Beyond The Pale- Clinical Approach to the Anaemic Patient

Presenters :

Marta Costa &Yvonne McGrotty

Date Nov 2025

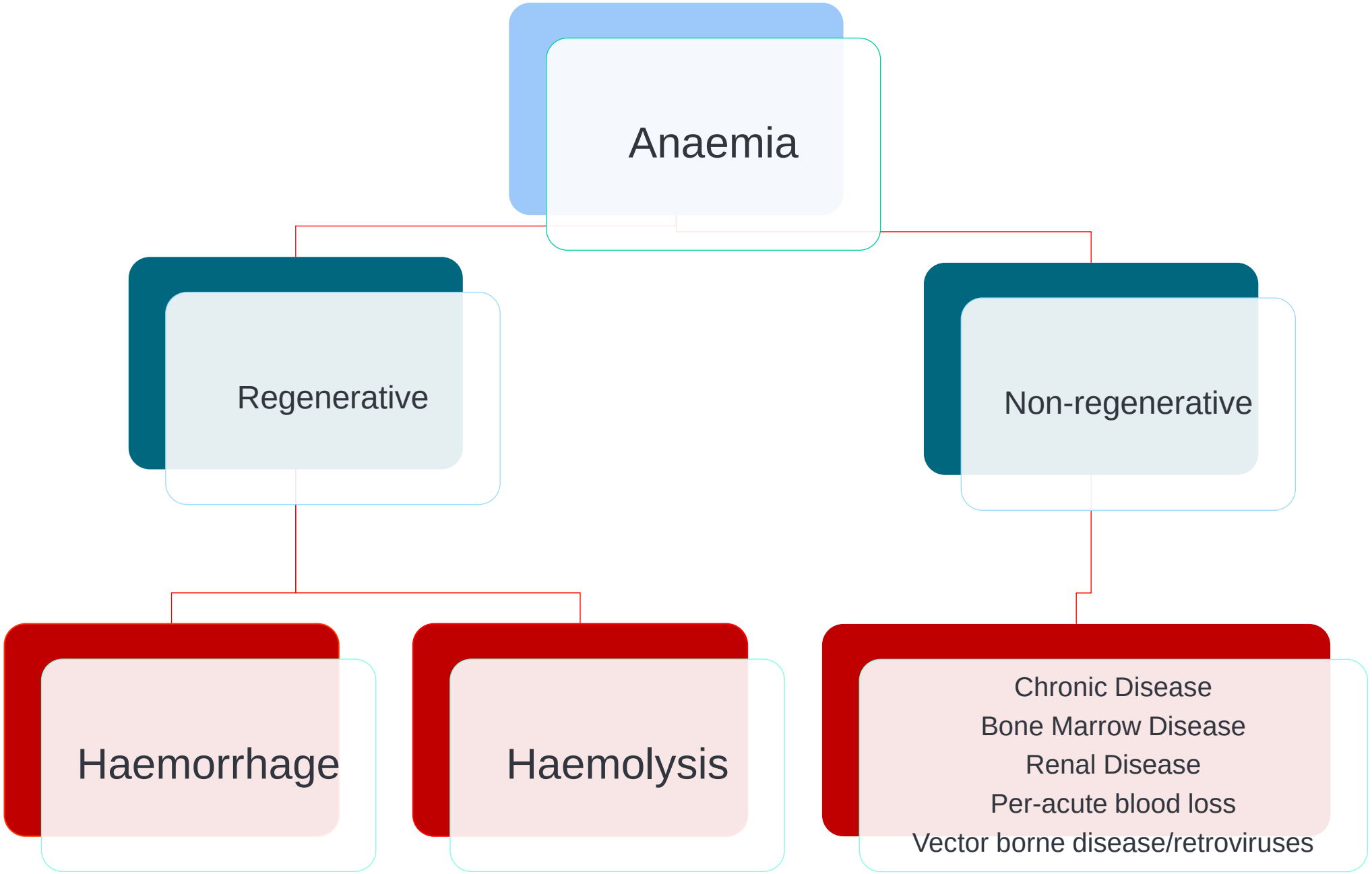
Disclosures:

Marta Costa
I am an employee of IDEXX Laboratories Ltd.

