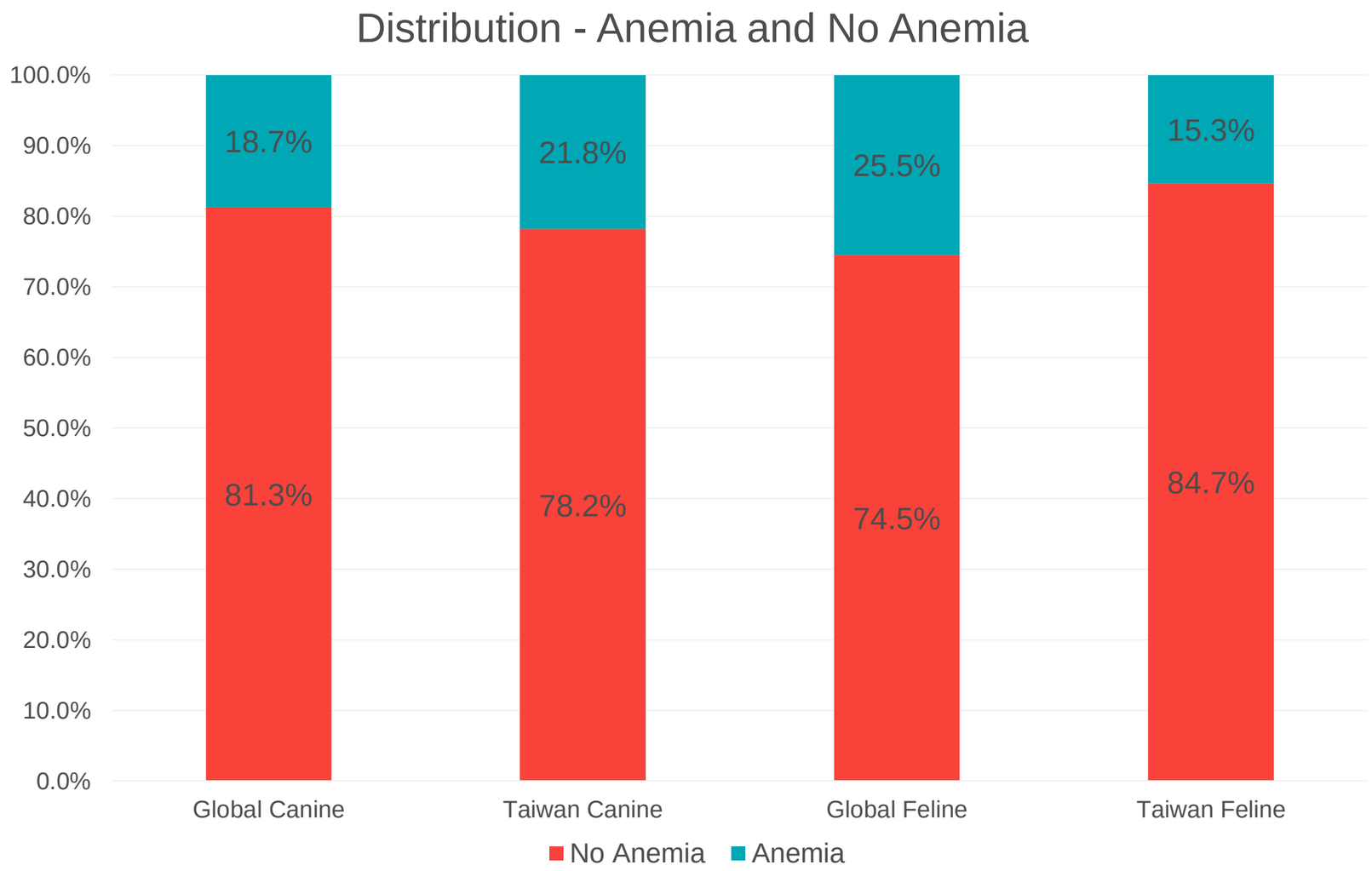
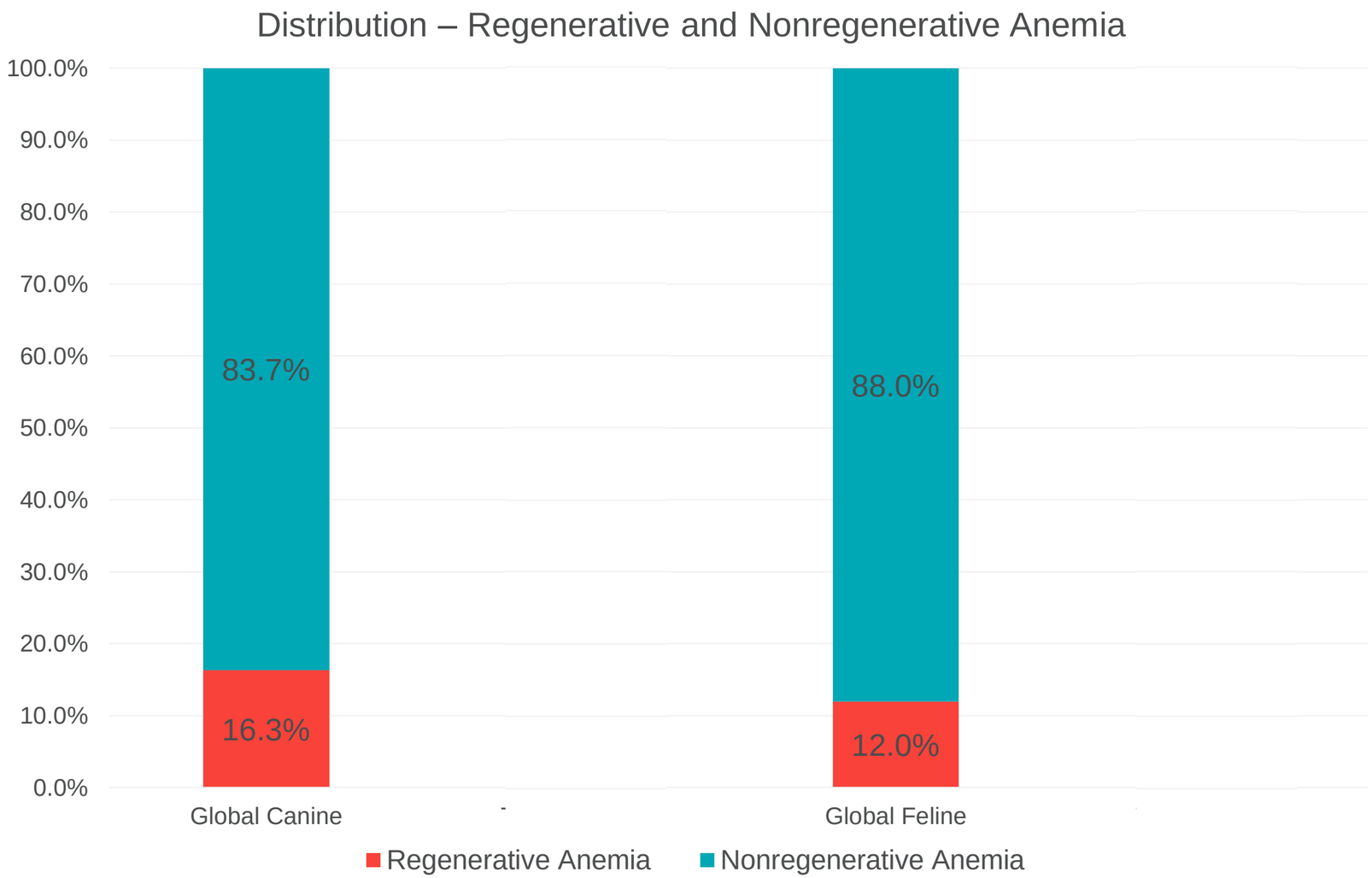


What is the prevalence of regenerative and nonregenerative anemia



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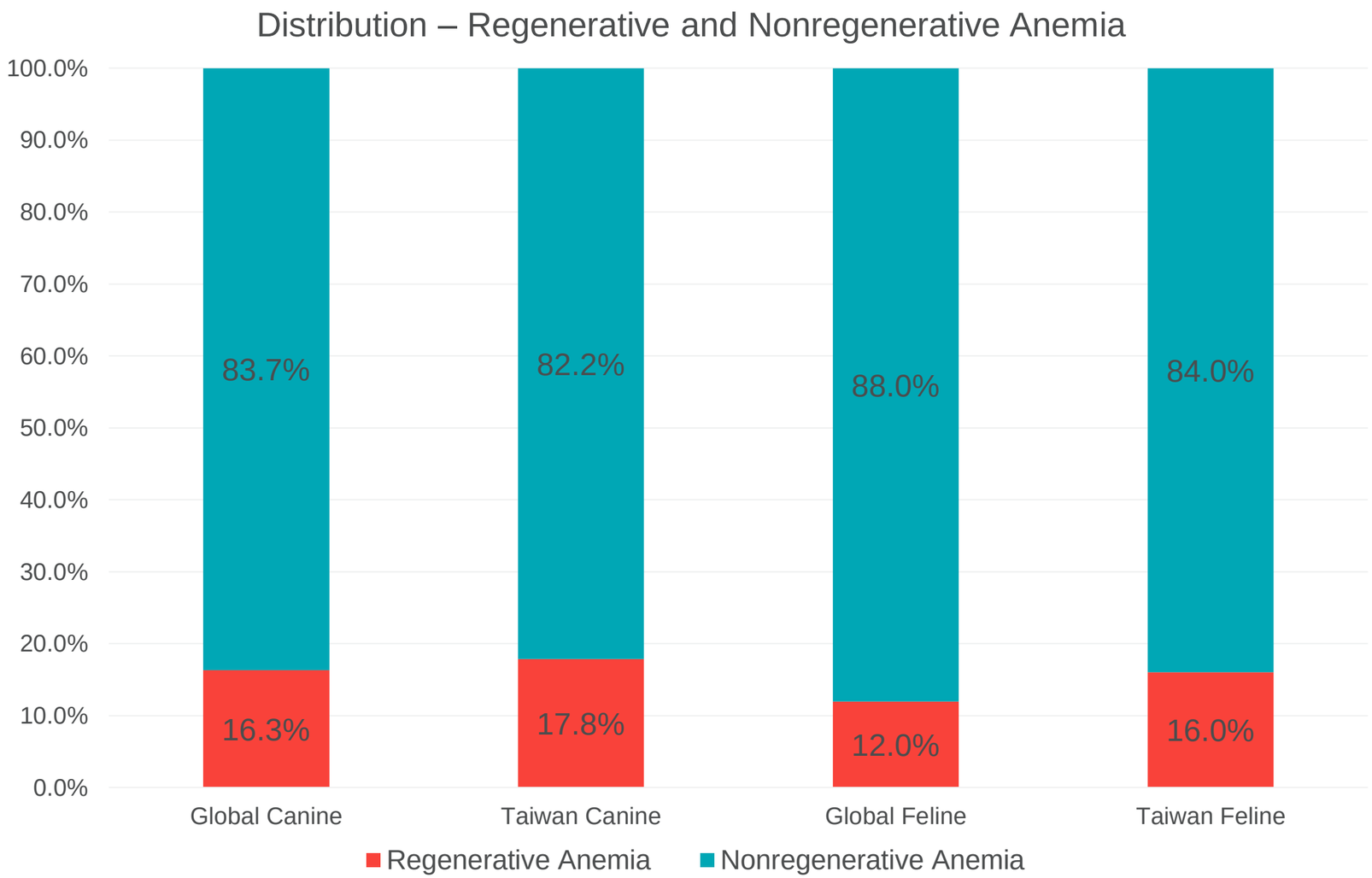

Characterization of bone marrow response in erythroid series

- How is a bone marrow response determined?

Characterization of bone marrow response in erythroid series

- How is a bone marrow response determined?
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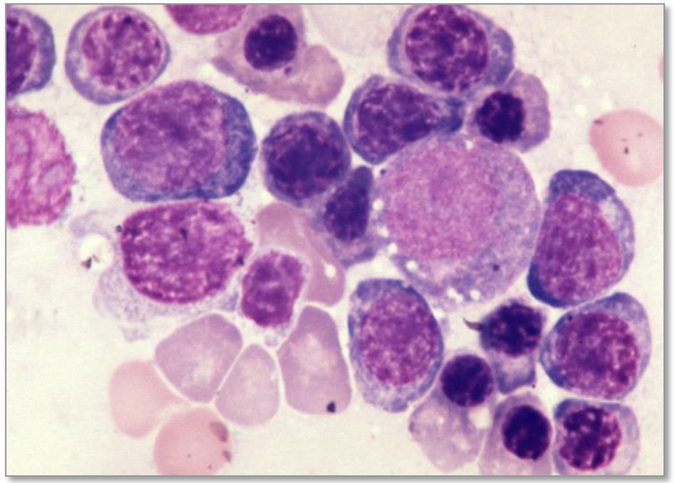
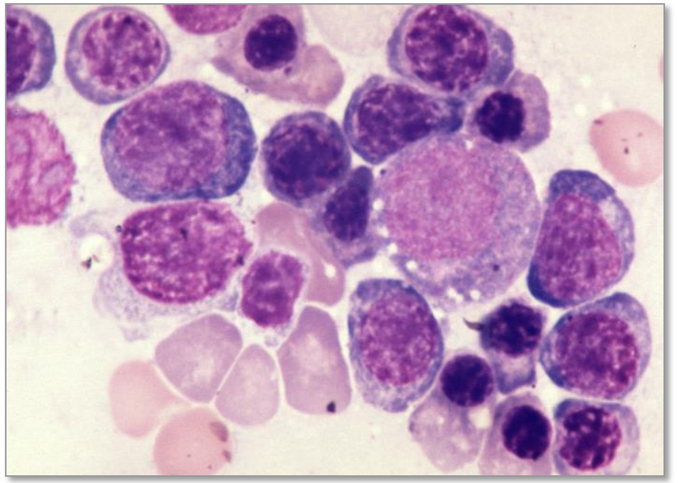
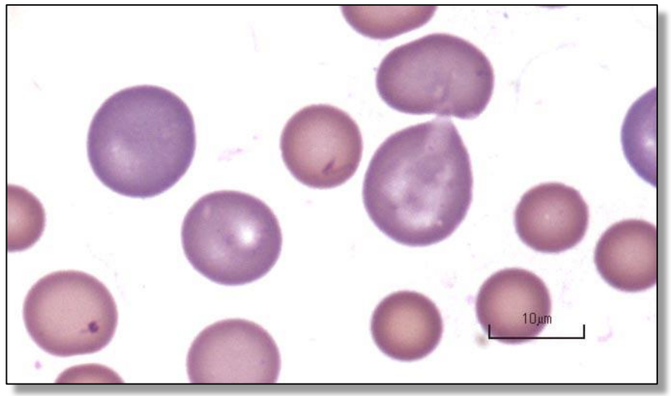


Characterization of bone marrow response in erythroid series

- How is a bone marrow response determined?
  - Direct examination of the bone marrow
  - Peripheral blood film review



Polychromasia
Anisocytosis



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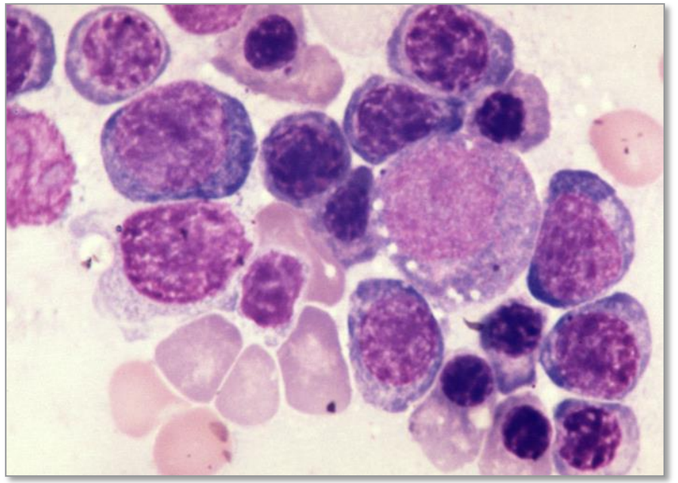
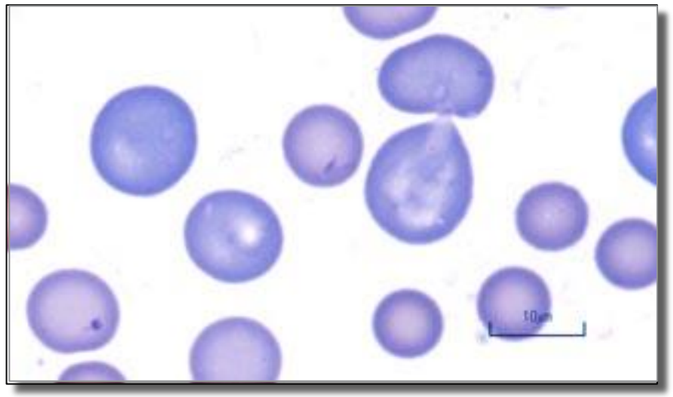


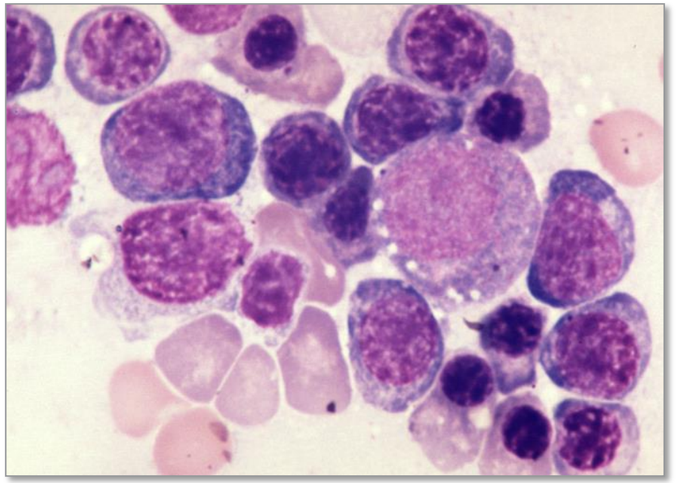
Polychromasia
Anisocytosis

Diff Quik stain



Characterization of bone marrow response in erythroid series

- How is a bone marrow response determined?
  - Direct examination of the bone marrow
  - Peripheral blood film review
  - Complete blood count data:
    - RBC indices—morphologic classification
    - Reticulocyte count—objective measure of bone marrow response



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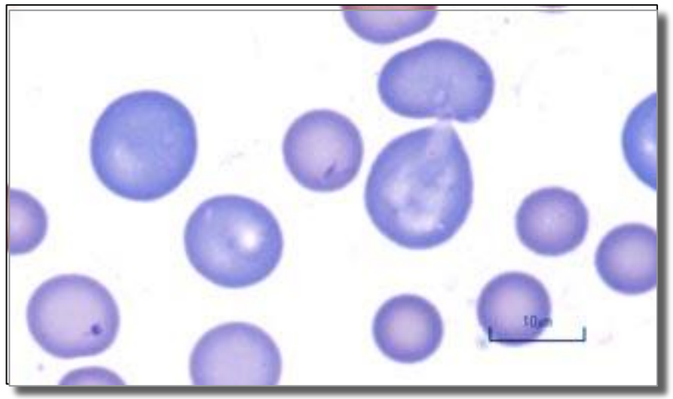
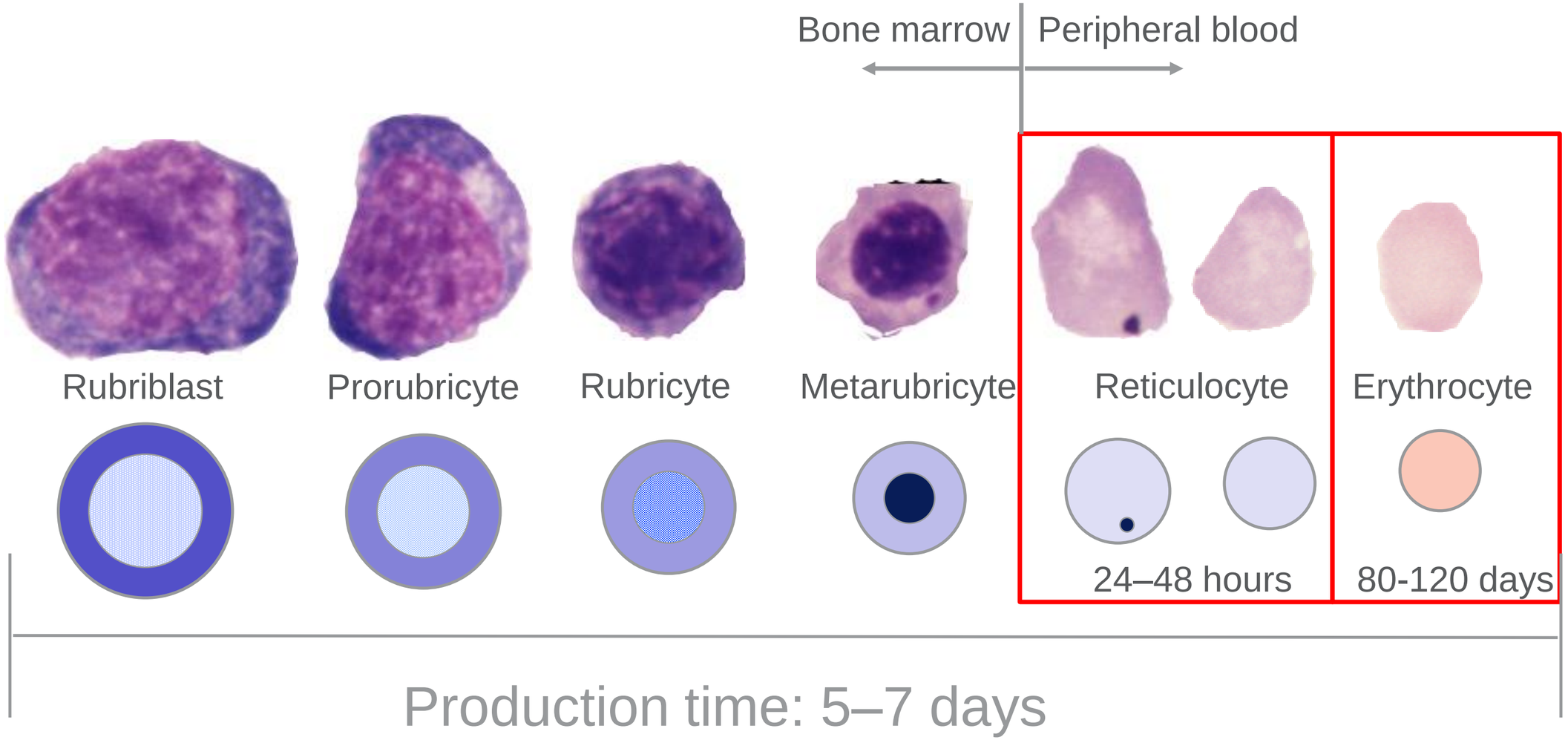