Yvonne McGrotty
-Employee of IDEXX, UK
-Employee of AniCura, France

Regenerative Anaemias

Haemorrhage vs Haemolysis



Regenerative Anaemia

+ Can take 3-5 days for bone marrow to respond

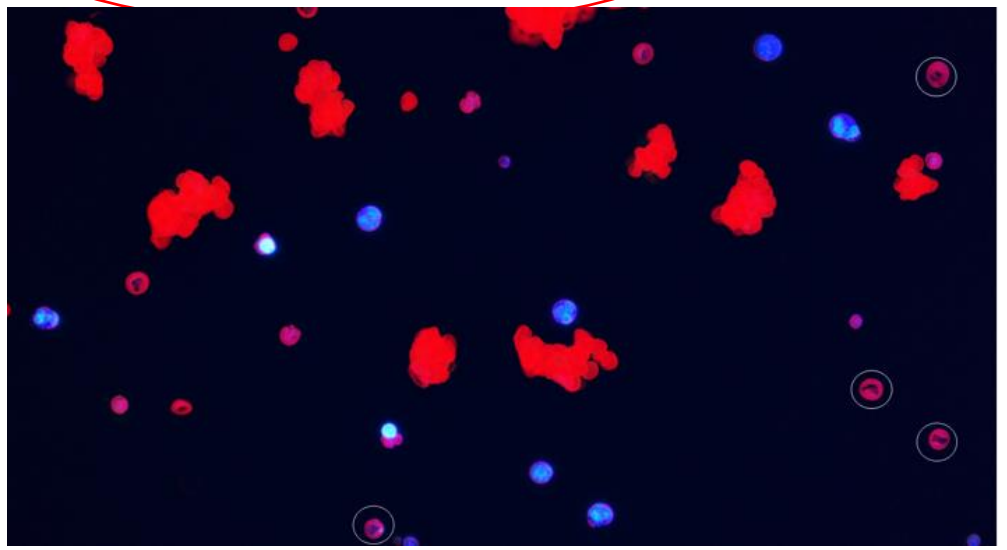
+ Haemorrhage
+ Haemolysis

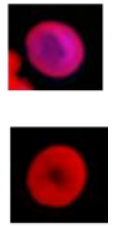
+ Polychromasia and reticulocytes assess degree of regeneration

+ Lasercyte & Procyte produce a reticulocyte count

+ InVue Dx provides RBC morphology assessment

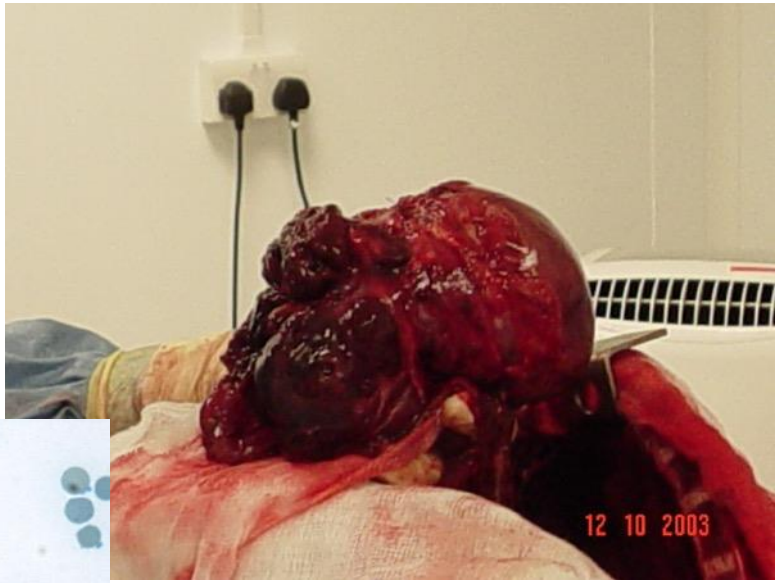
Haematology	20/02/2025 17:47	
RBC	3.85	5.65 - 8.87 x10^12/L
Haematocrit	0.237	0.373 - 0.617 L/L
Haemoglobin	82	131 - 205 g/L
MCV	61.6	61.6 - 73.5 fL
MCH	21.4	21.2 - 25.9 pg
MCHC	347	320 - 379 g/L
RDW	14.1	13.6 - 21.7 %
% Reticulocytes	8.4	%
Reticulocytes	321.6	10.0 - 110.0 K/µL

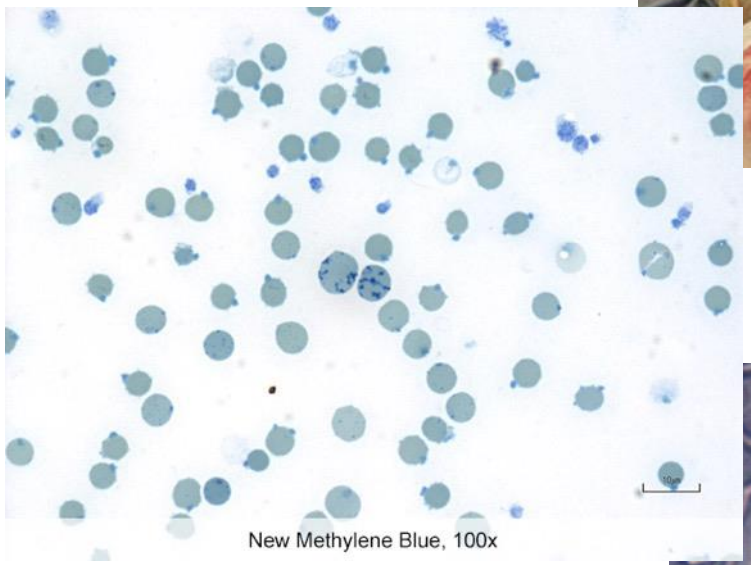


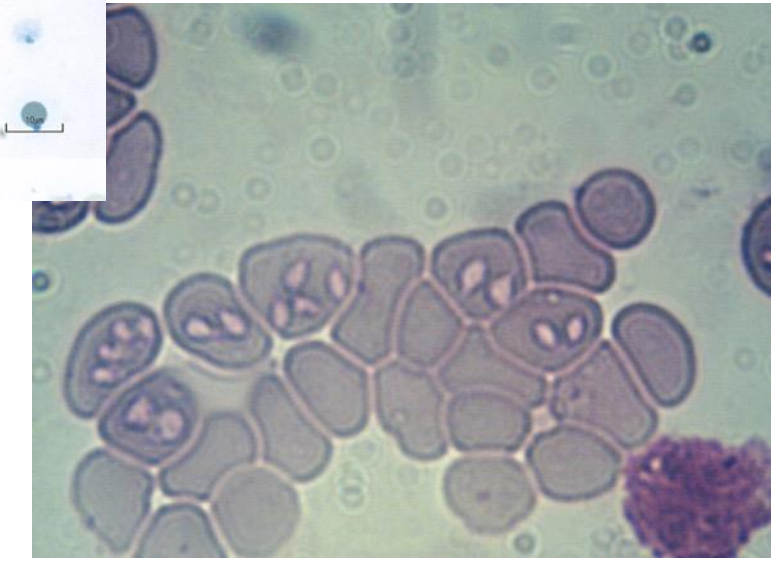


Haemolytic Anaemias

- Immune mediated
  - Associative or non-associative
- Mechanical Injury
  - Vascular neoplasms
  - Heartworm
- Oxidative Injury
  - Heinz bodies
- Red Cell Parasites
  - Haemomycoplasma
  - *Babesia spp*