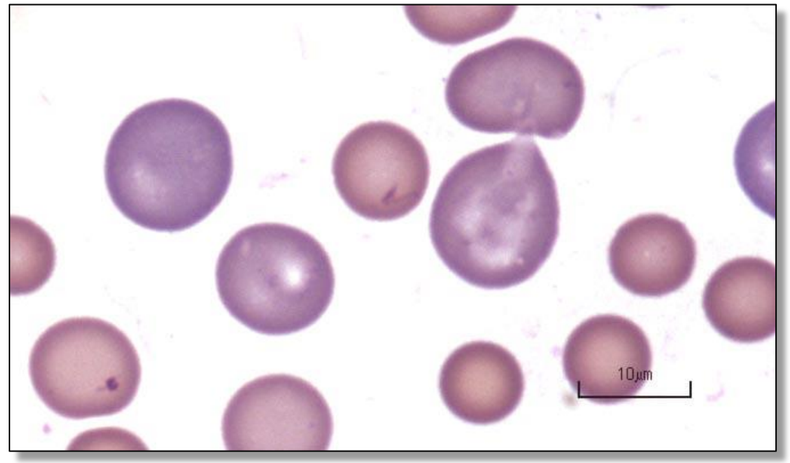
Erythropoiesis

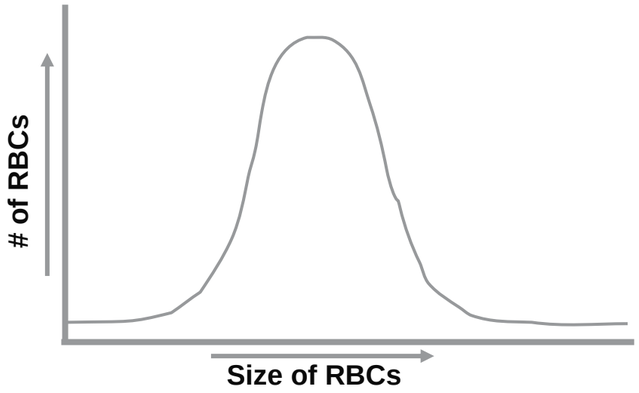
Compared to mature RBC, Reticulocytes:
1. Larger (increased MCV)
2. Less HGB (decreased MCHC
3. Contribute to anisocytosis



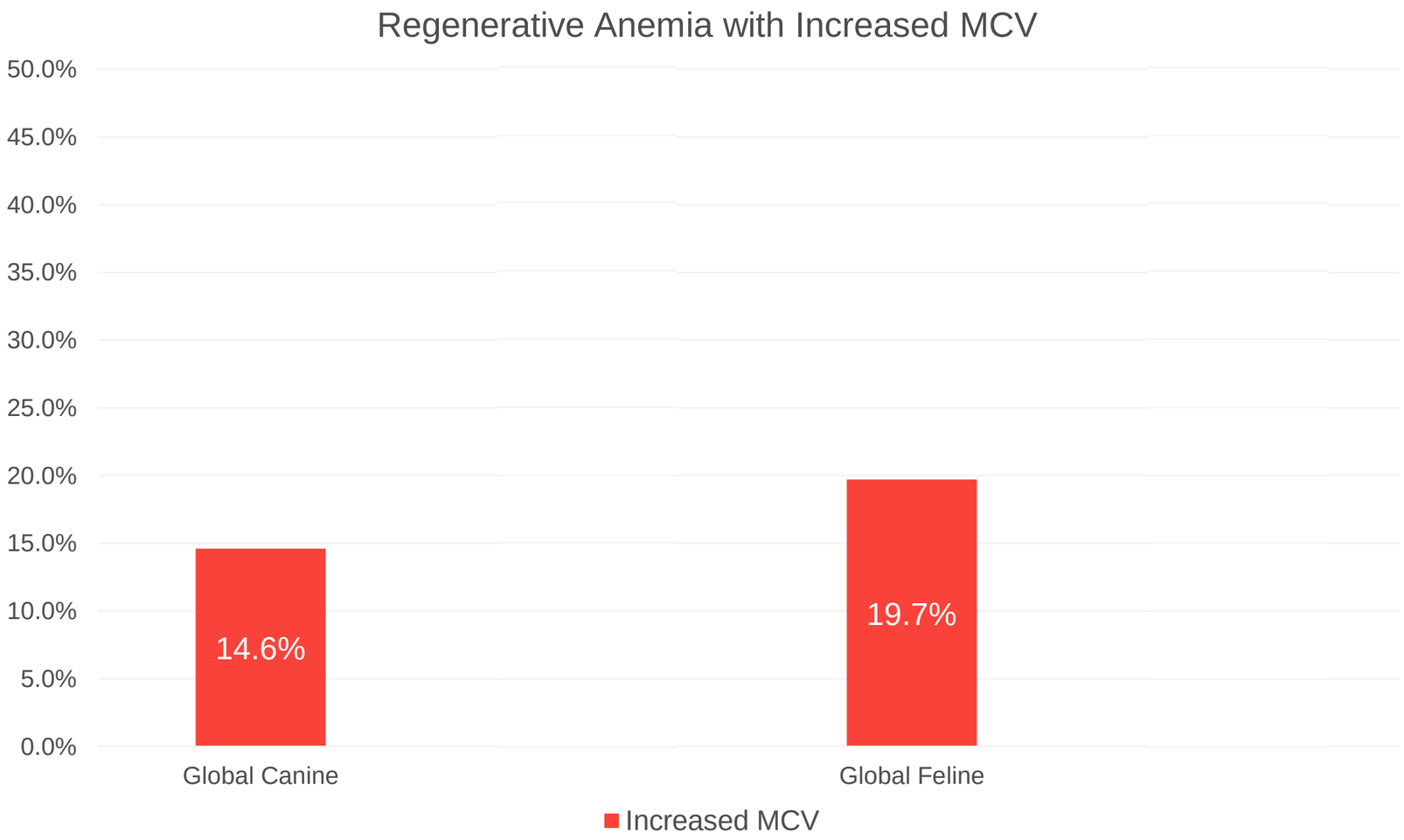
Red blood cell indices

- Numerical values describing blood film morphologic changes:
  - MCV—mean corpuscular volume:
    - Immature RBCs are larger than mature RBCs.
    - Relatively rare conditions with increased MCV not associated with regeneration:
      - Miniature and toy poodles, greyhounds, FeLV infections
  - MCHC—mean corpuscular hemoglobin concentration:
    - Immature RBCs have less hemoglobin than mature RBCs.
    - Advanced stages of chronic blood loss—iron deficiency.
  - RDW—red cell distribution width:
    - Objective measure of variability of RBC size
    - Not specific for mixture of normal and large RBCs:
      - Normal and large cells
      - Normal and small cells
      - Normal, large, and small cells





Prevalence of Increased MCV with Regenerative Anemia



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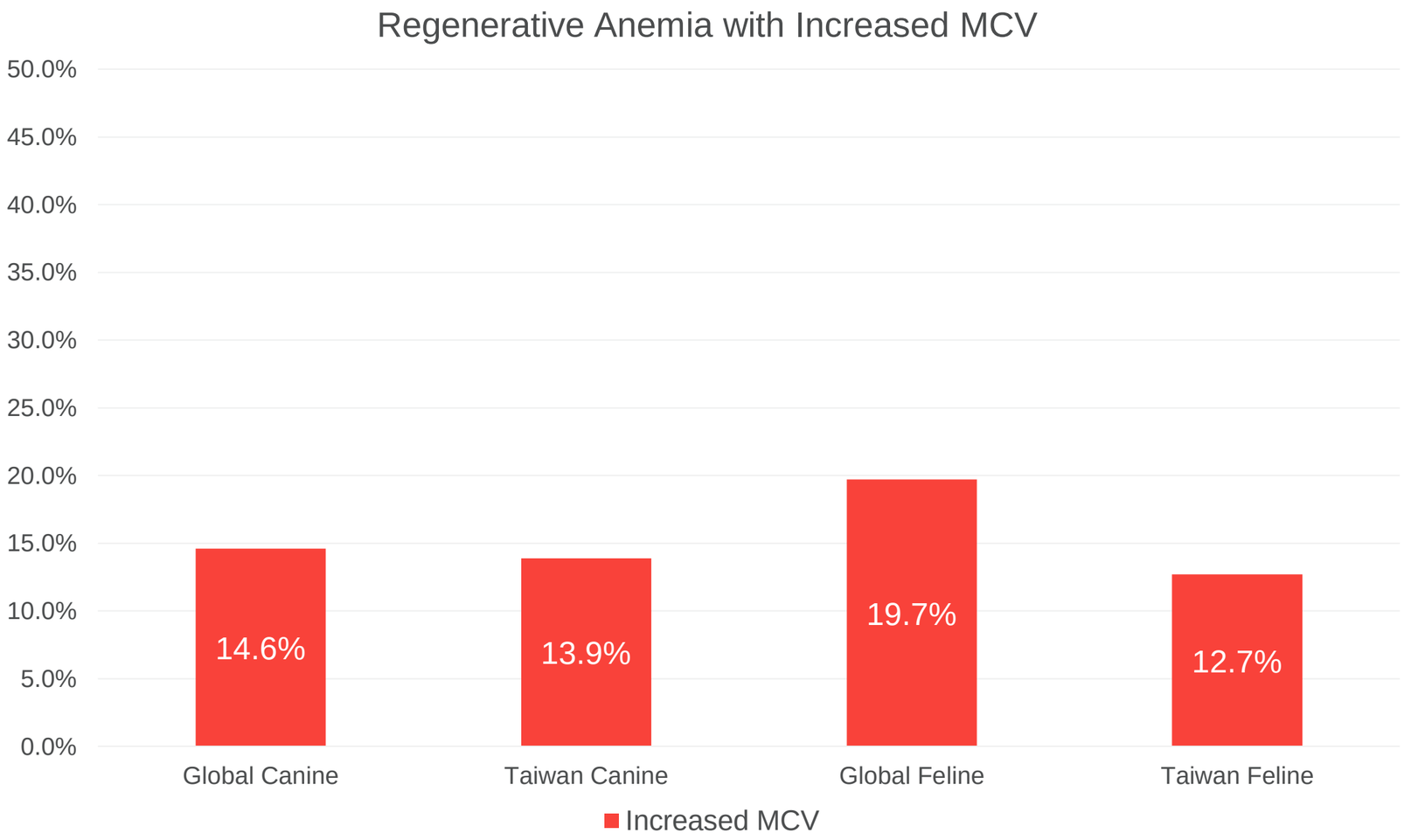
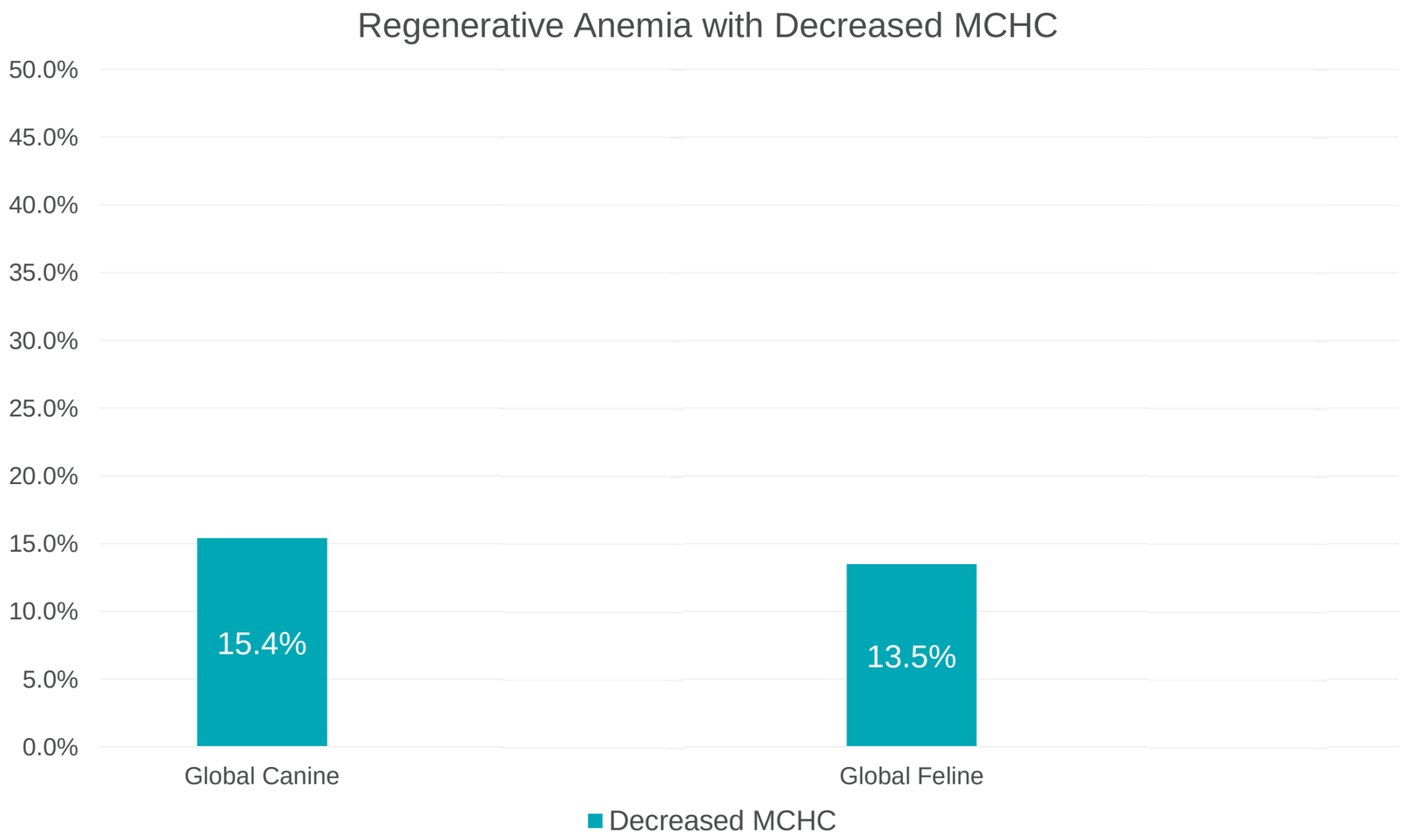
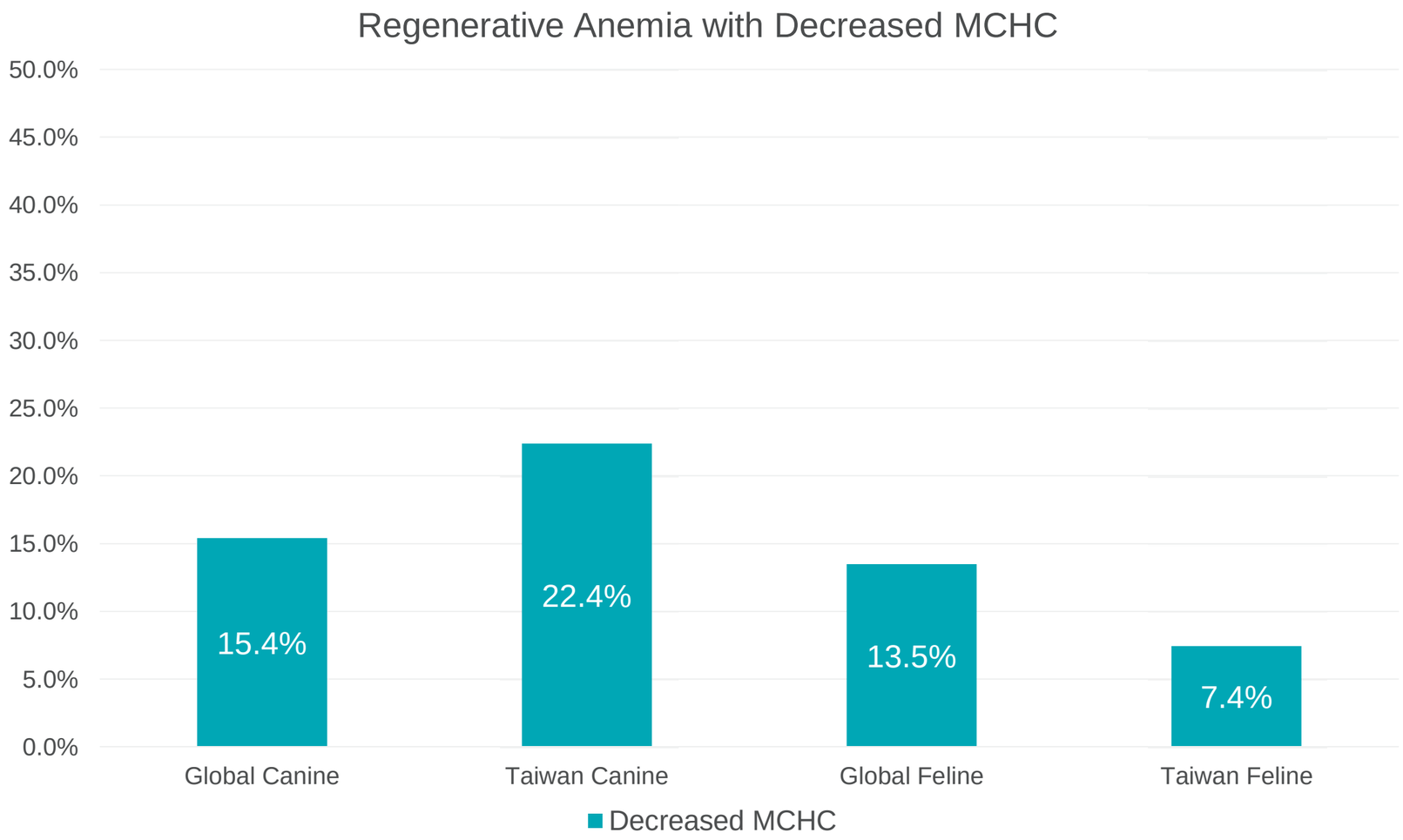


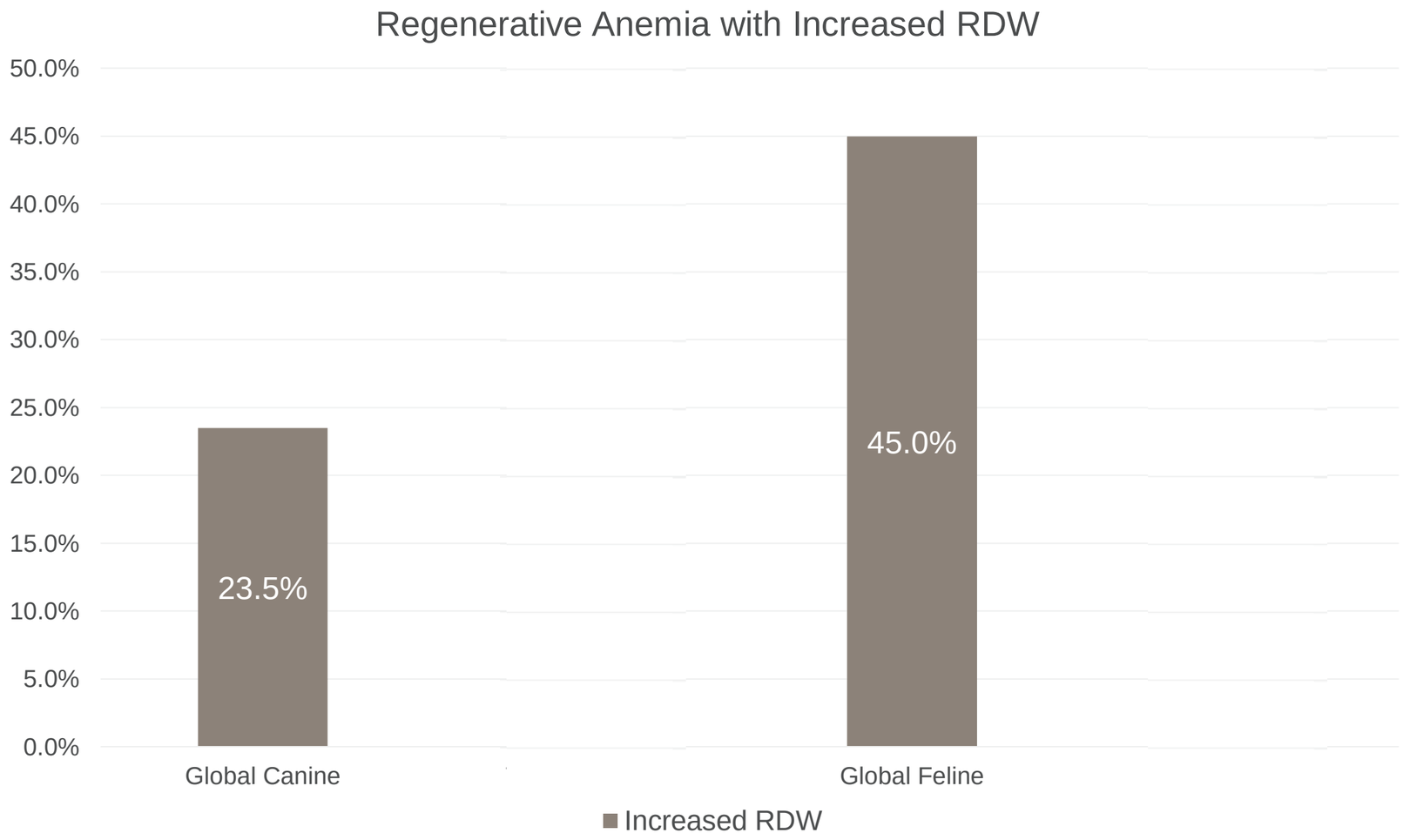
Prevalence of Decreased MCHC with Regenerative Anemia



Prevalence of Decreased MCHC with Regenerative Anemia



Prevalence of Increased RDW with Regenerative Anemia



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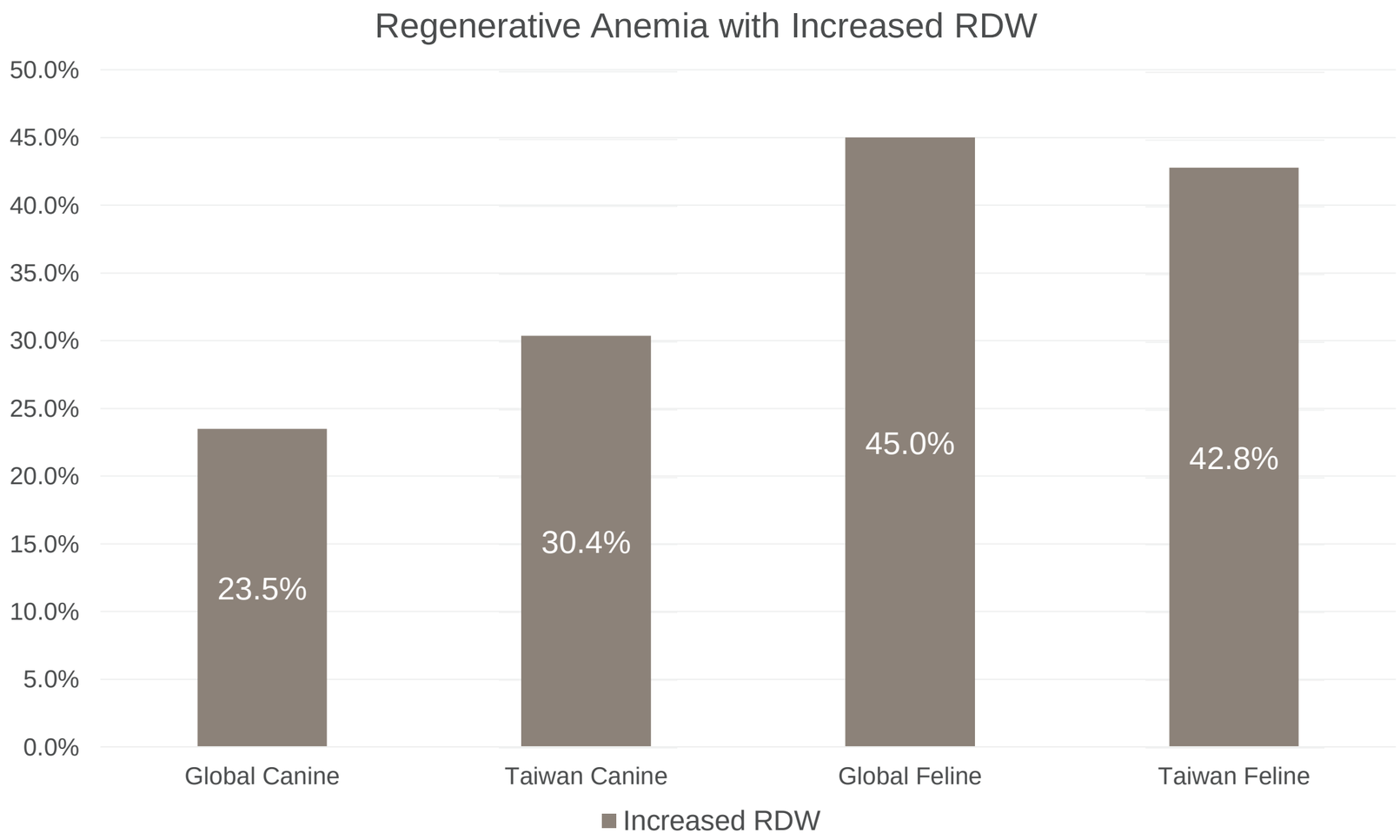
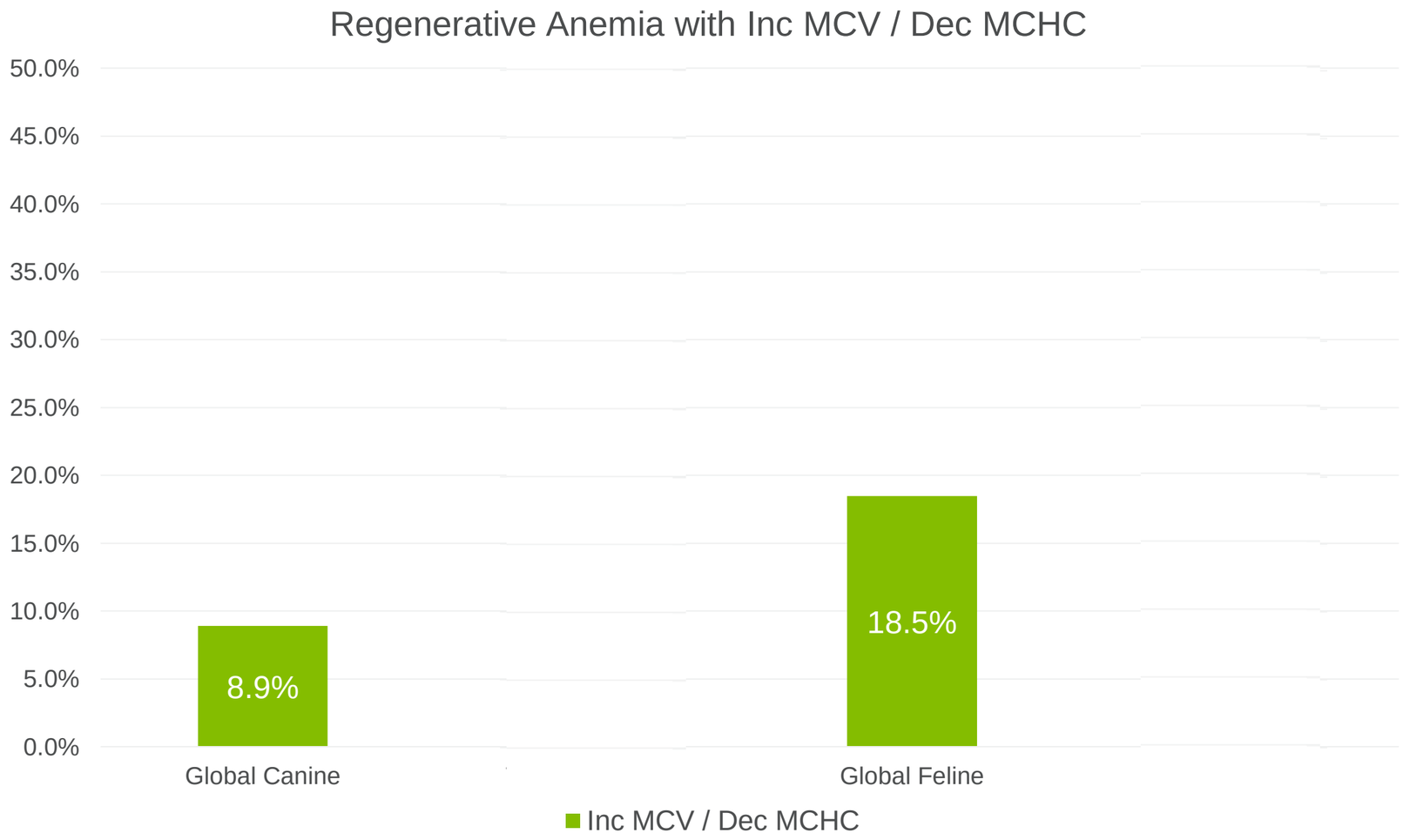


Prevalence of Inc MCV / Dec MCHC with Regenerative Anemia



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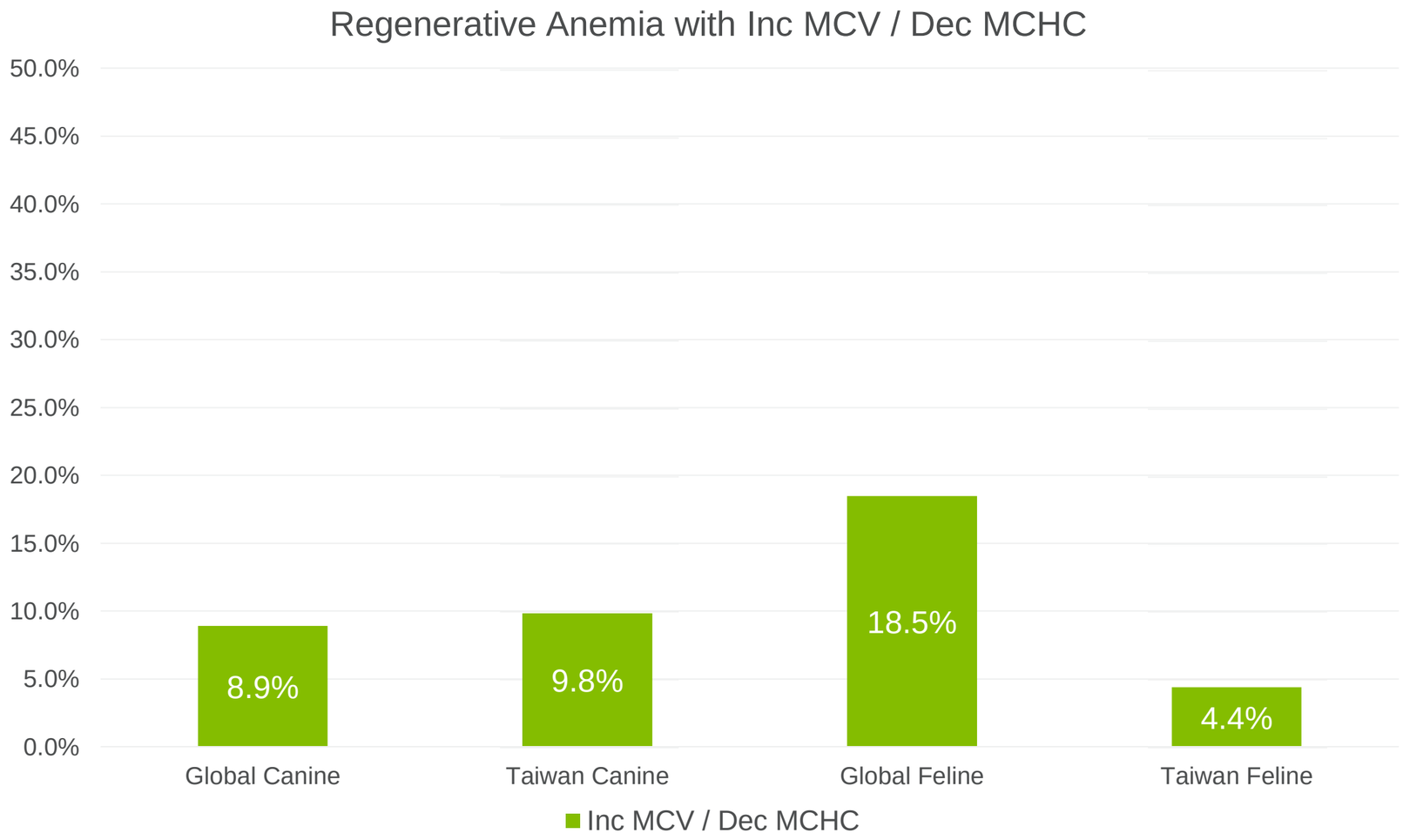
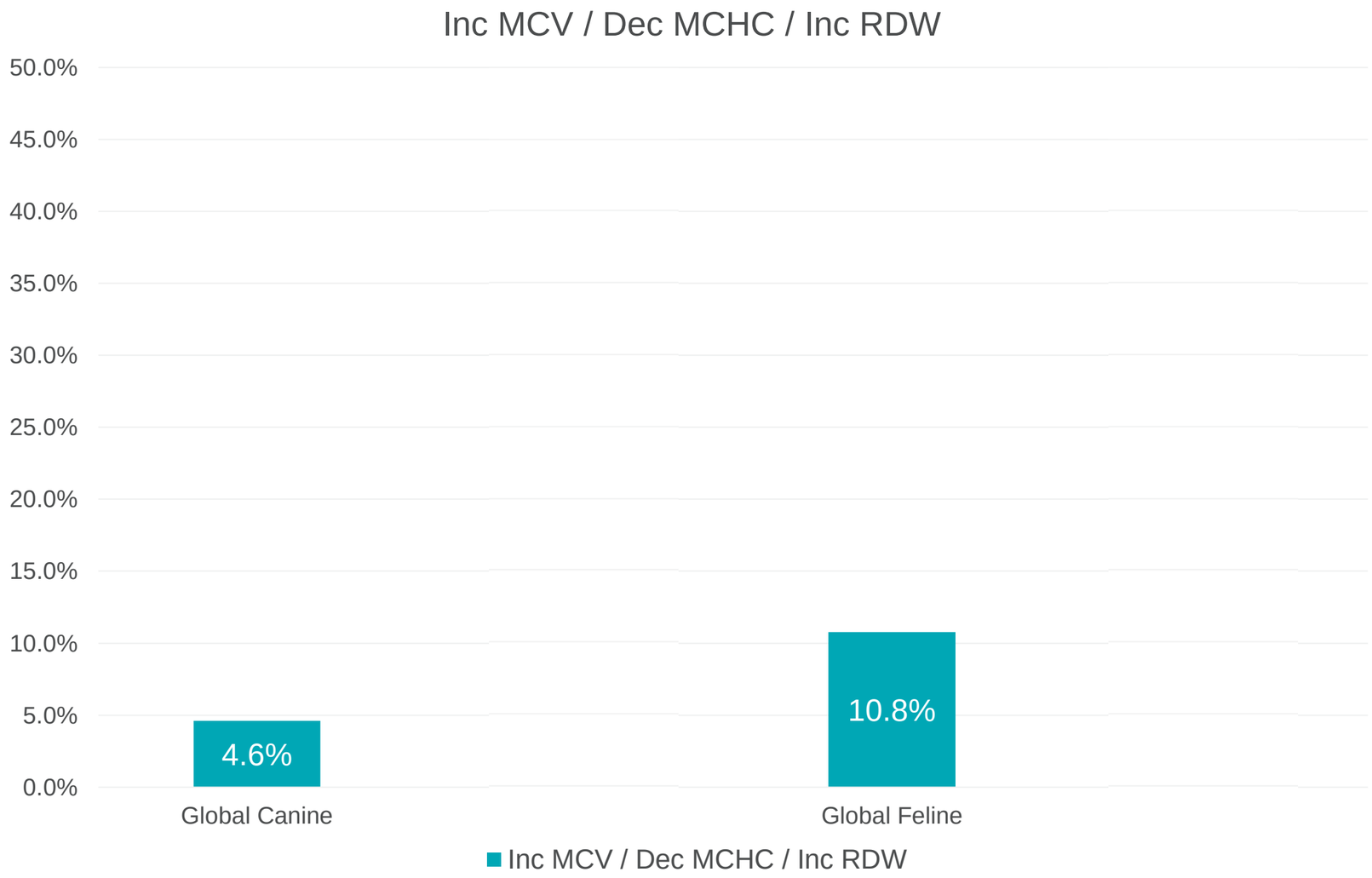
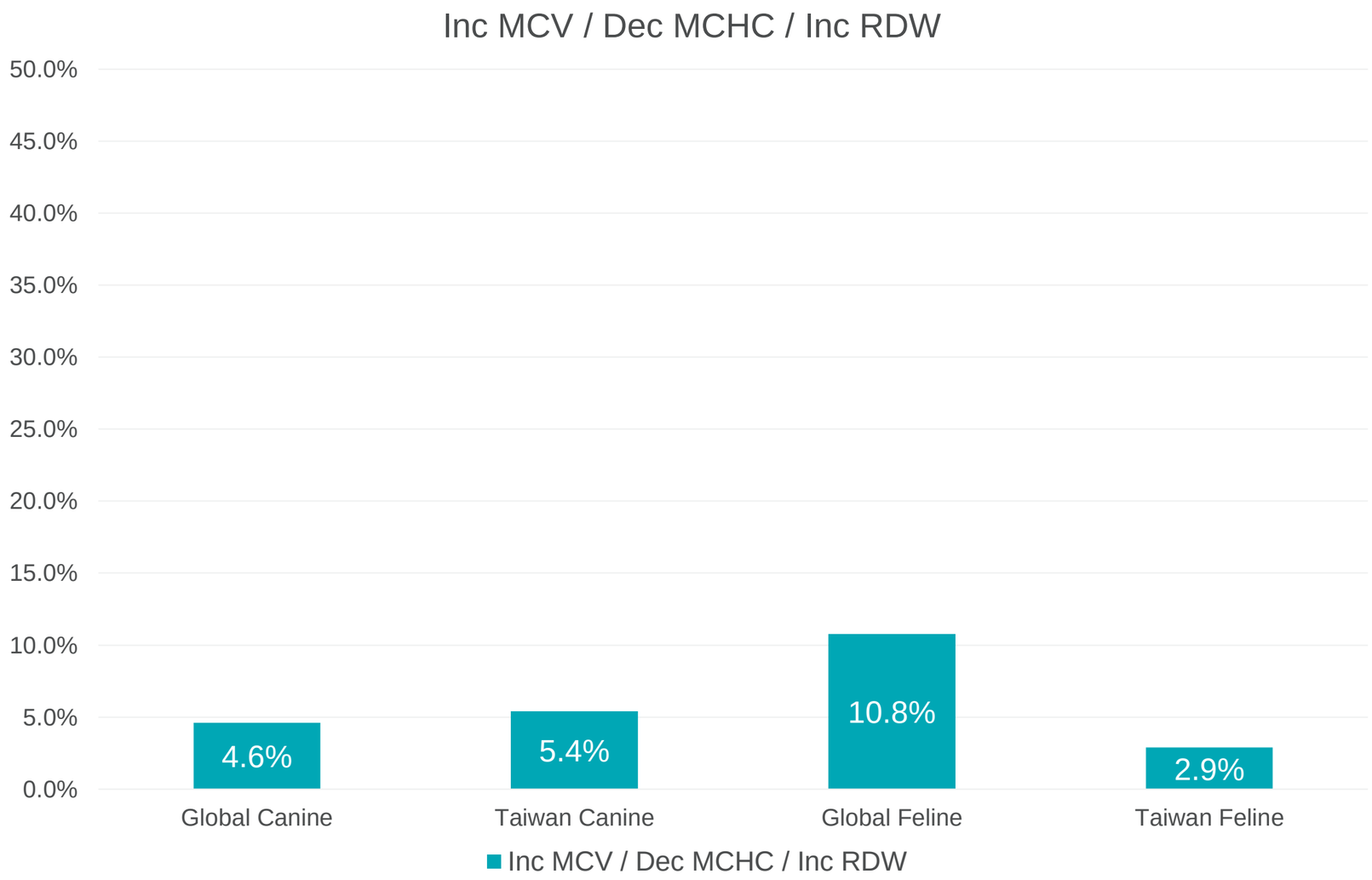


Prevalence of Inc MCV / Dec MCHC / Inc RDW with Regenerative Anemia

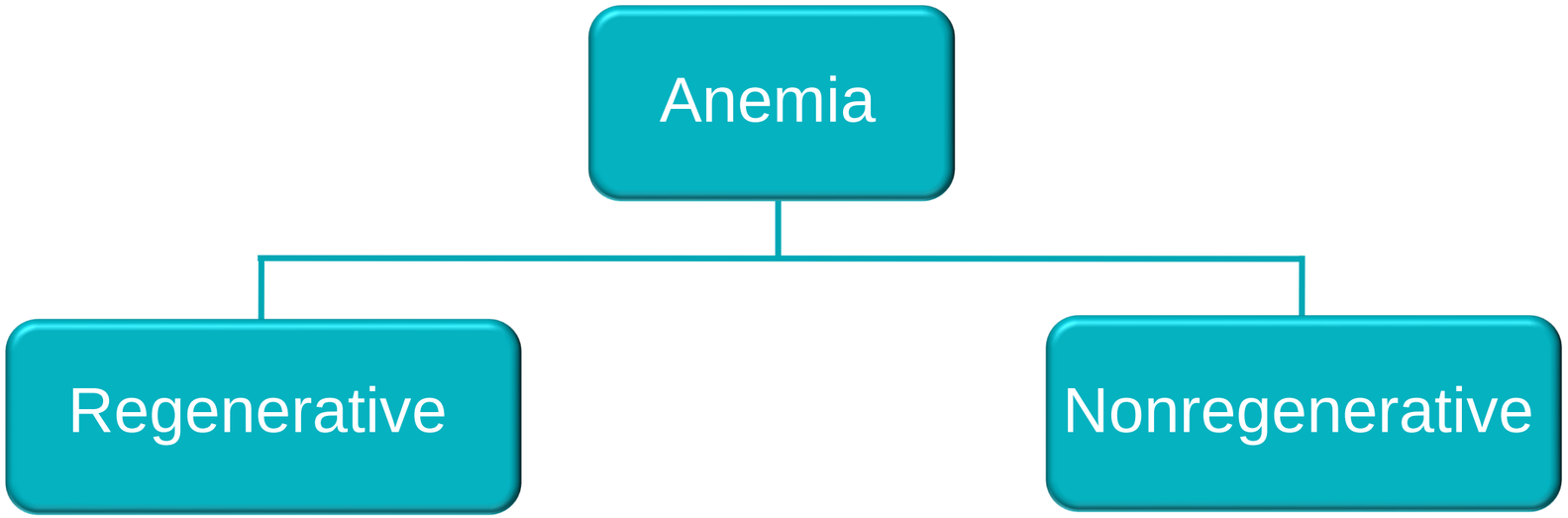


Prevalence of Inc MCV / Dec MCHC / Inc RDW with Regenerative Anemia



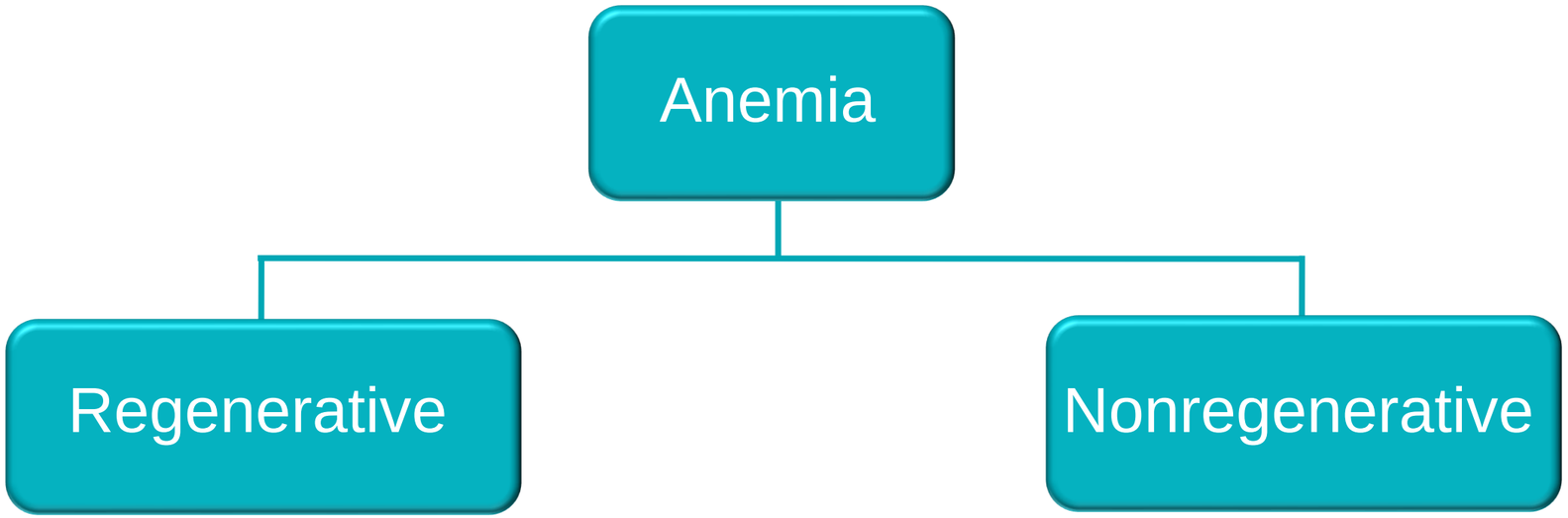
Conclusions regarding anemia characterization

- Absolute reticulocyte counts are ESSENTIAL for correct characterization of the anemia



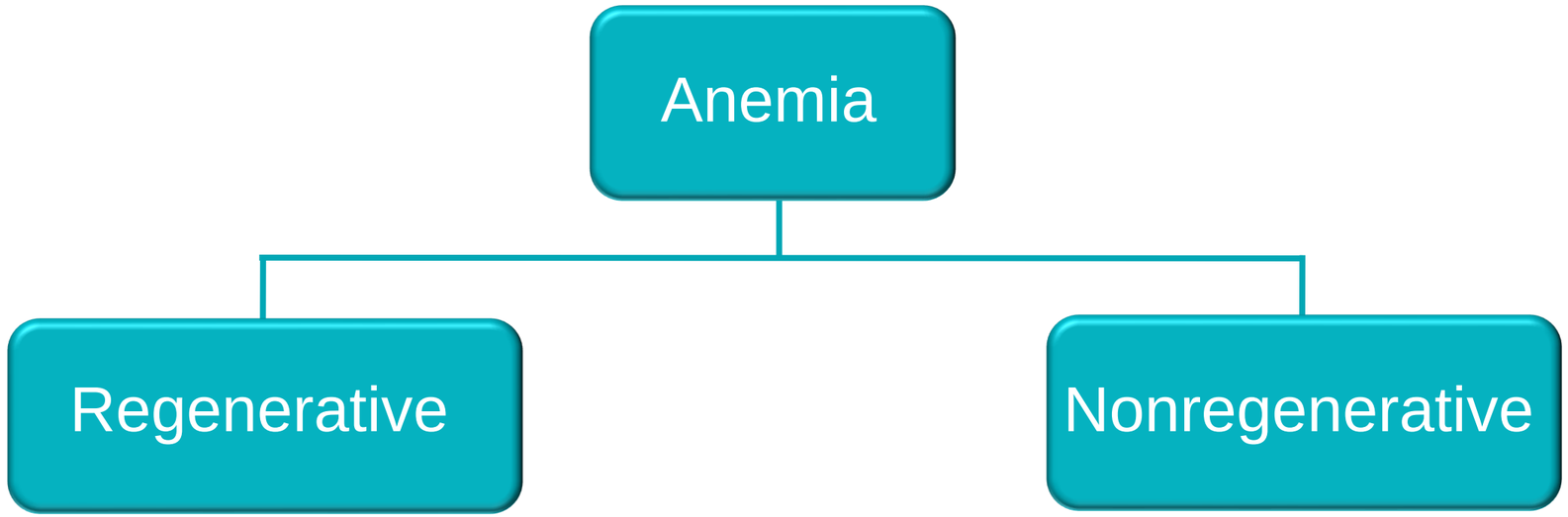
Conclusions regarding anemia characterization