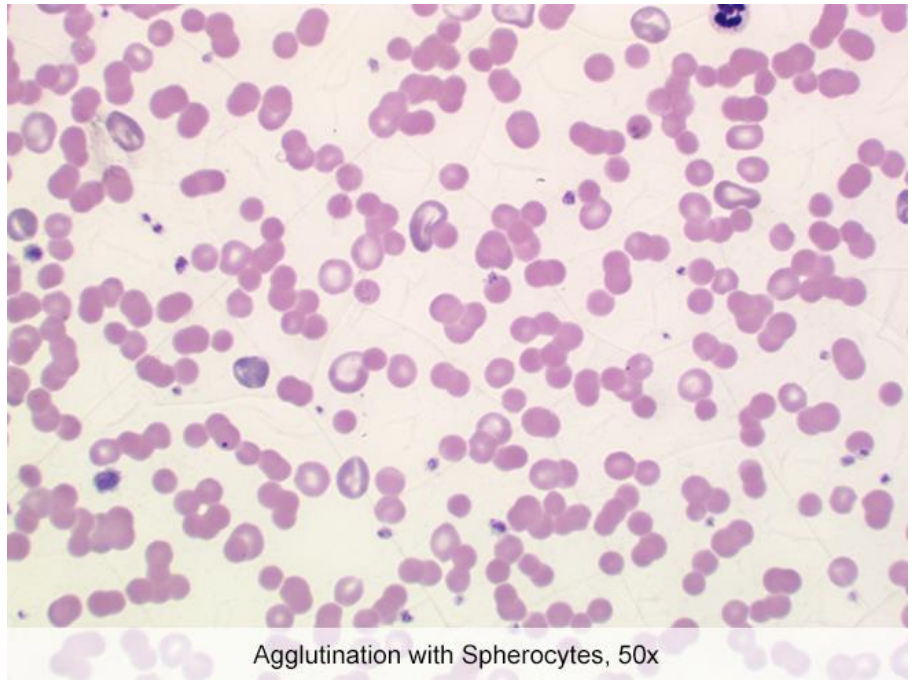



New Methylene Blue, 100x

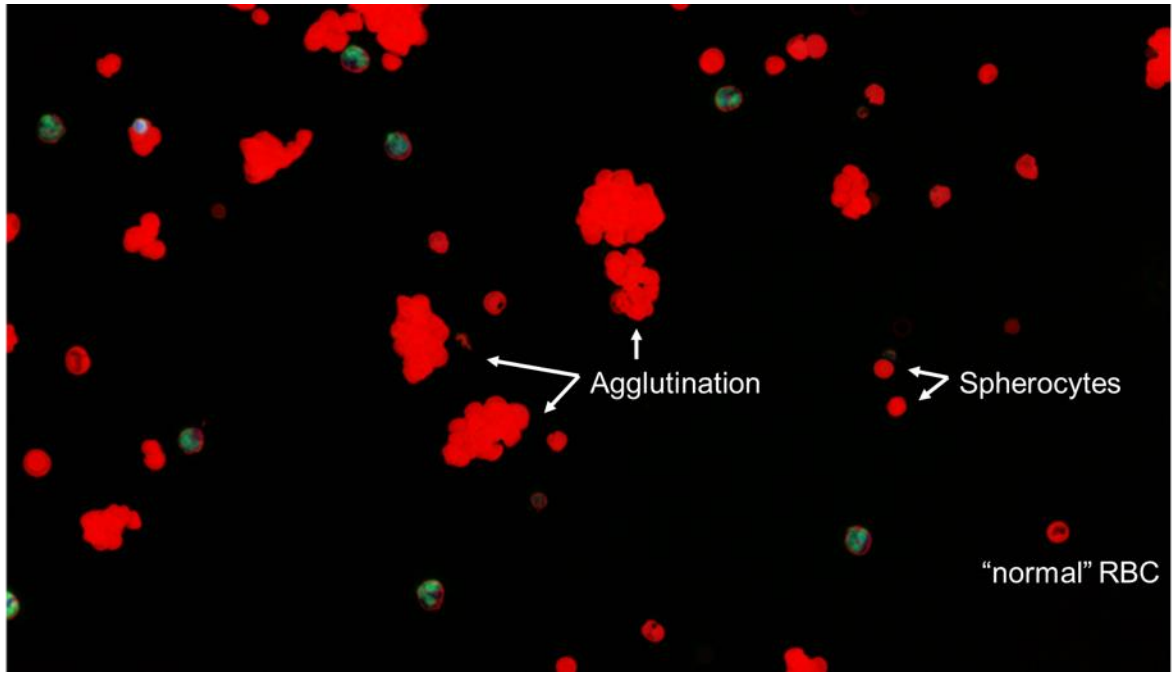


Haemolysis

- Regenerative response
  - Polychromasia
  - Anisocytosis
  - Reticulocytes
- Neutrophilia
- Spherocytes
  - Immune-mediated
- Autoagglutination?