- Absolute reticulocyte counts are ESSENTIAL for correct characterization of the anemia
- Standard RBC Indices (MCV, MCHC, RDW) have extreme low sensitivity and specificity



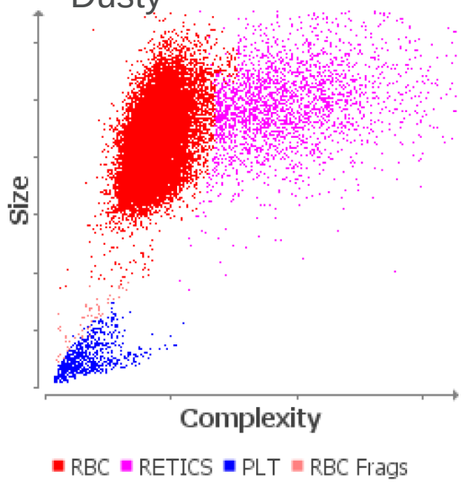
Conclusions regarding anemia characterization

- Absolute reticulocyte counts are ESSENTIAL for correct characterization of the anemia
- Standard RBC Indices (MCV, MCHC, RDW) have extreme low sensitivity and specificity
- What to do if your analyzer does not provide a reticulocyte count
  - Blood film is essential
  - Manual reticulocyte count may be needed

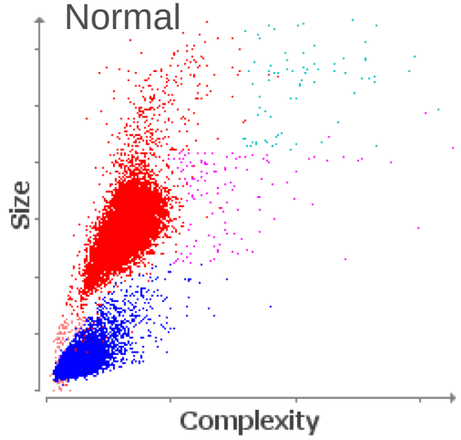


Molly – 11-year-old, Fs, Beagle-Mix

Dusty



Normal



Dot plot review

Good separation of cell types – trusted data

Molly – 11-year-old, Fs, Beagle-Mix

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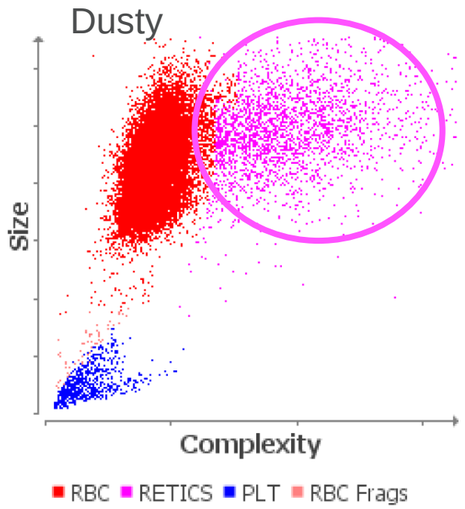

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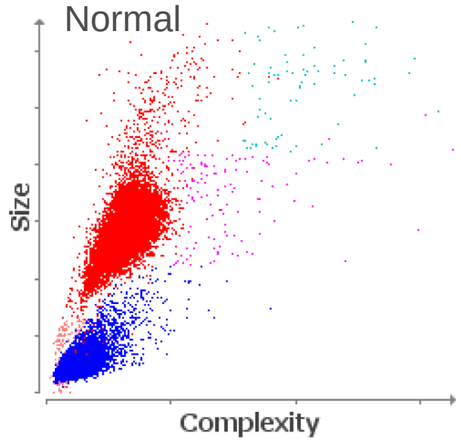

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- Marked increase in RETIC cluster

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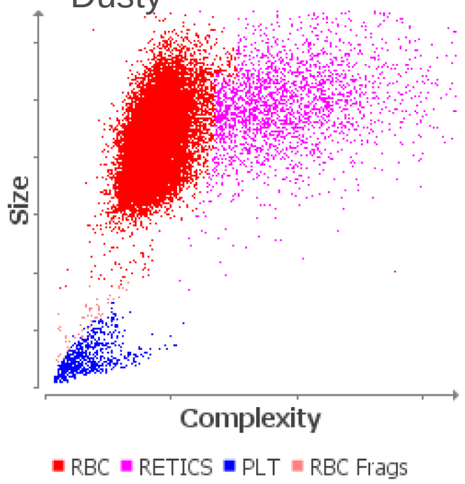
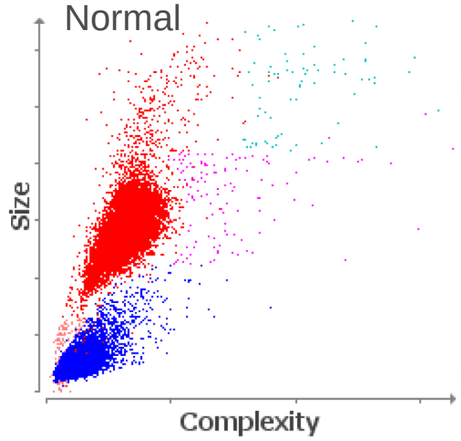


Normal



Dot plot review

- Good separation of cell types – trusted data
- Marked increase in RETIC cluster

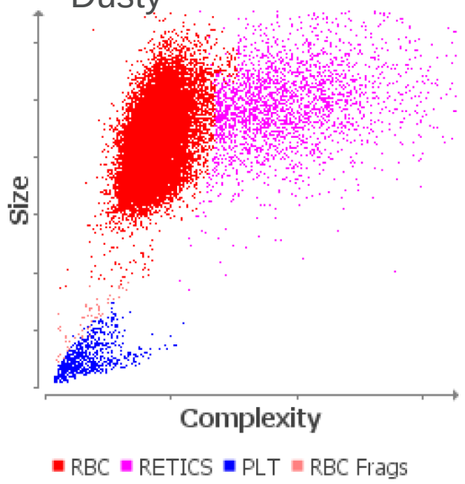
Data review

- Marked anemia with marked regeneration (RETIC)

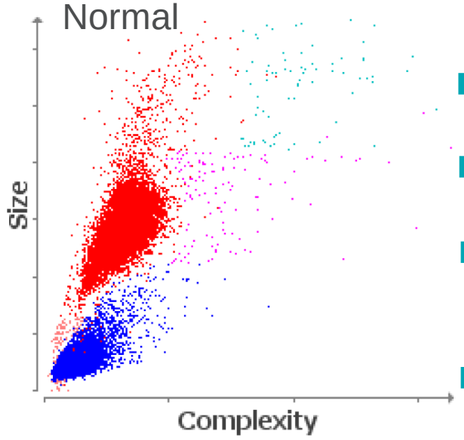
Test	Results	Reference Interval	LOW / NORMAL / HIGH
ProCyte One (July 7, 2021 3:05 PM)			
RBC	2.45 M/µL	5.65 - 8.87	LOW
HCT	18.9 %	37.3 - 61.7	LOW
HGB	3.4 g/dL	13.1 - 20.5	LOW
MCV	77.0 fL	61.6 - 73.5	HIGH
MCH	14.1 pg	21.2 - 25.9	LOW
MCHC	18.2 g/dL	32.0 - 37.9	LOW
RDW	11.3 %	13.6 - 21.7	LOW
%RETIC	17.0 %		
RETIC	416.6 K/µL	10.0 - 110.0	HIGH

Molly – 11-year-old, Fs, Beagle-Mix

Dusty



Normal



Dot plot review

- Good separation of cell types – trusted data
- Marked increase in RETIC cluster

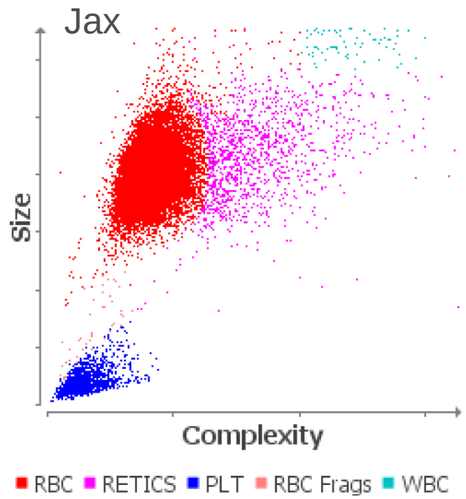
Data review

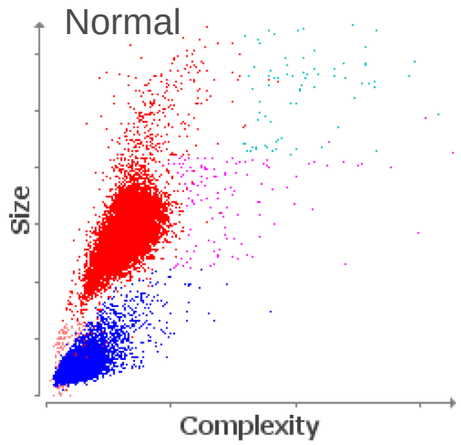
- Marked anemia with marked regeneration (RETIC)
- Classic (‘textbook’) RBC indices for ‘regenerative anemia’
  - Macrocytic – increased MCV
  - Hypochromic – decreased MCHC

ProCyte One (July 7, 2021 3:05 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	2.45 M/µL	5.65 - 8.87	LOW
HCT	18.9 %	37.3 - 61.7	LOW
HGB	3.4 g/dL	13.1 - 20.5	LOW
MCV	77.0 fL	61.6 - 73.5	HIGH
MCH	14.1 pg	21.2 - 25.9	LOW
MCHC	18.2 g/dL	32.0 - 37.9	LOW
RDW	11.3 %	13.6 - 21.7	LOW
%RETIC	17.0 %		
RETIC	416.6 K/µL	10.0 - 110.0	HIGH

Jax – 5-year-old, Mn, Boxer

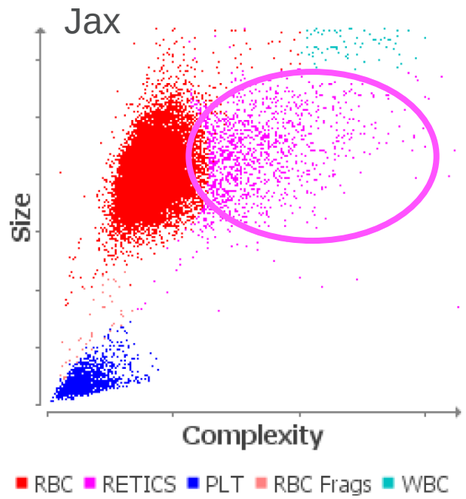


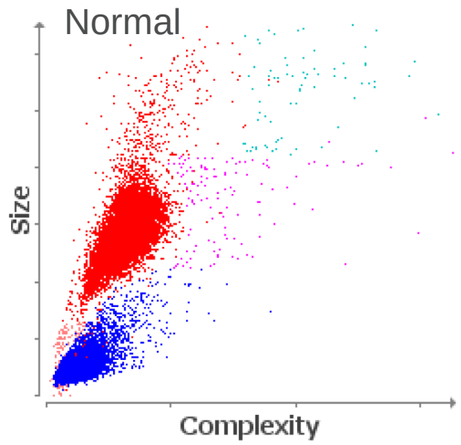


Dot plot review

Good separation of cell types – trusted data

Jax – 5-year-old, Mn, Boxer

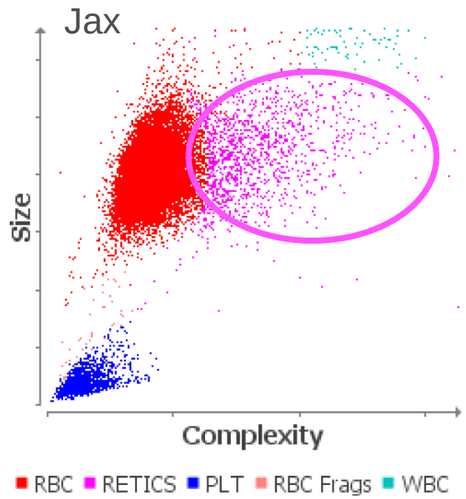


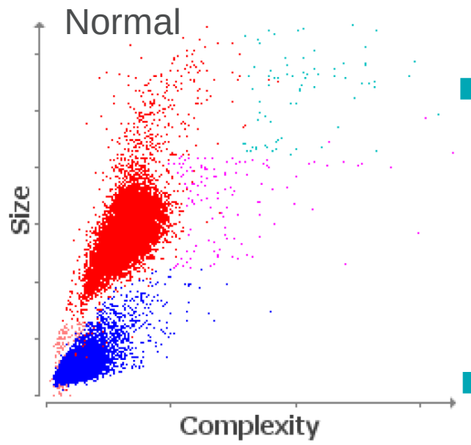


Dot plot review

- Good separation of cell types – trusted data
- Moderate increase in RETIC cluster

Jax – 5-year-old, Mn, Boxer





Dot plot review

- Good separation of cell types – trusted data
- Moderate increase in RETIC cluster

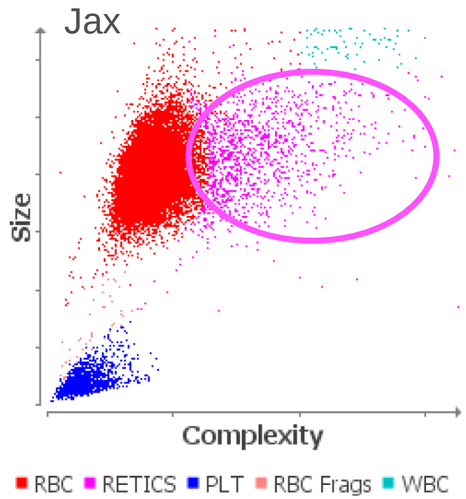
Data review

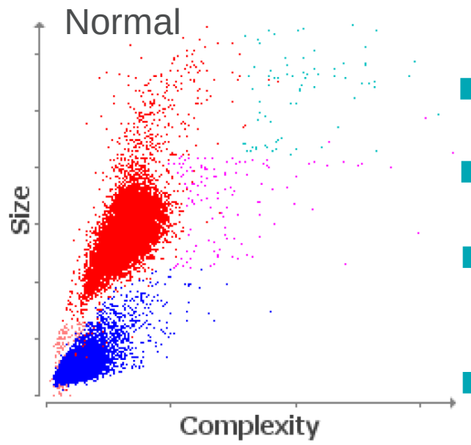
- Moderate anemia with Moderate regeneration (RETIC)

ProCyte One (August 3, 2021 12:51 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	3.07 M/µL	5.65 - 8.87	LOW
HCT	22.1 %	37.3 - 61.7	LOW
HGB	6.3 g/dL	13.1 - 20.5	LOW
MCV	72.1 fL	61.6 - 73.5	
MCH	20.4 pg	21.2 - 25.9	LOW
MCHC	28.3 g/dL	32.0 - 37.9	LOW
RDW	11.6 %	13.6 - 21.7	LOW
%RETIC	7.3 %		
RETIC	223.0 K/µL	10.0 - 110.0	HIGH

Jax – 5-year-old, Mn, Boxer





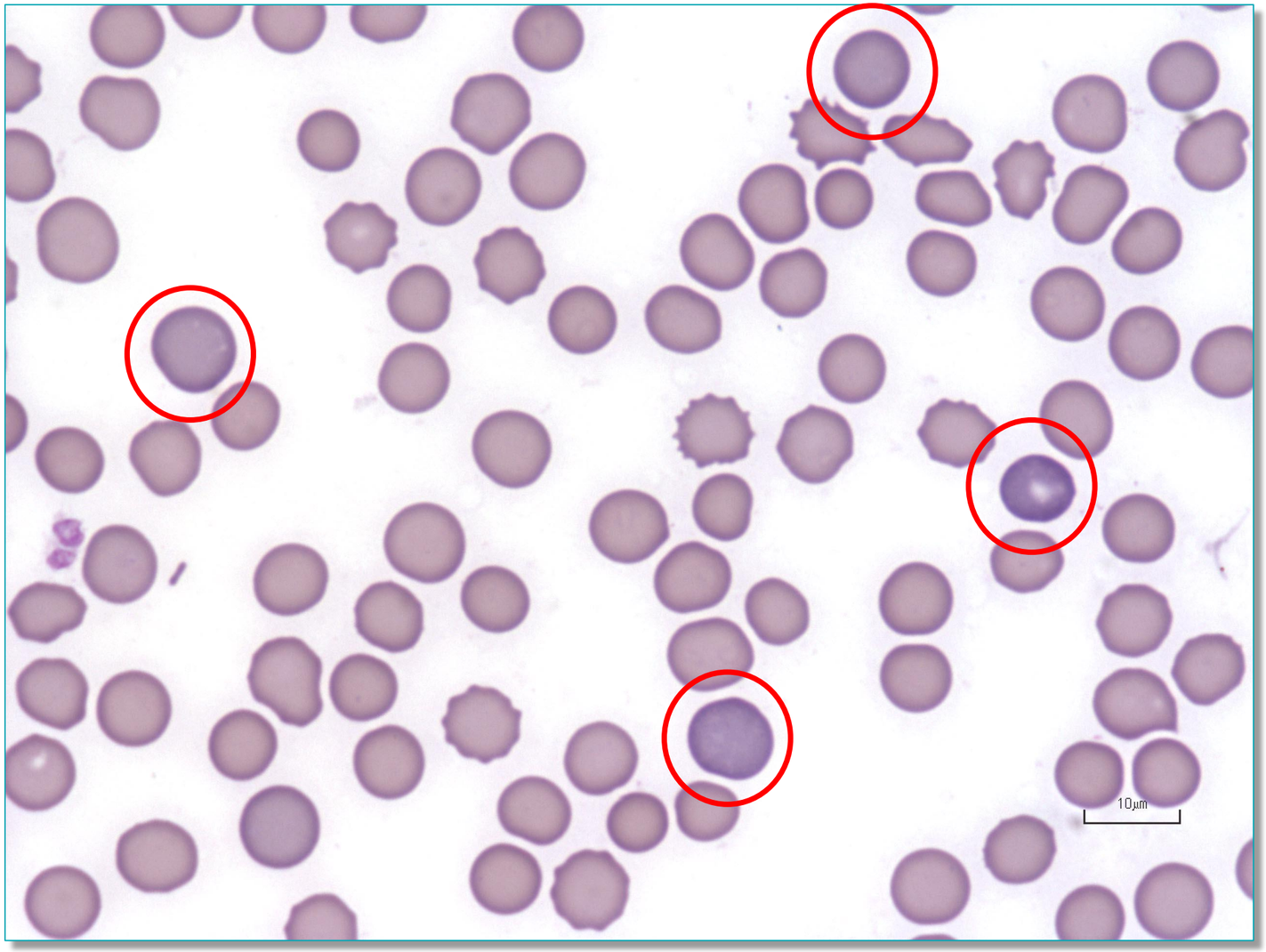
Dot plot review
- Good separation of cell types – trusted data
- Moderate increase in RETIC cluster

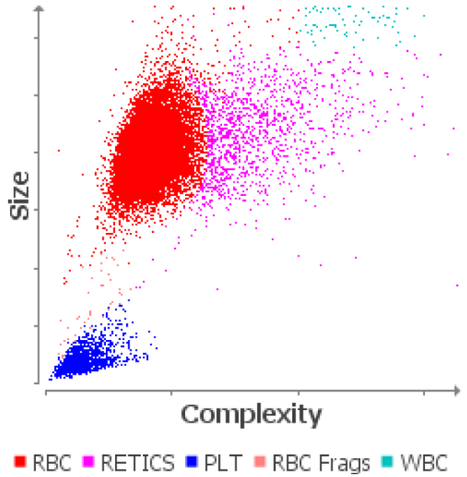
Data review
- Moderate anemia with Moderate regeneration (RETIC)
- Classic (‘textbook’) RBC indices for ‘regenerative anemia’ not evident
  - Normocytic – normal MCV
  - Hypochromic – decreased MCHC

ProCyte One (August 3, 2021 12:51 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	3.07 M/µL	5.65 - 8.87	LOW
HCT	22.1 %	37.3 - 61.7	LOW
HGB	6.3 g/dL	13.1 - 20.5	LOW
MCV	72.1 fL	61.6 - 73.5	
MCH	20.4 pg	21.2 - 25.9	LOW
MCHC	28.3 g/dL	32.0 - 37.9	LOW
RDW	11.6 %	13.6 - 21.7	LOW
%RETIC	7.3 %		
RETIC	223.0 K/µL	10.0 - 110.0	HIGH

Jax – 5-year-old, Mn, Boxer

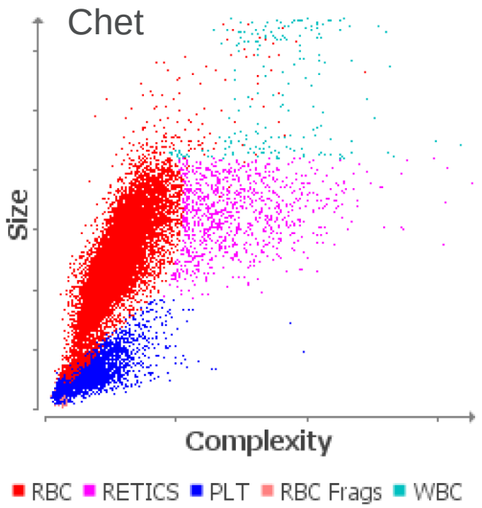


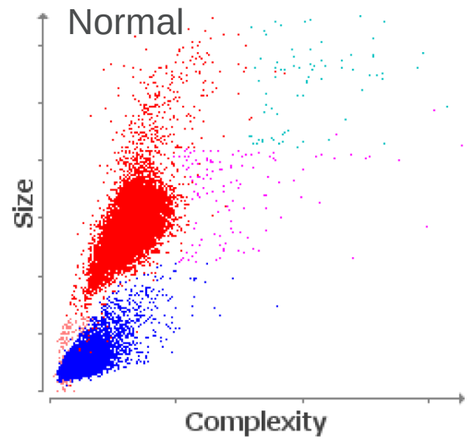


Easily identified polychromatophils
1-2 / 100x Oil Immersion FOV

Additional confirmation of reticulocytosis

Chet – 12-year-old, Mn, Domestic shorthair

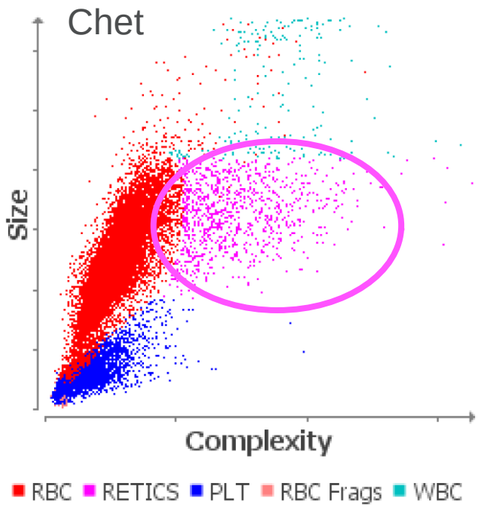


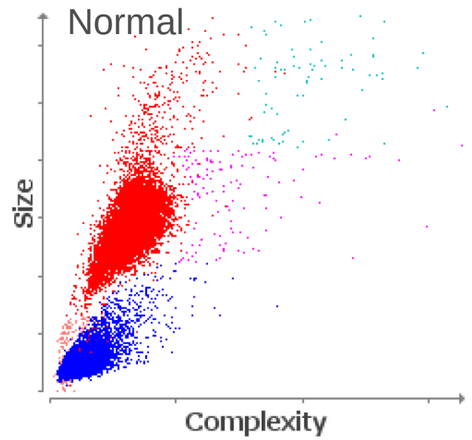


Dot plot review

Good separation of cell types – trusted data

Chet – 12-year-old, Mn, Domestic shorthair

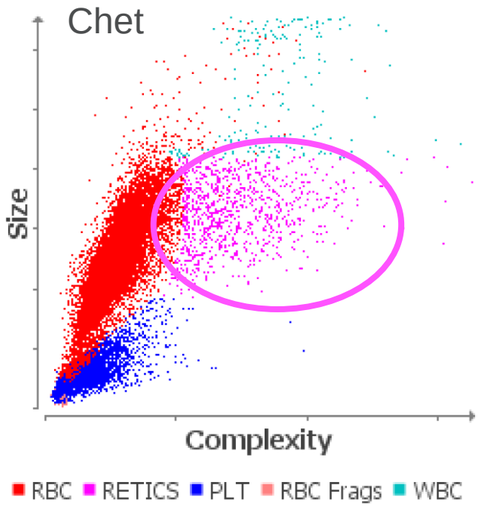


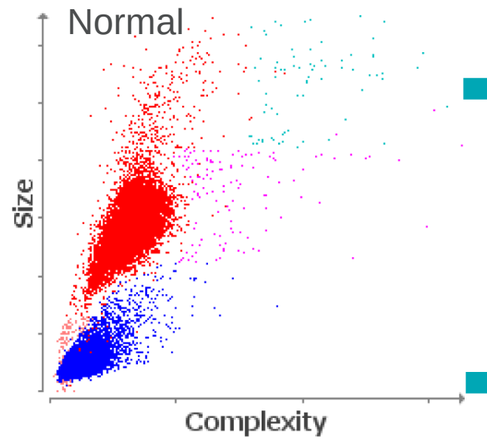


Dot plot review

- Good separation of cell types – trusted data
- Moderate to marked increase in RETIC cluster

Chet – 12-year-old, Mn, Domestic shorthair





Dot plot review

- Good separation of cell types – trusted data
- Moderate to marked increase in RETIC cluster

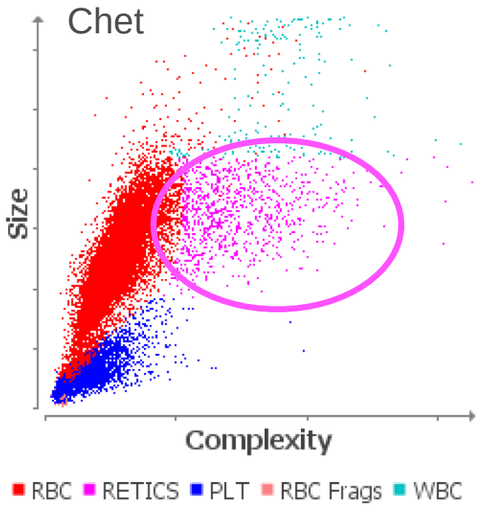
Data review

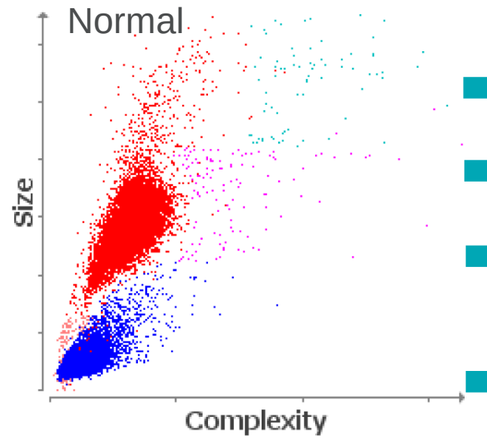
- Moderate anemia with Moderate regeneration (RETIC)

ProCyte One (July 8, 2021 4:52 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	* 3.29 M/µL	6.54 - 12.20	LOW
HCT	* 13.4 %	30.3 - 52.3	LOW
HGB	1.7 g/dL	9.8 - 16.2	LOW
MCV	* 40.7 fL	35.9 - 53.1	
MCH	* 5.1 pg	11.8 - 17.3	LOW
MCHC	* 12.4 g/dL	28.1 - 35.8	LOW
RDW	* 21.6 %	15.0 - 27.0	
%RETIC	* 5.5 %		
RETIC	* 179.3 K/µL	3.0 - 50.0	HIGH

Chet – 12-year-old, Mn, Domestic shorthair





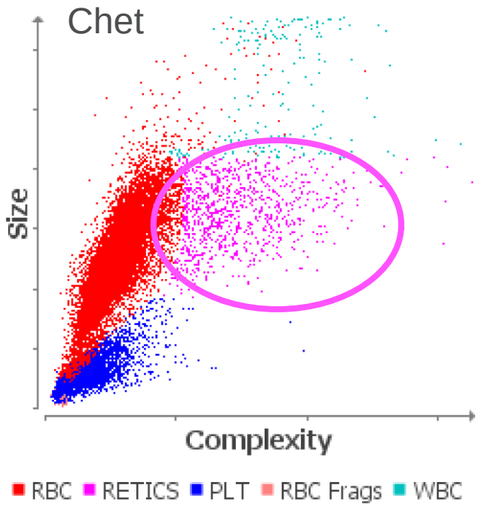
Dot plot review
- Good separation of cell types – trusted data
- Moderate to marked increase in RETIC cluster

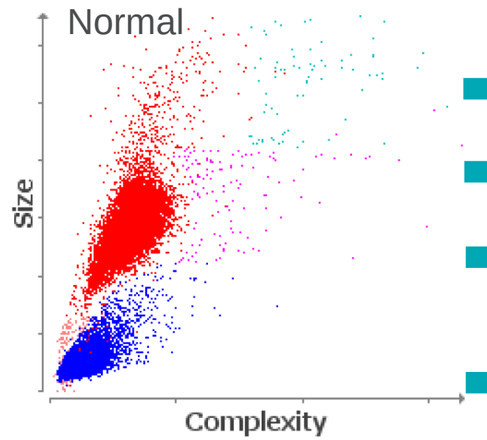
Data review
- Moderate anemia with Moderate regeneration (RETIC)
- Classic (‘textbook’) RBC indices for ‘regenerative anemia’ not evident
  - Normocytic – normal MCV
  - Hypochromic – decreased MCHC

ProCyte One (July 8, 2021 4:52 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	* 3.29 M/µL	6.54 - 12.20	LOW
HCT	* 13.4 %	30.3 - 52.3	LOW
HGB	* 1.7 g/dL	9.8 - 16.2	LOW
MCV	* 40.7 fL	35.9 - 53.1	
MCH	* 5.1 pg	11.8 - 17.3	LOW
MCHC	* 12.4 g/dL	28.1 - 35.8	LOW
RDW	* 21.6 %	15.0 - 27.0	
%RETIC	* 5.5 %		
RETIC	* 179.3 K/µL	3.0 - 50.0	HIGH

Chet – 12-year-old, Mn, Domestic shorthair





Dot plot review
- Good separation of cell types – trusted data
- Moderate to marked increase in RETIC cluster

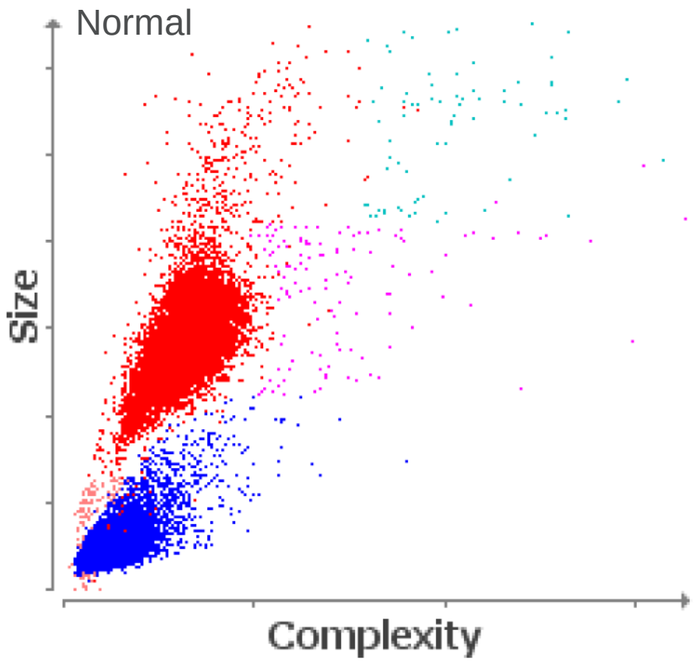
Data review
- Moderate anemia with Moderate regeneration (RETIC)
- Classic ('textbook') RBC indices for 'regenerative anemia' not evident
  - Normocytic – normal MCV
  - Hypochromic – decreased MCHC

NOTE – Many results are qualified (*)

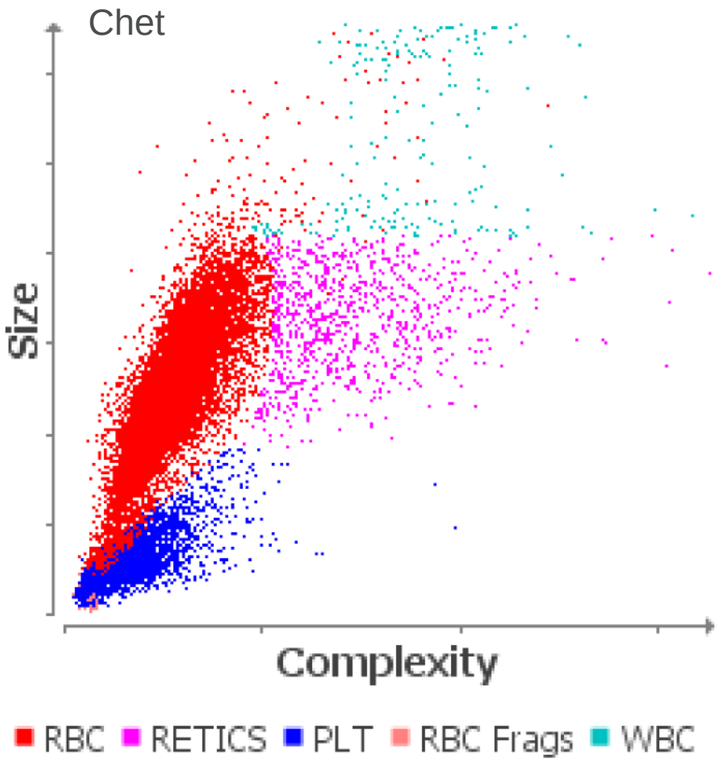
ProCyte One (July 8, 2021 4:52 PM)

Test	Results	Reference Interval	LOW / NORMAL / HIGH
RBC	* 3.29 M/µL	6.54 - 12.20	LOW
HCT	* 13.4 %	30.3 - 52.3	LOW
HGB	1.7 g/dL	9.8 - 16.2	LOW
MCV	* 40.7 fL	35.9 - 53.1	
MCH	* 5.1 pg	11.8 - 17.3	LOW
MCHC	* 12.4 g/dL	28.1 - 35.8	LOW
RDW	* 21.6 %	15.0 - 27.0	
%RETIC	* 5.5 %		
RETIC	* 179.3 K/µL	3.0 - 50.0	HIGH

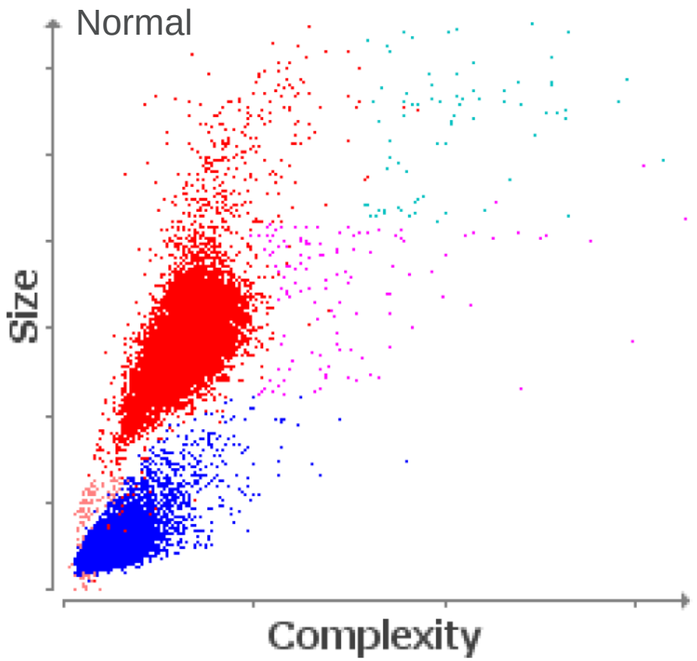
Chet – 12-year-old, Mn, Domestic shorthair



Abnormal RBC cluster shape

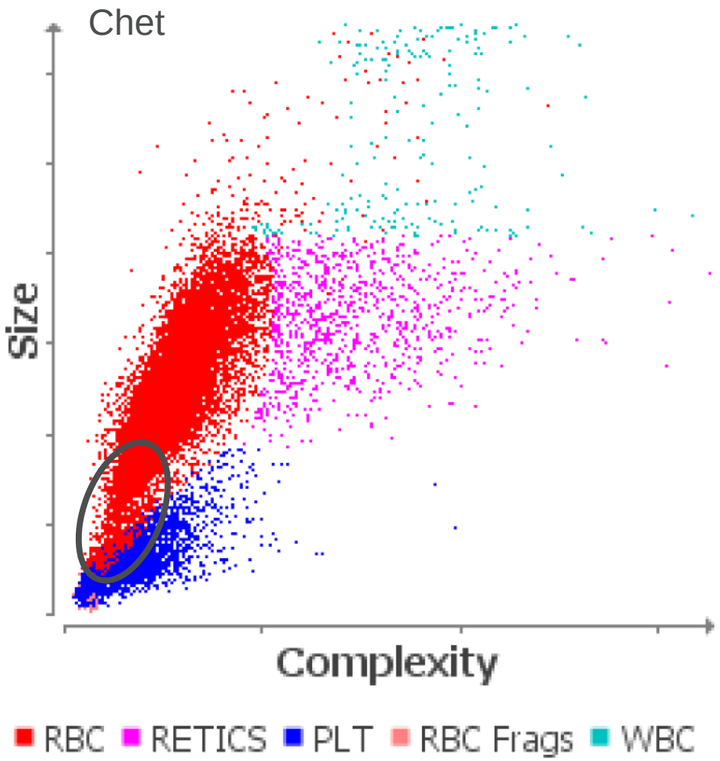


Chet – 12-year-old, Mn, Domestic shorthair

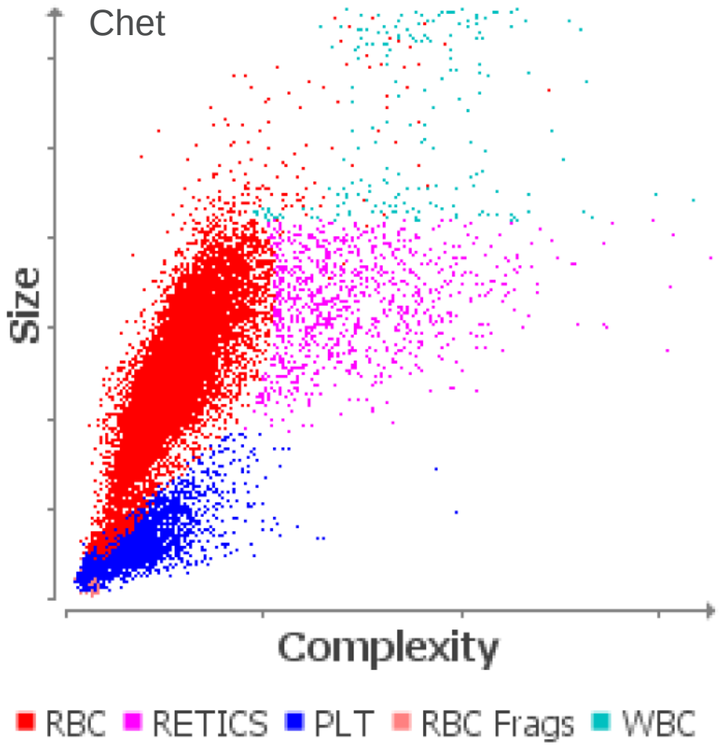


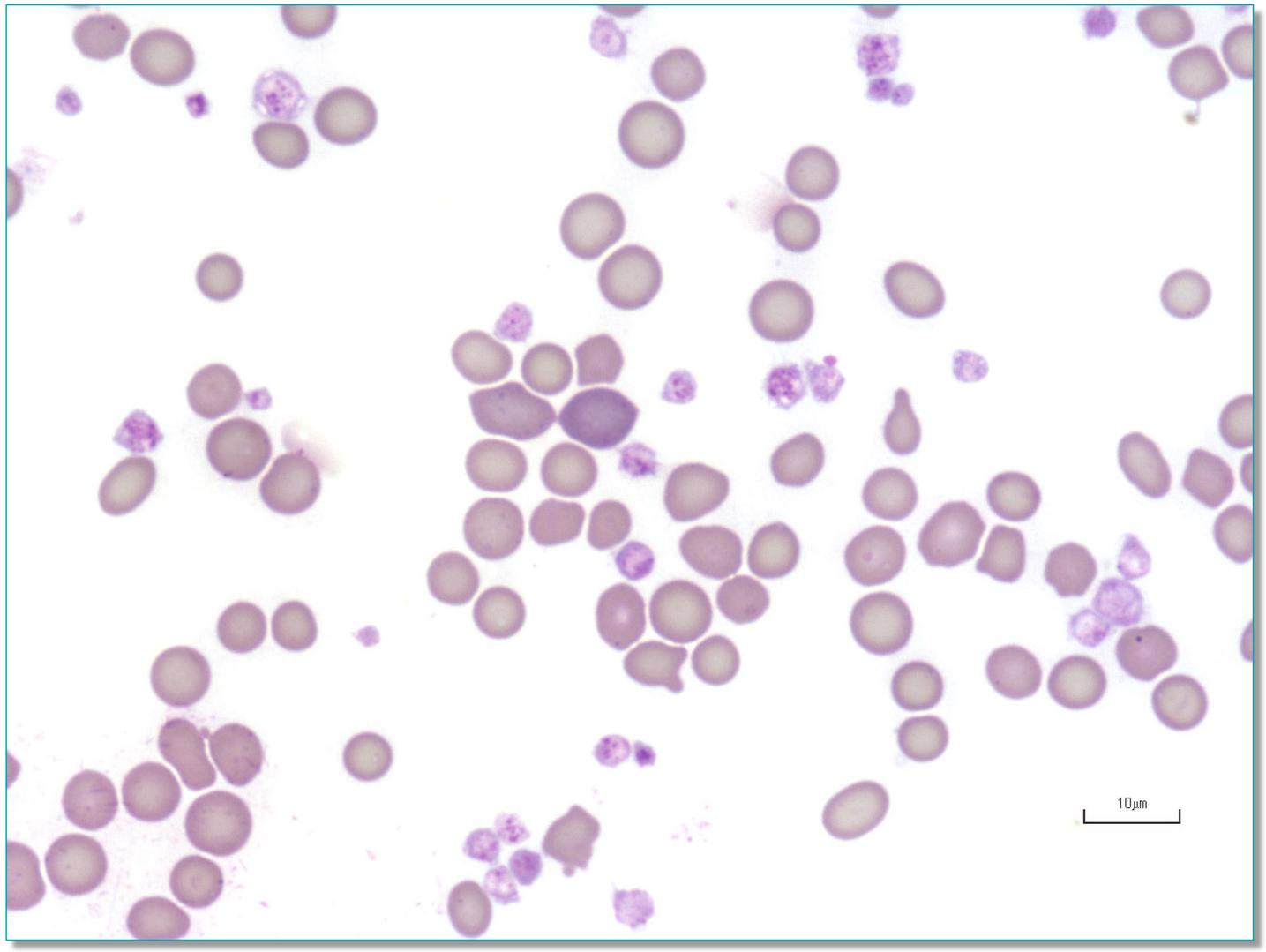
Abnormal RBC cluster shape

Many small (and pathologic) RBCs

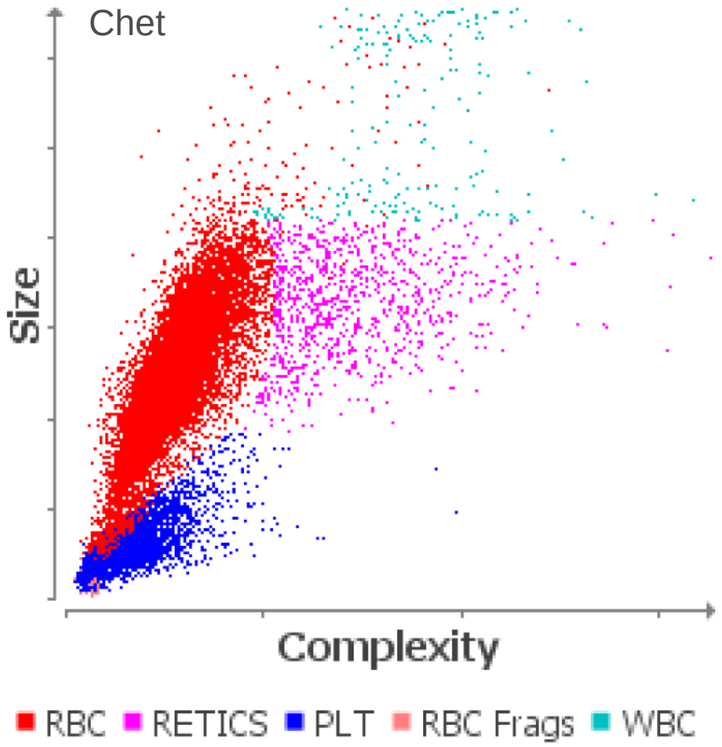


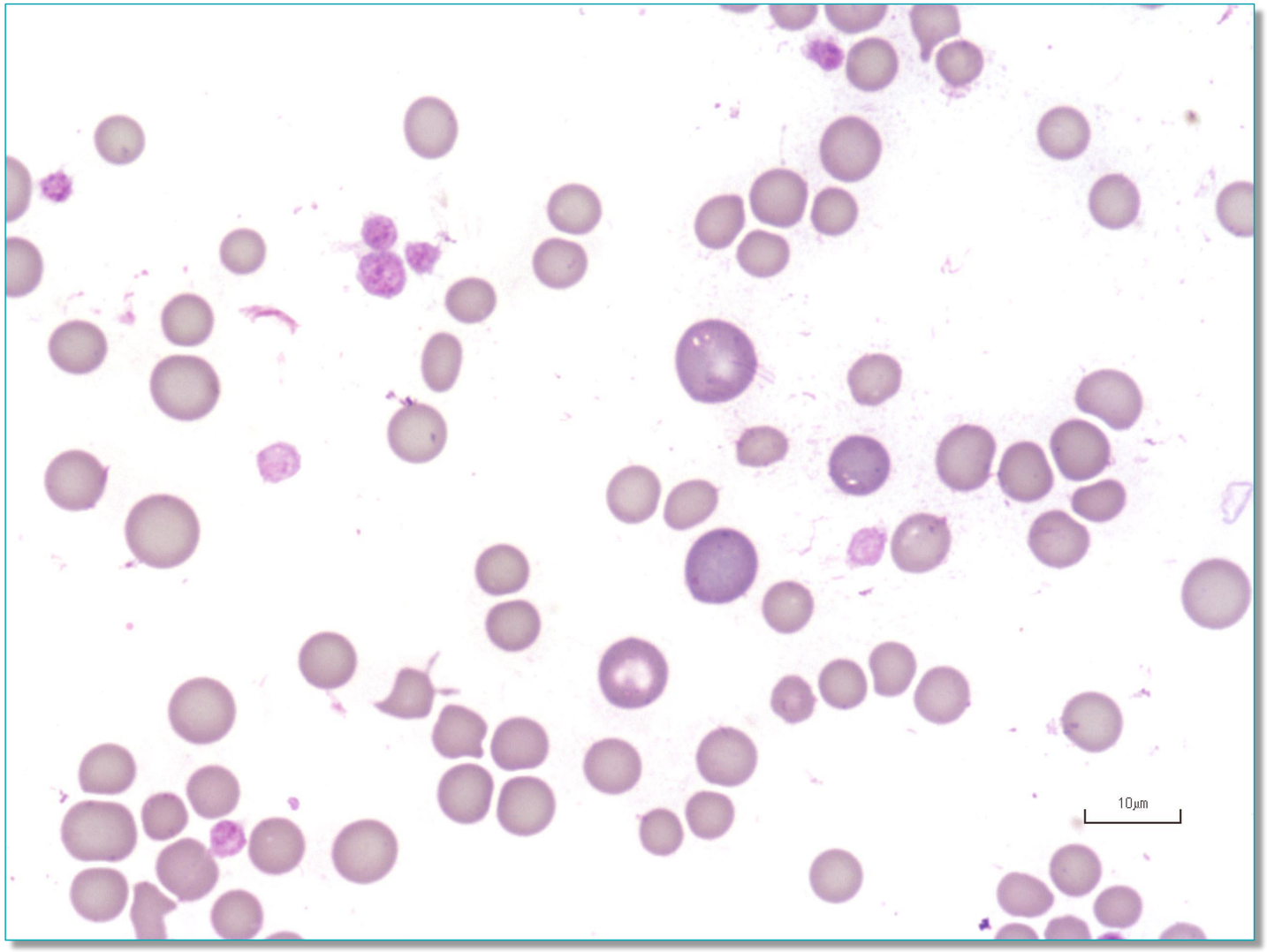
Chet – 12-year-old, Mn, Domestic shorthair