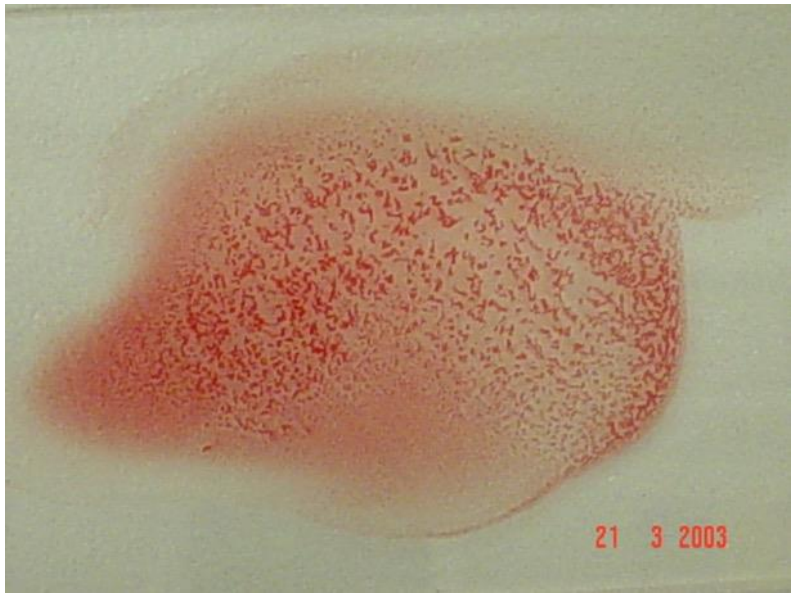


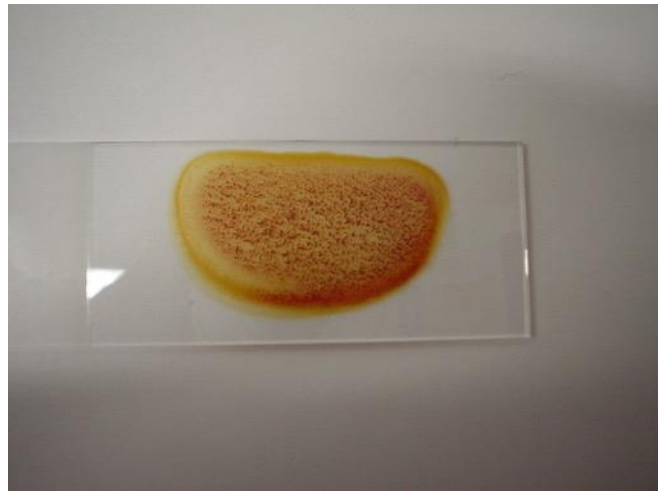
Agglutination with Spherocytes, 50x



In Saline Agglutination Test

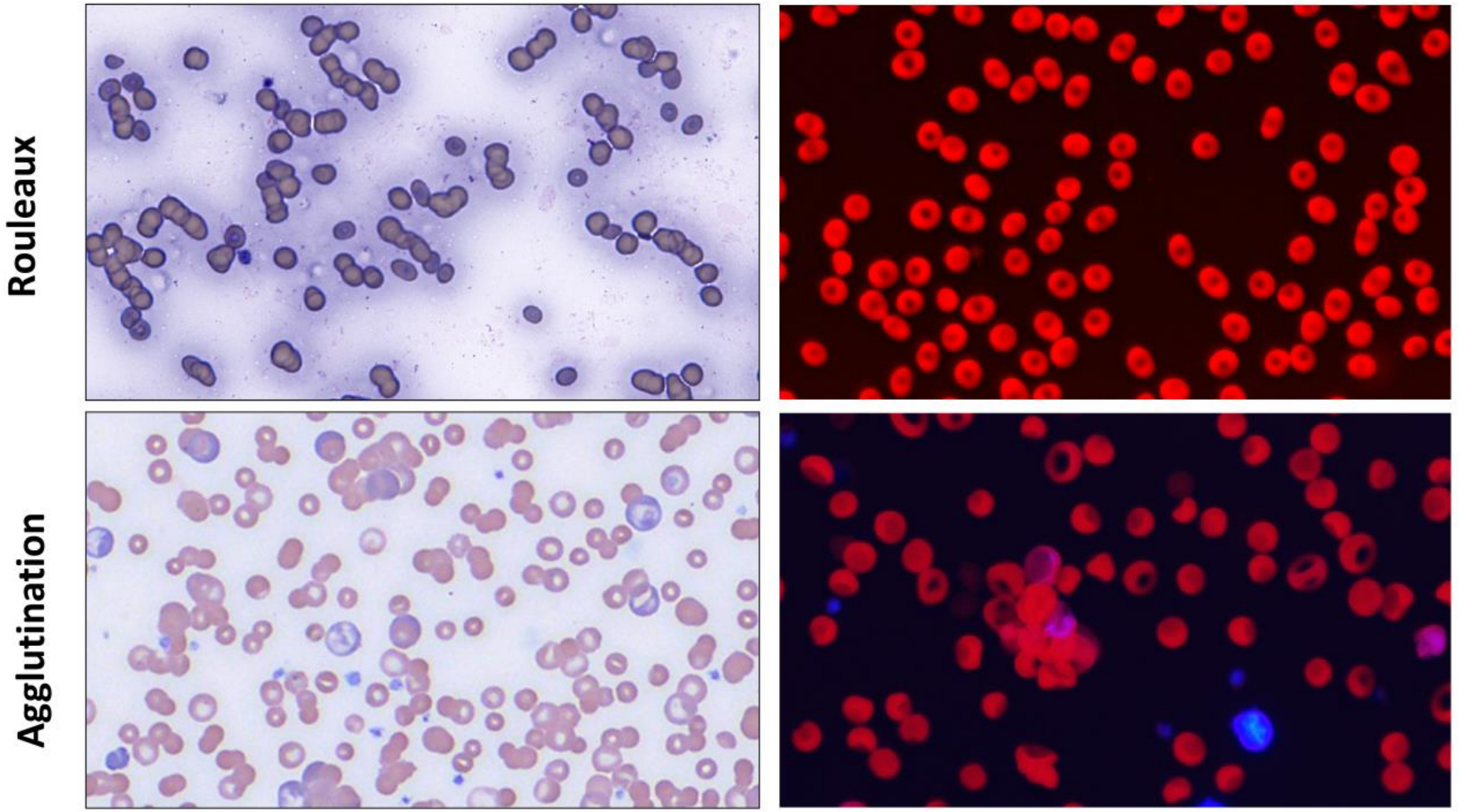
+ Place 1 drop of EDTA blood on glass slide
+ Add at least 4 drops of saline
+ Gently rock to mix blood and saline
+ Distinguishes rouleaux from agglutination





Agglutination vs Rouleaux

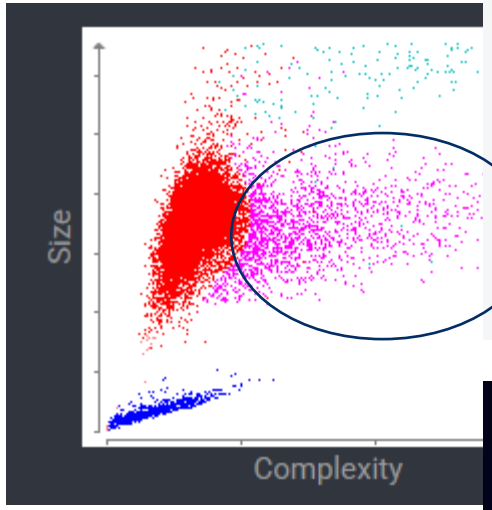
inVue Dx™ solves clinical confusion of rouleaux and agglutination