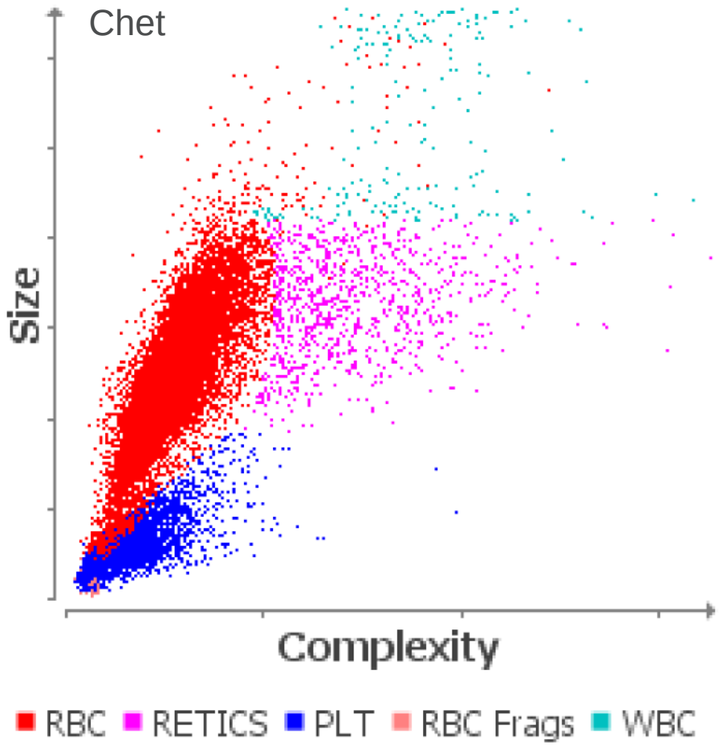


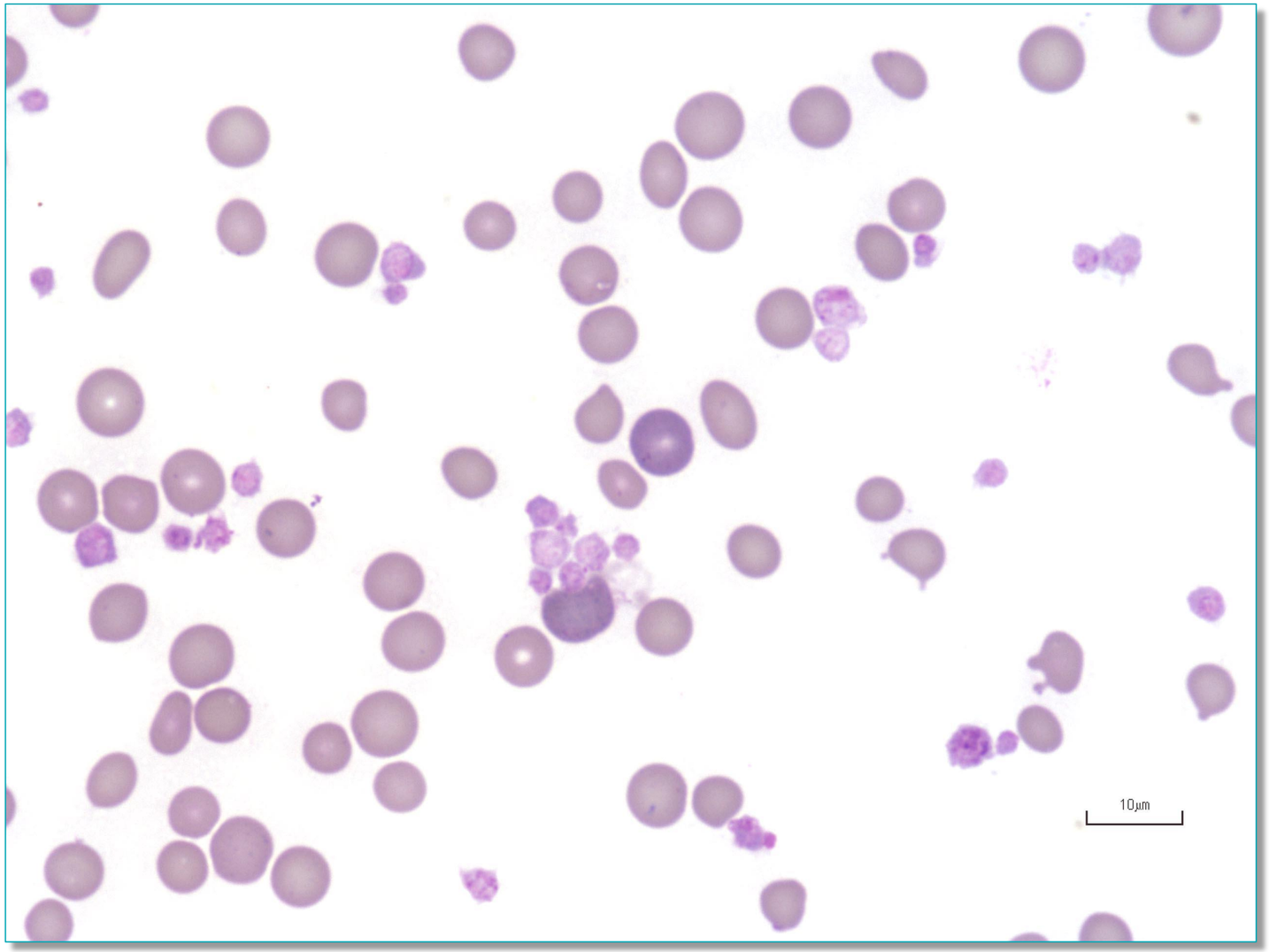
Chet – 12-year-old, Mn, Domestic shorthair



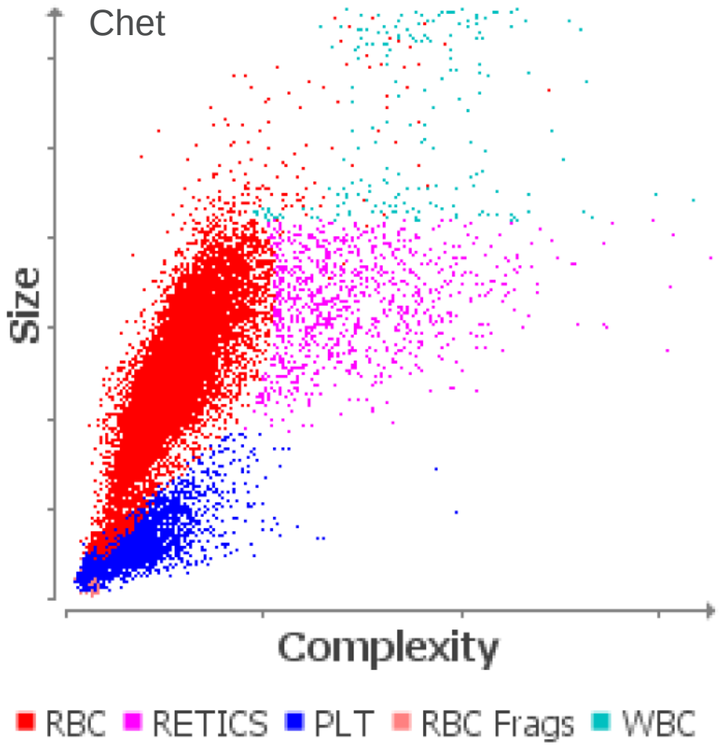


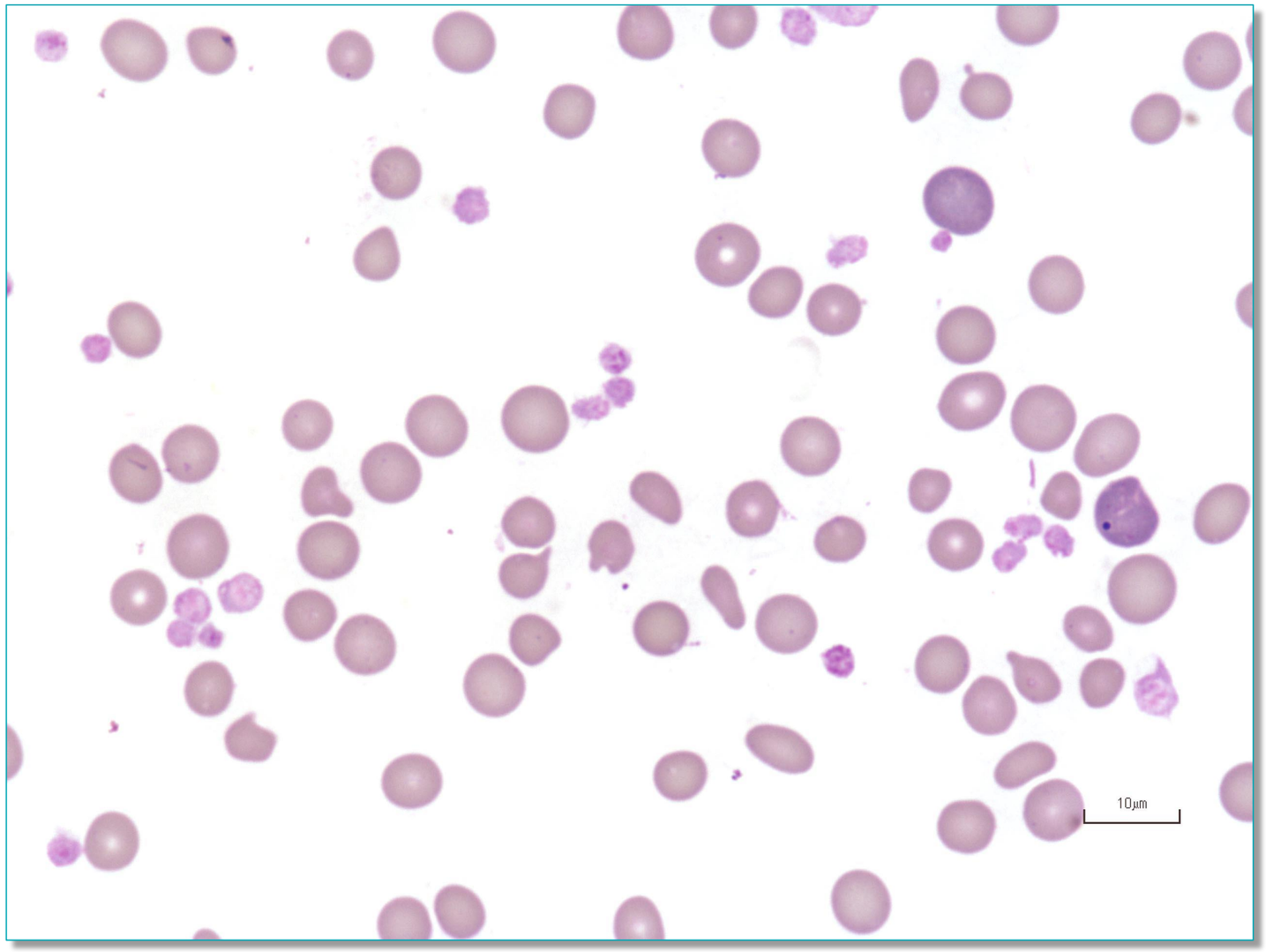
Chet – 12-year-old, Mn, Domestic shorthair





Chet – 12-year-old, Mn, Domestic shorthair

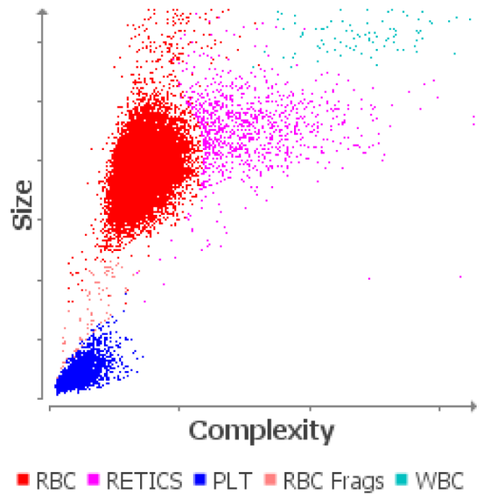




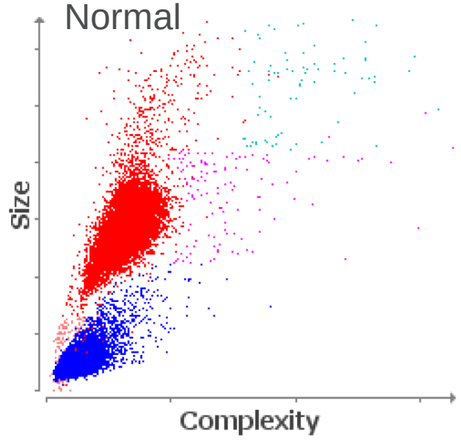
Value of Reticulocytes in the Non-Anemic Patient

Merone – 1-year-old, F, Mixed breed dog

Merone



Normal

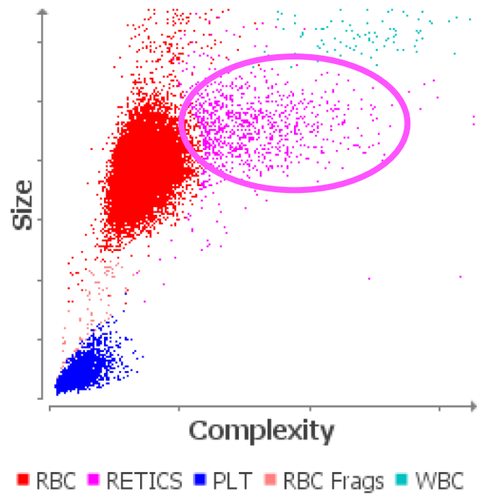


Dot plot review

Good separation of cell types – trusted data

Merone – 1-year-old, F, Mixed breed dog

Merone



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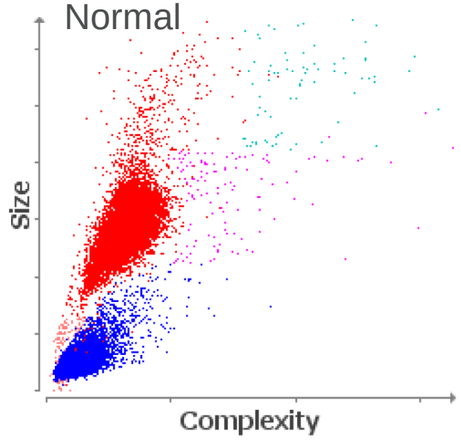
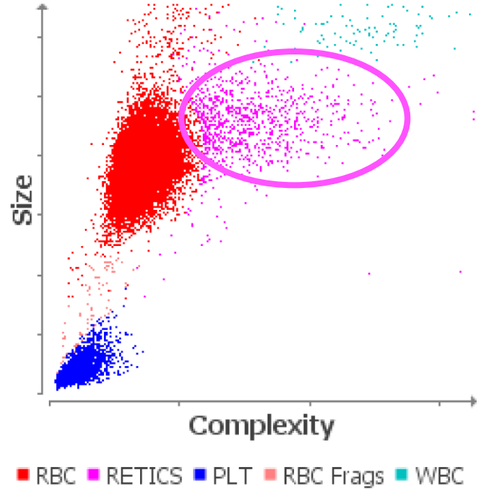


Dot plot review

- Good separation of cell types – trusted data
- Mild to moderate increase in RETIC cluster

Merone – 1-year-old, F, Mixed breed dog

Merone



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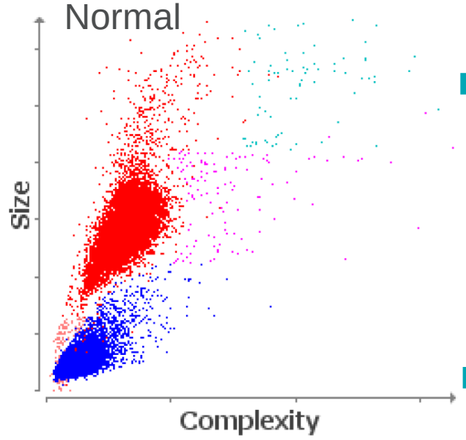


Dot plot review

- Good separation of cell types – trusted data
- Mild to moderate increase in RETIC cluster

Data review

- Reticulocytosis without anemia

Test	Results	Reference Interval		LOW NORMAL HIGH
ProCyte One (July 9, 2021 10:28 AM)				
RBC	7.11 M/µL	5.65 - 8.87		
HCT	48.0 %	37.3 - 61.7		
HGB	13.6 g/dL	13.1 - 20.5		
MCV	67.6 fL	61.6 - 73.5		
MCH	19.1 pg	21.2 - 25.9	LOW	
MCHC	28.2 g/dL	32.0 - 37.9	LOW	
RDW	19.6 %	13.6 - 21.7		
%RETIC	2.2 %			
RETIC	155.4 K/µL	10.0 - 110.0	HIGH	

“Slightly” Outside RI Limits – How much of a change is significant

- How often will this occur?
- How do I define “slightly”?
  - ± 2 SD = 95.44% of clinically normal animals
  - ± 3 SD = 99.64% of clinically normal animals
  - Add and subtract 1 SD to and from the upper and lower RI limits
- How do I determine 1 SD?

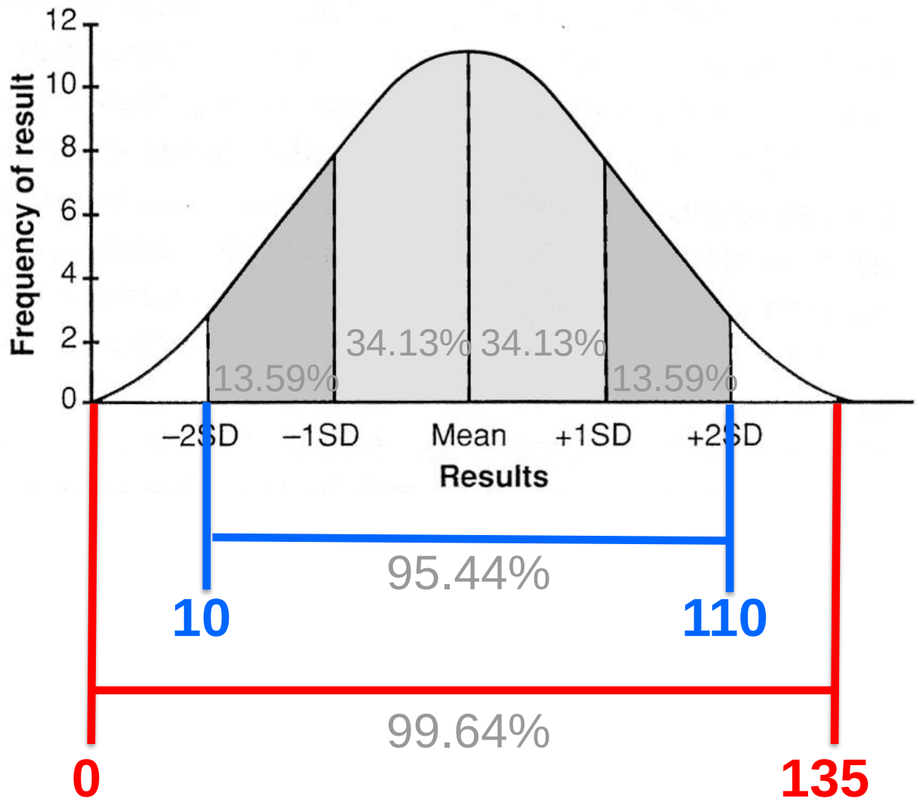
  1 SD = (Upper RI limit – Lower RI limit) ÷ 4

Example: RI for RETIC is 10 – 110 U/L (canine)

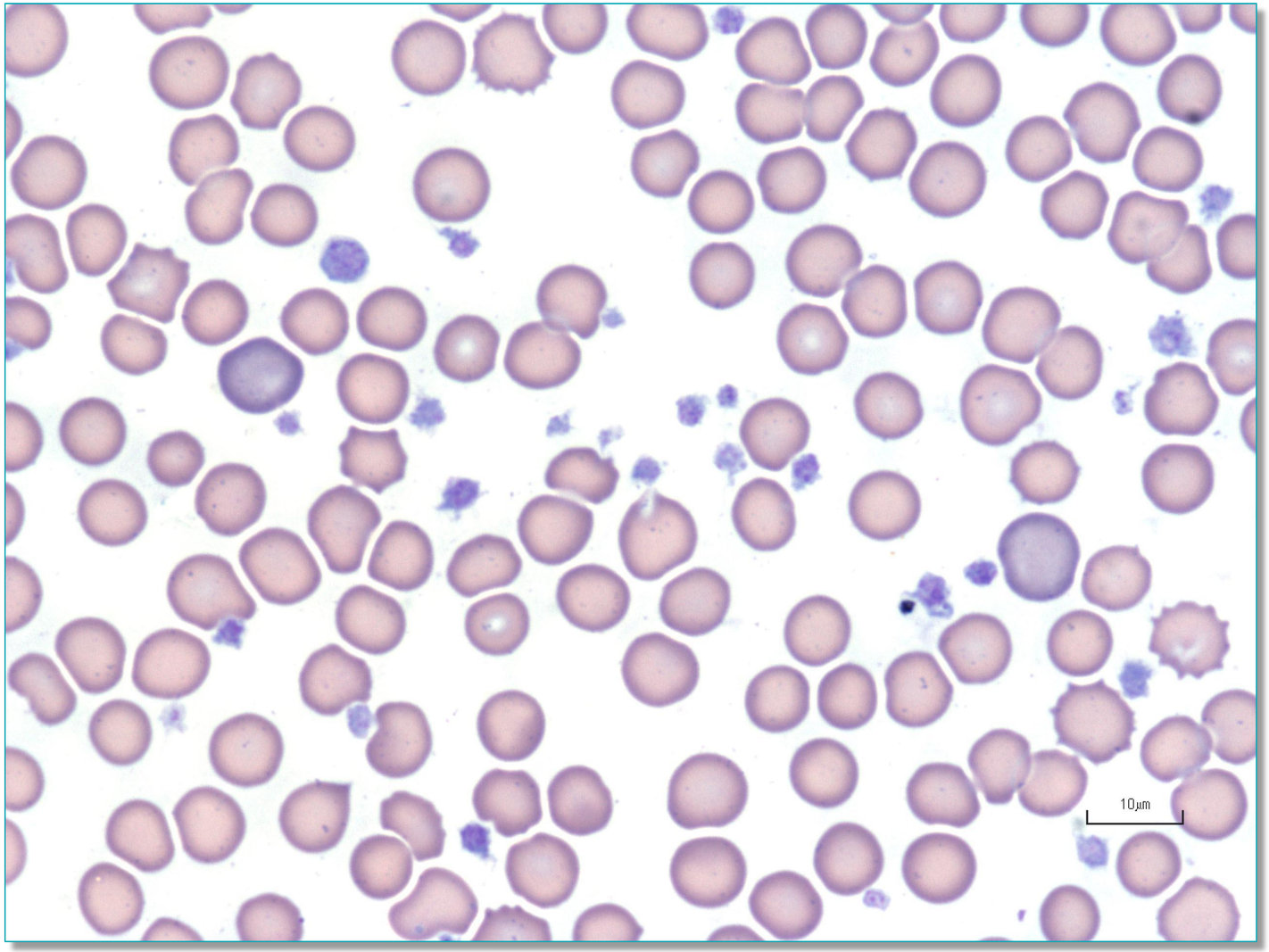
(110 – 10) = 100

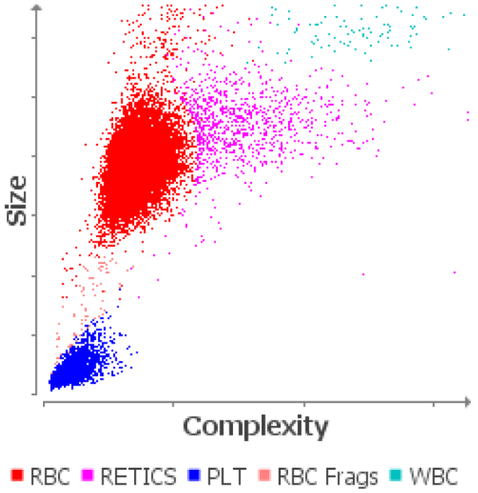
(100 ÷ 4) = 25

1 SD = 25 U/L



Merone – 1-year-old, F, Mixed breed dog





Easily identified polychromatophils
1-2 / 100x Oil Immersion FOV

Additional confirmation of reticulocytosis

Suspect spherocytosis but no obvious significant morphologic abnormalities

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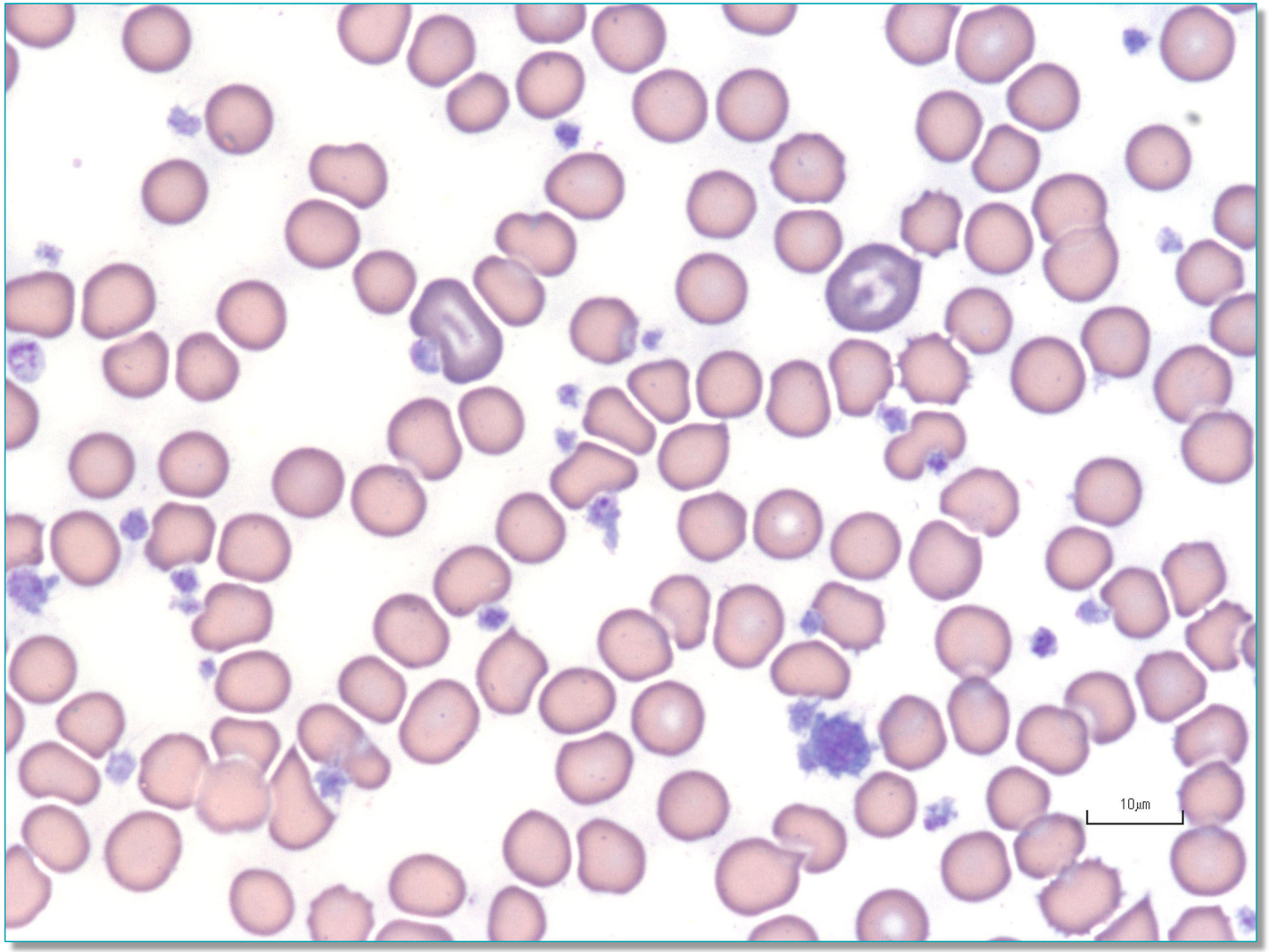

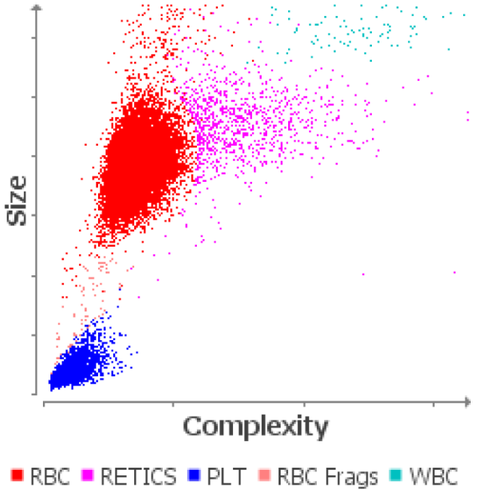

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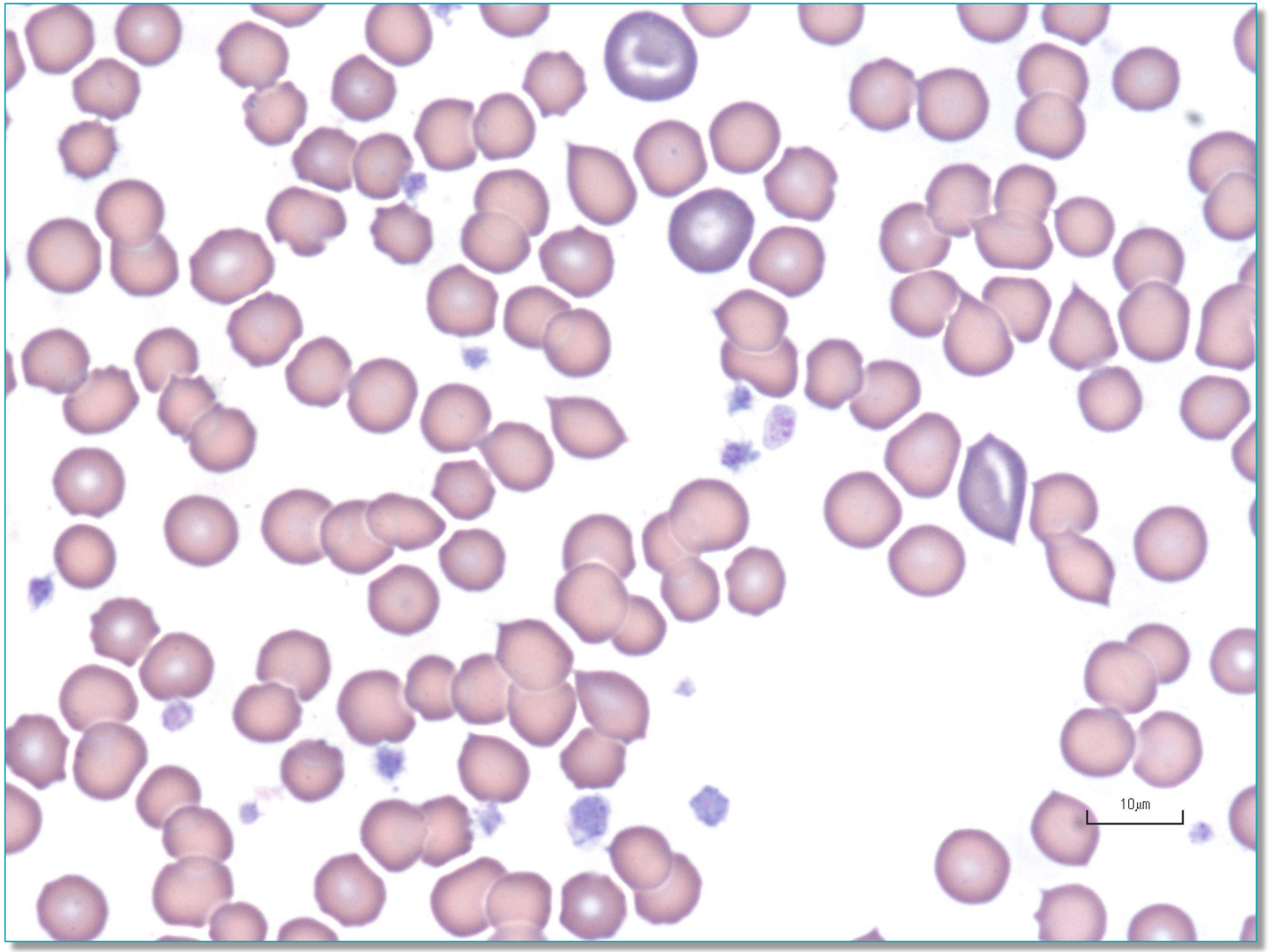

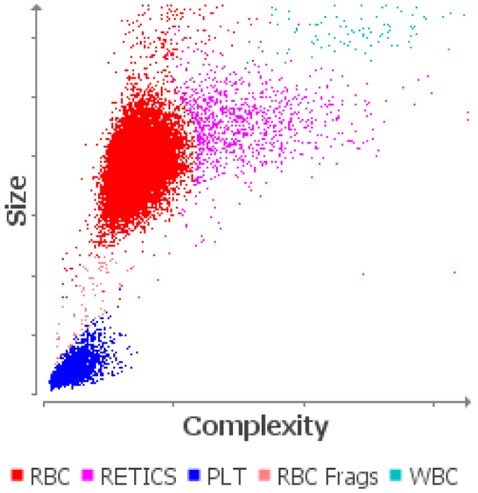

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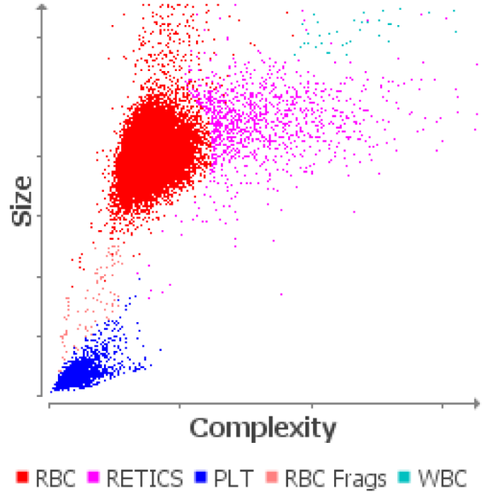
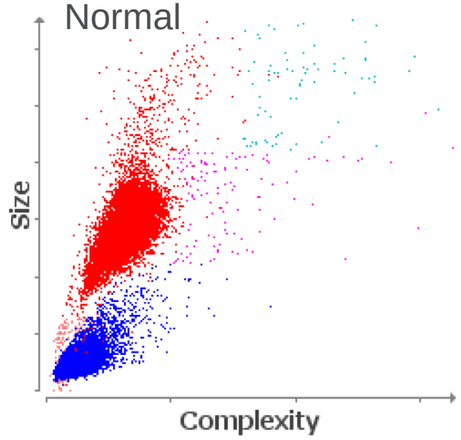
Finlee – 3-year-old, F, Mixed breed dog

Finlee



Normal

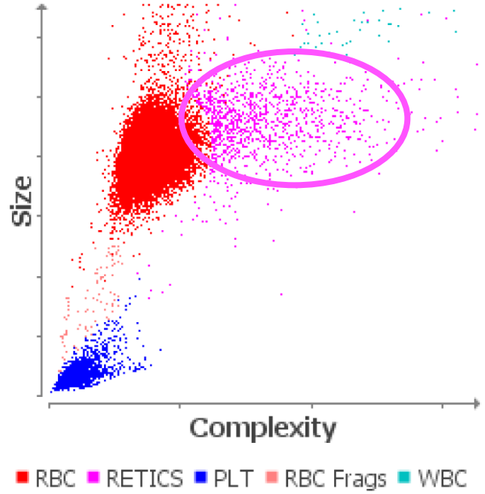


Dot plot review

Good separation of cell types – trusted data

Finlee – 3-year-old, F, Mixed breed dog

Finlee



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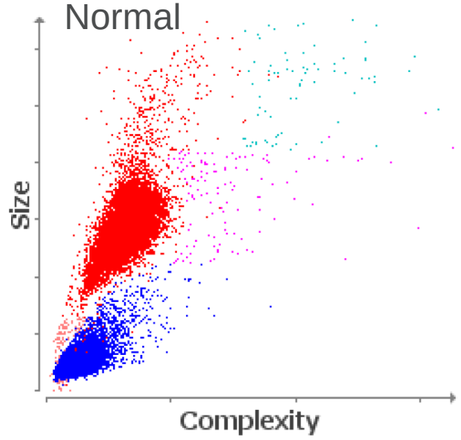

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- Good separation of cell types – trusted data
- Mild to moderate increase in RETIC cluster

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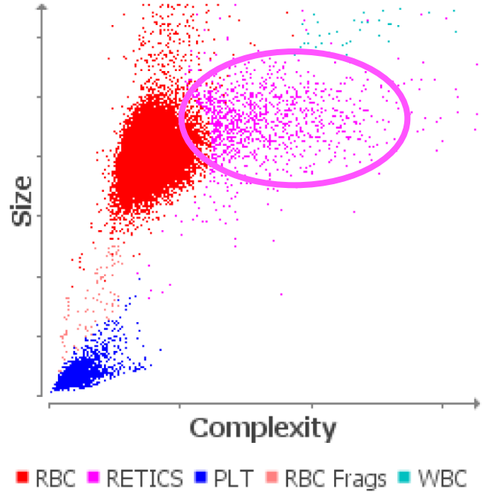

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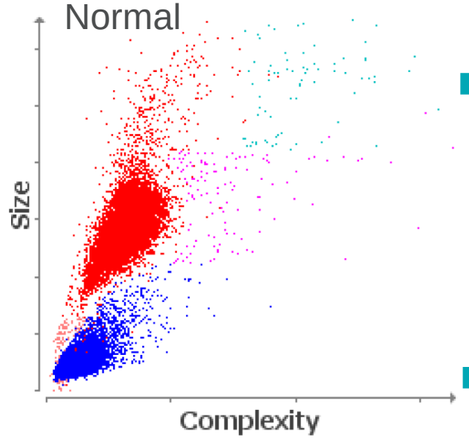

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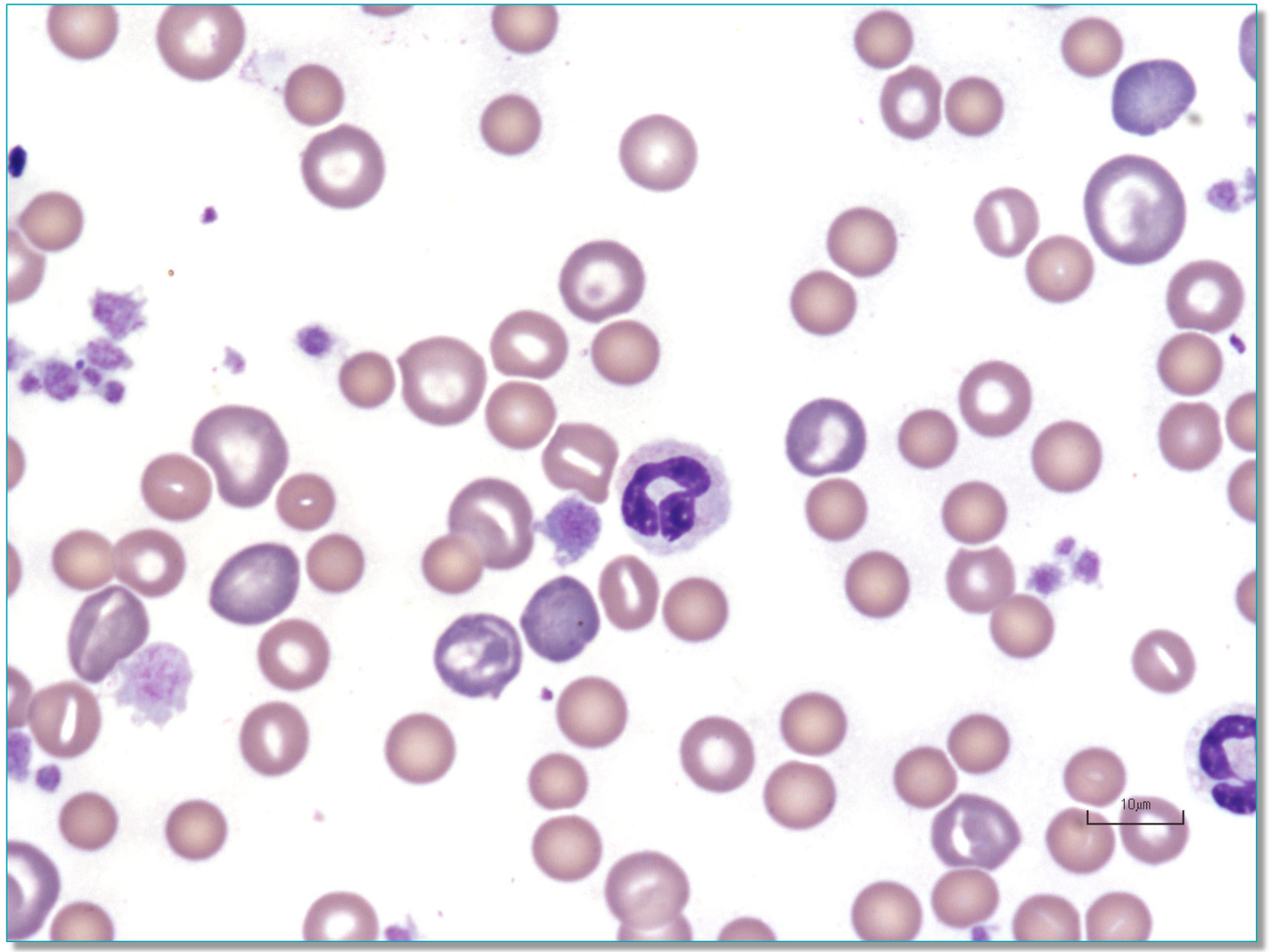
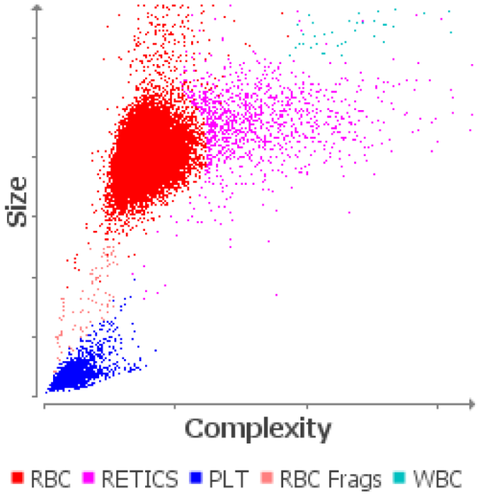
Data review

- Reticulocytosis without anemia

Test	Results	Reference Interval		LOW NORMAL HIGH
ProCyte One (July 9, 2021 10:28 AM)				
RBC	7.11 M/µL	5.65 - 8.87		
HCT	48.0 %	37.3 - 61.7		
HGB	13.6 g/dL	13.1 - 20.5		
MCV	67.6 fL	61.6 - 73.5		
MCH	19.1 pg	21.2 - 25.9	LOW	
MCHC	28.2 g/dL	32.0 - 37.9	LOW	
RDW	19.6 %	13.6 - 21.7		
%RETIC	2.2 %			
RETIC	155.4 K/µL	10.0 - 110.0	HIGH	

Finlee – 3-year-old, F, Mixed breed dog





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Additional confirmation of reticulocytosis