2

Reticulocytes

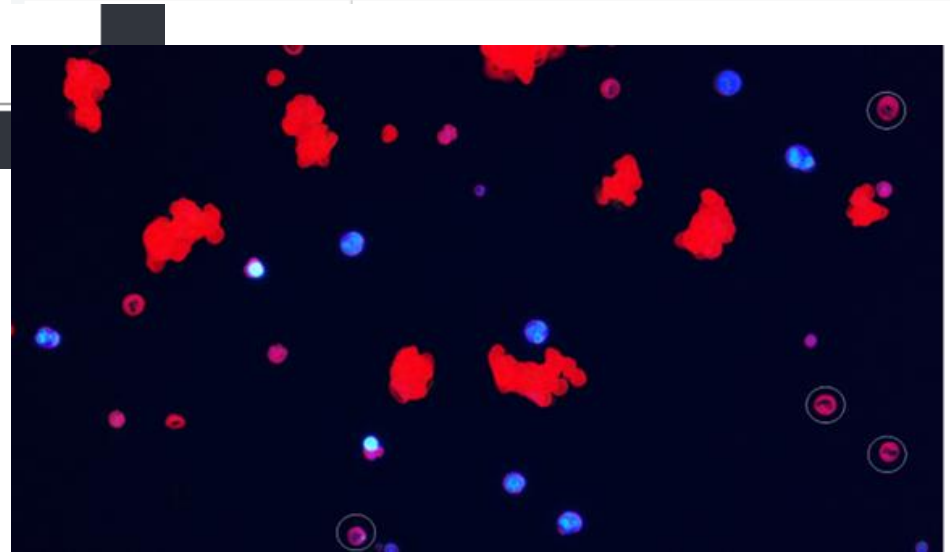
+ Evaluates response to anaemia
+ Immature RBCs
+ Increased mRNA
+ Identified with
  + Flow cytometry
  + New methylene blue stain
  + InVue Dx

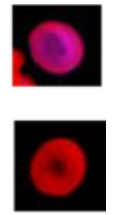


Haematology

20/02/2025
17:47

RBC	3.85	5.65 - 8.87 x10^12/L
Haematocrit	0.237	0.373 - 0.617 L/L
Haemoglobin	82	131 - 205 g/L
MCV	61.6	61.6 - 73.5 fL
MCH	21.4	21.2 - 25.9 pg
MCHC	347	320 - 379 g/L
RDW	14.1	13.6 - 21.7 %
% Reticulocytes	8.4	%
Reticulocytes	321.6	10.0 - 110.0 K/µL