Spherocytosis supporting immune-mediated extravascular destruction

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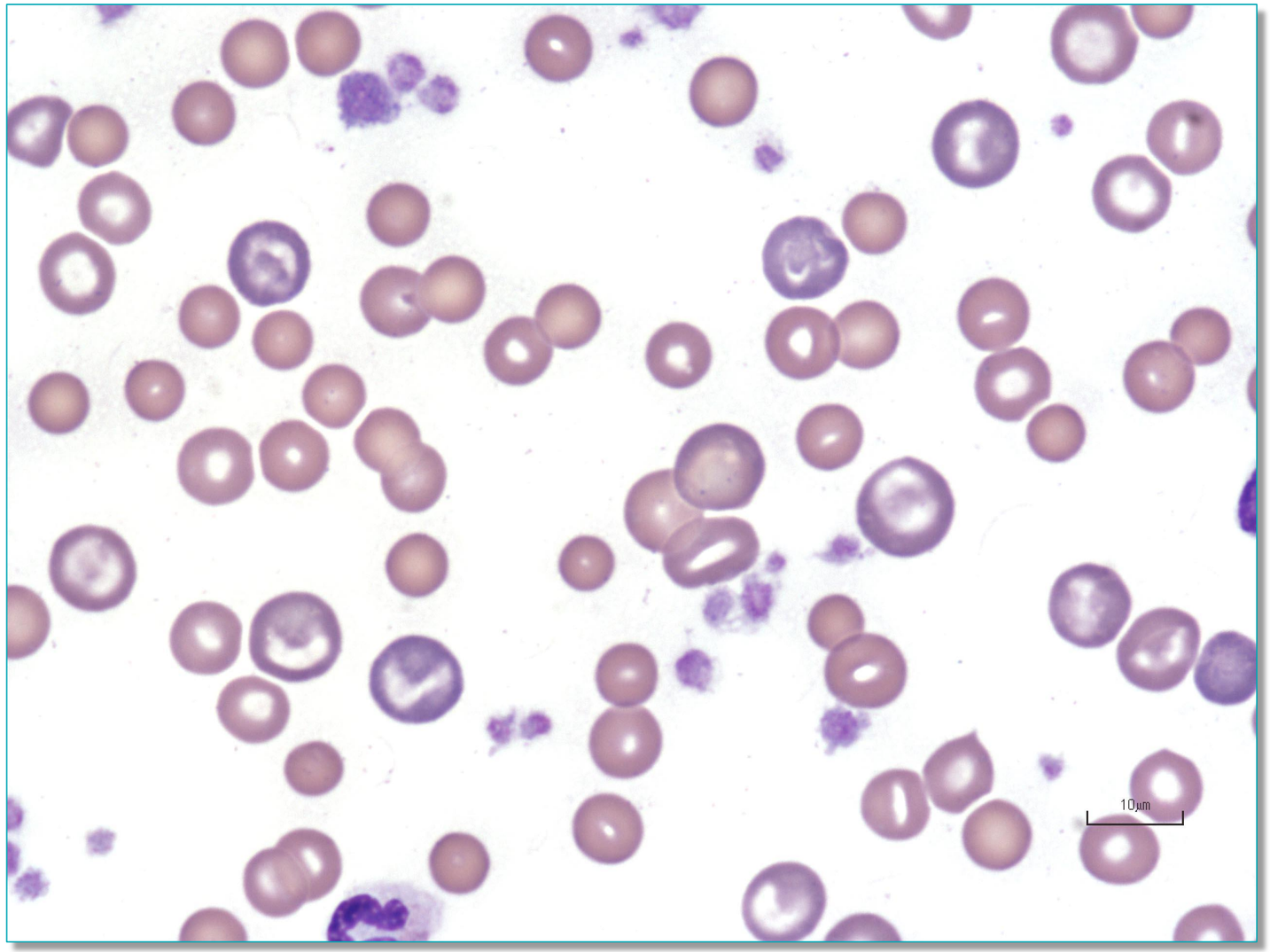

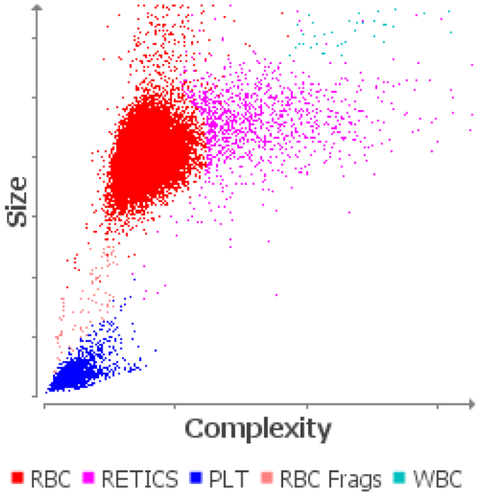

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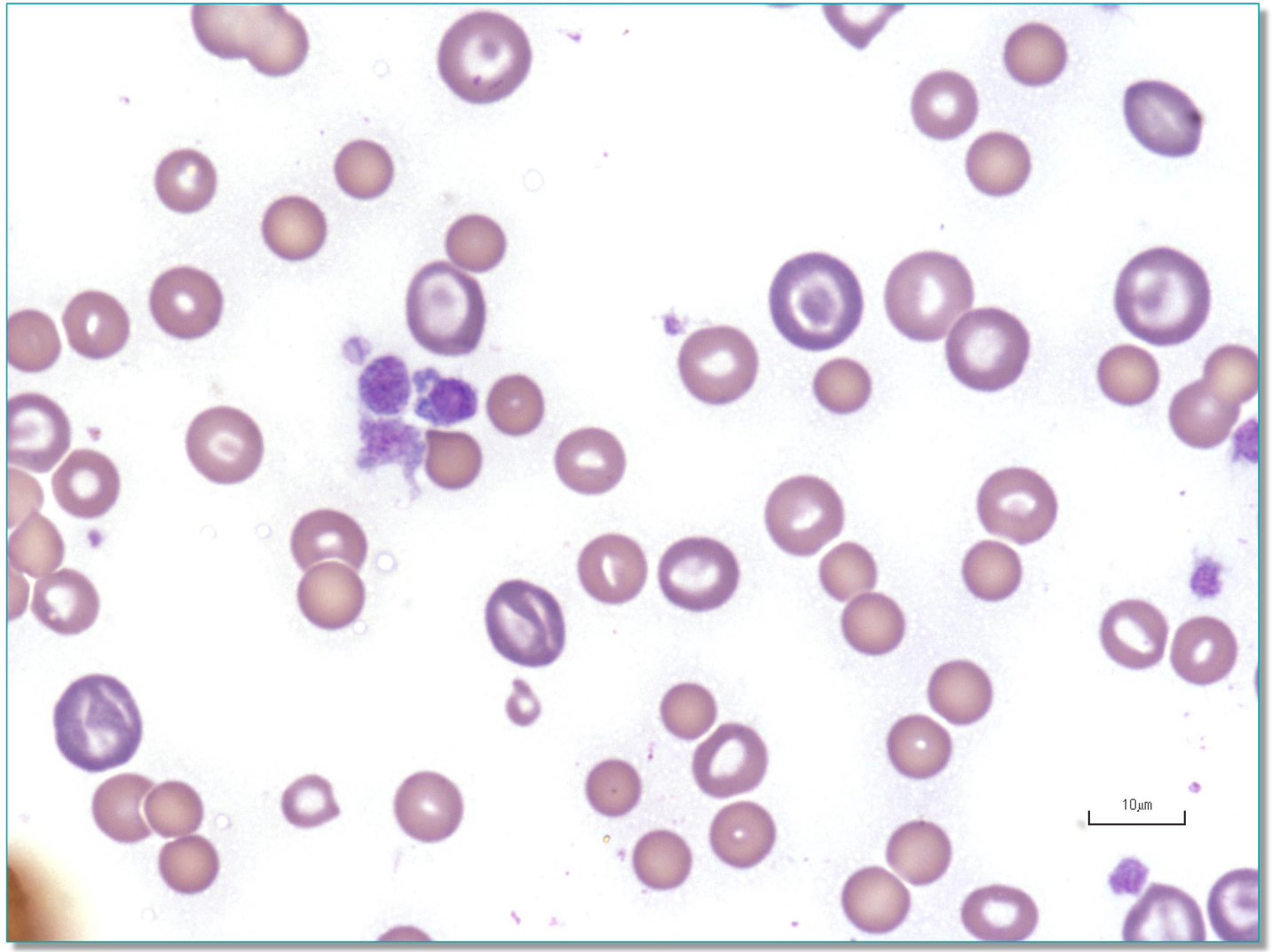

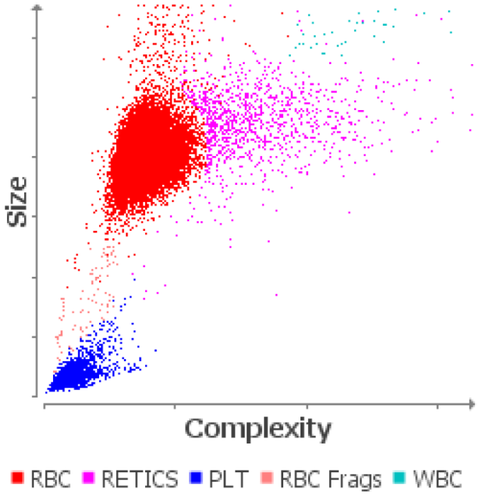

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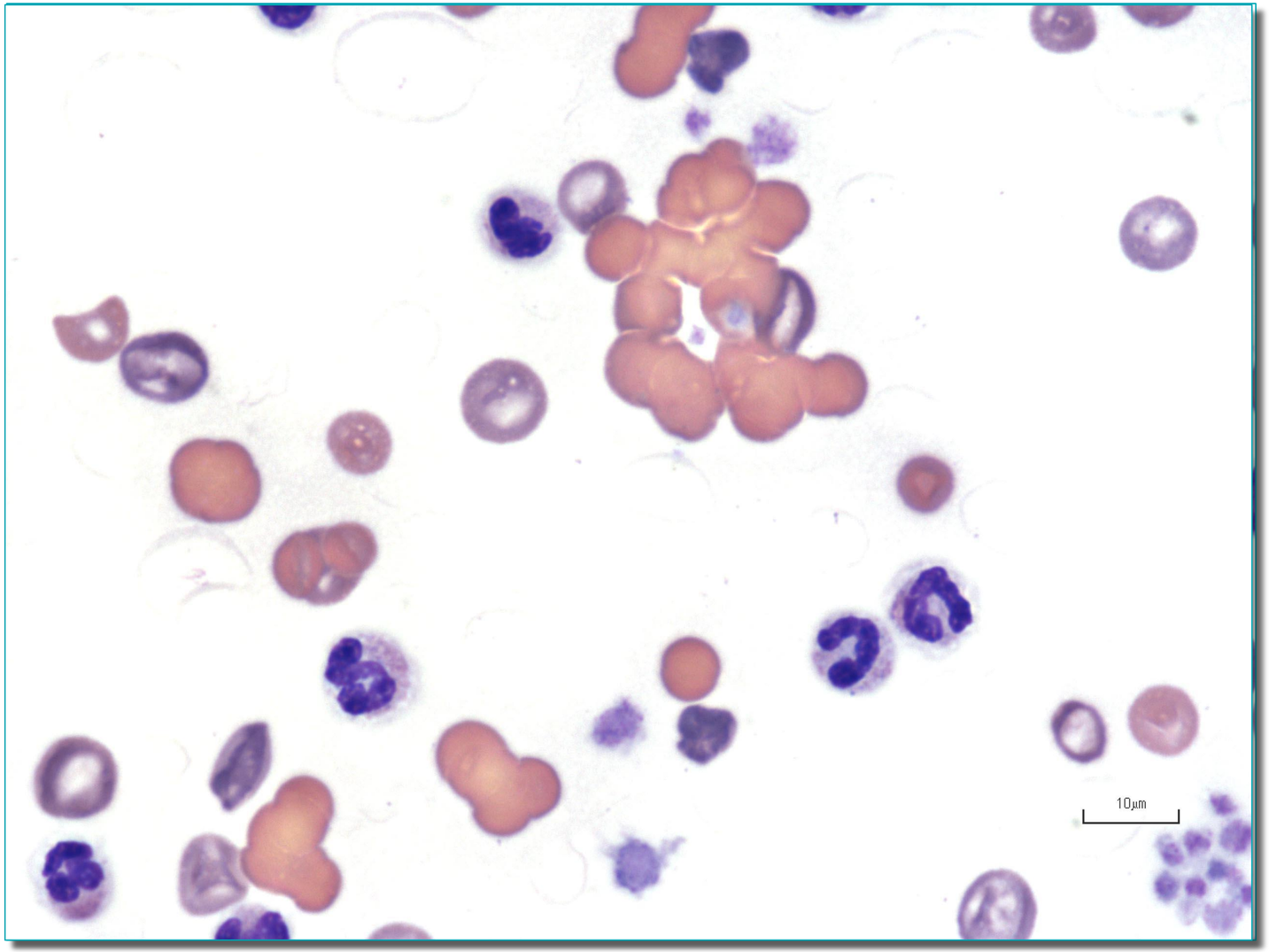

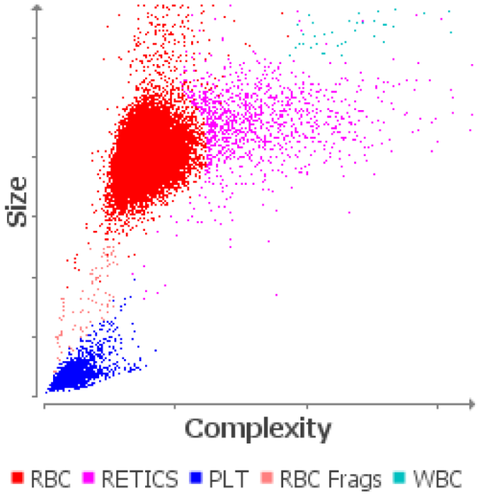

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Additional confirmation of reticulocytosis

Agglutination suggested in body of blood film

Blood loss (internal/external)	Hemolytic disease
Trauma	Immune-mediated
GI ulceration	Mechanic injury
Thrombocytopenia	Oxidative injury
Coagulopathy	Metabolic
Thrombocytopathia	Infectious
Neoplasia	Hereditary
Parasites	Misc. conditions

- **Anemia** when …
  - Rate of blood loss or hemolytic disease

    Overwhelms the bone marrow capacity to respond.

Bone marrow capacity

Decreasing RBC mass

= Anemia

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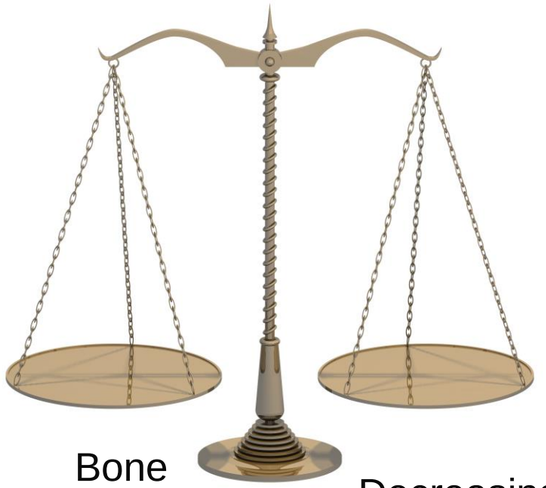
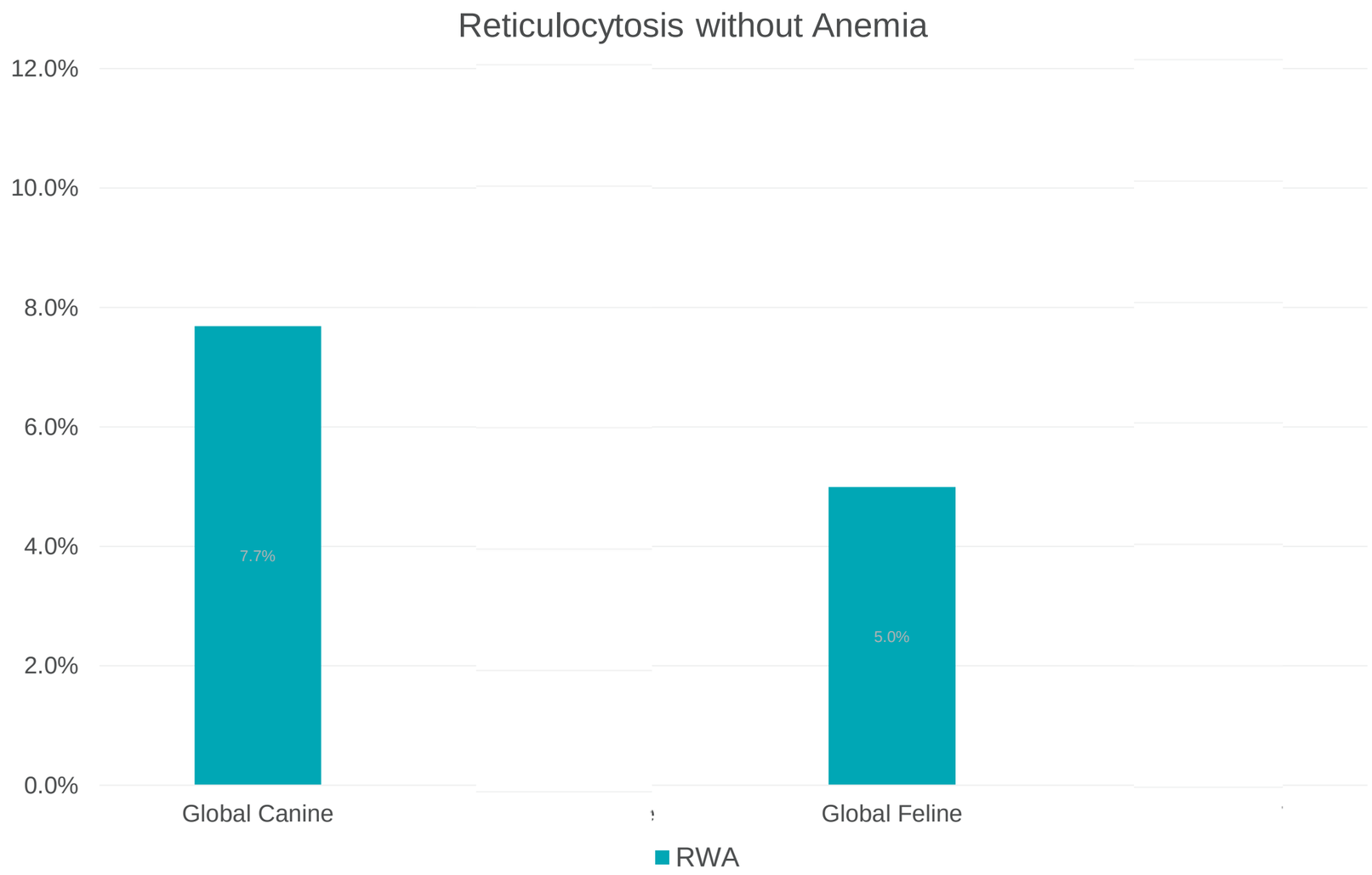
- **No anemia** when …
  - Rate of blood loss or hemolytic disease

    Is mild or early enough and does not overwhelm the bone marrow capacity to respond.



= No anemia

Prevalence of Reticulocytosis without Anemia



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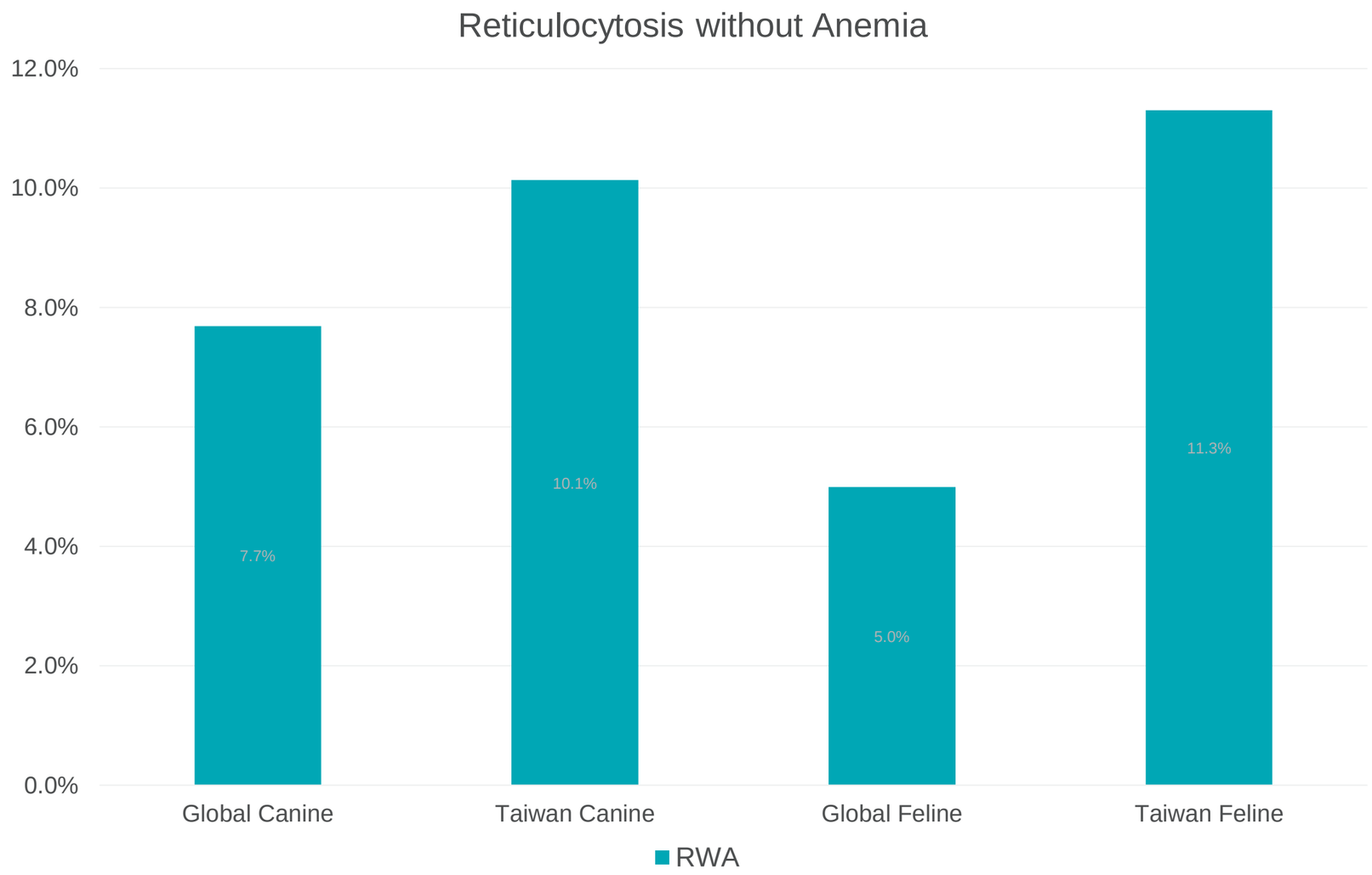

Increasing prevalence of iron deficiency: Study

Pattullo KM, Kidney BA, Taylor SM, Jackson ML. Reticulocytosis in nonanemic dogs: increasing prevalence and potential etiologies. *Vet Clin Pathol*. 2015;44(1):26–36.

- Increased rate of microcytosis noted in the nonanemic dogs with reticulocytosis
- Iron profiles more consistent with iron deficiency
  - Lower total Fe and % transferrin saturation
  - Higher total iron binding capacity (Fe free transferrin)
- Potential associated with increased rate of osteoarthritis
  - Anti-inflammatory medications
  - Neutraceuticals

Reticulocytosis without anemia (RWA): Study

Fuchs J, Moritz A, Grußendorf E, et al. Reticulocytosis in non-anemic cats and dogs. *J Small Anim Pract*. 2018. Accepted for publication, January, 2018.

- Low proportion of nonanemic dogs and cats:
  - 3.1% cats
  - 4.4% dogs
- Mainly in animals with disease
  - Blood loss
  - Cardiac/respiratory disease
  - Gastrointestinal disease
  - Inflammatory disease
  - Cancer
- High mortality rate associated with RWA

Conclusions regarding reticulocytosis without anemia (RWA)

- RWA can provide valuable information about possible occult clinical disease
  - Directs the veterinarian to re-evaluate the patient
  - If no underlying disease is discovered, more frequent laboratory testing should be considered

Conclusions regarding reticulocytosis without anemia (RWA)

- RWA can provide valuable information about possible occult clinical disease
  - Directs the veterinarian to re-evaluate the patient
  - If no underlying disease is discovered, more frequent laboratory testing should be considered
- What to do if your analyzer does not provide a reticulocyte count
  - Blood film is essential
  - Manual reticulocyte count may be needed

Questions?

dbdenicola@roadrunner.com