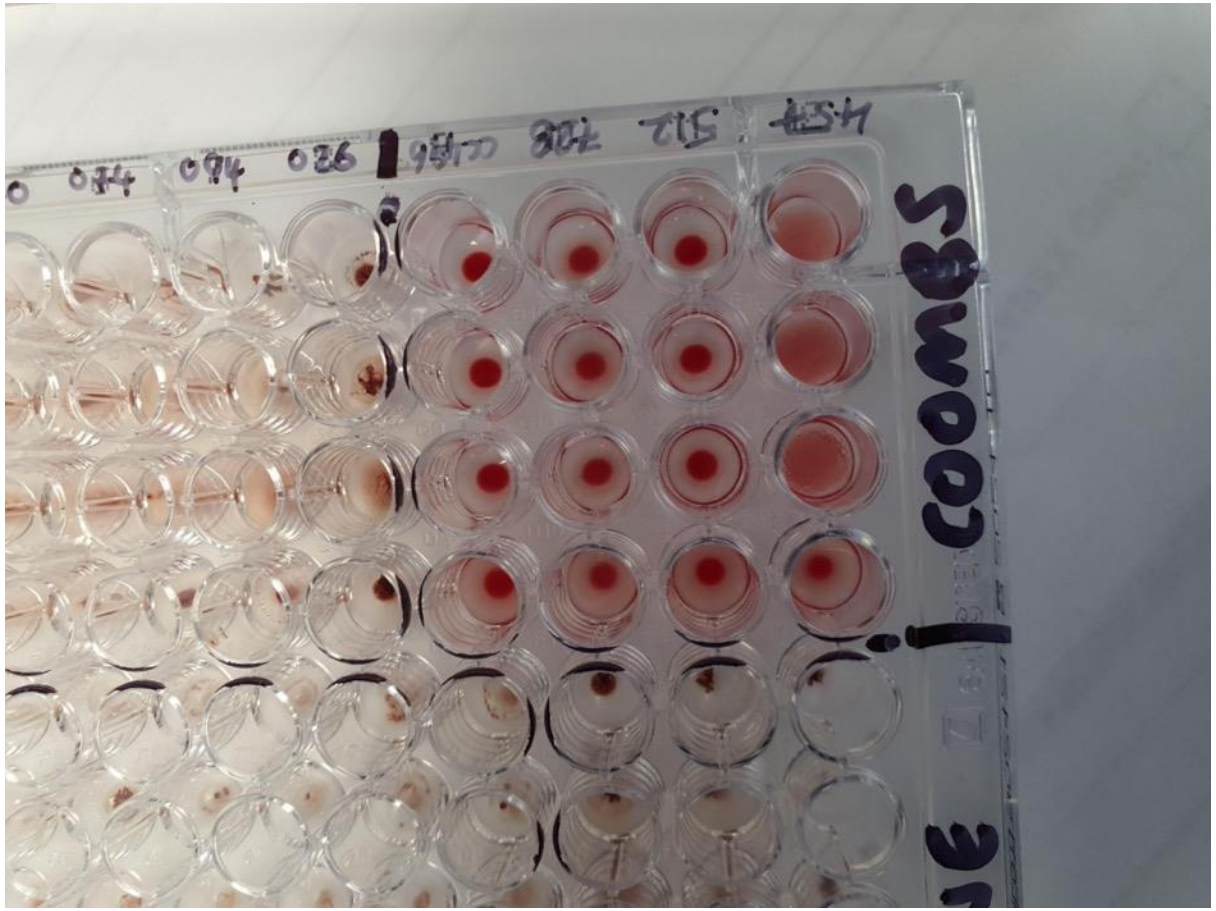




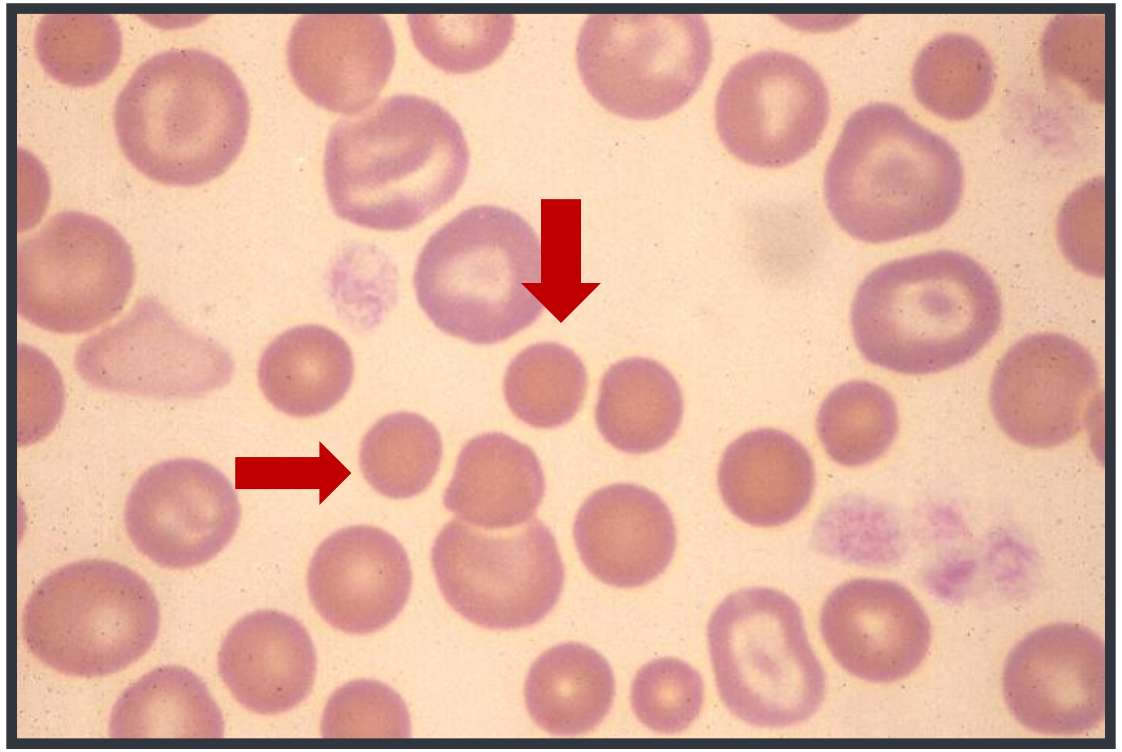
All polychromatophilic red blood cells are reticulocytes, *but* not all reticulocytes are polychromatophilic

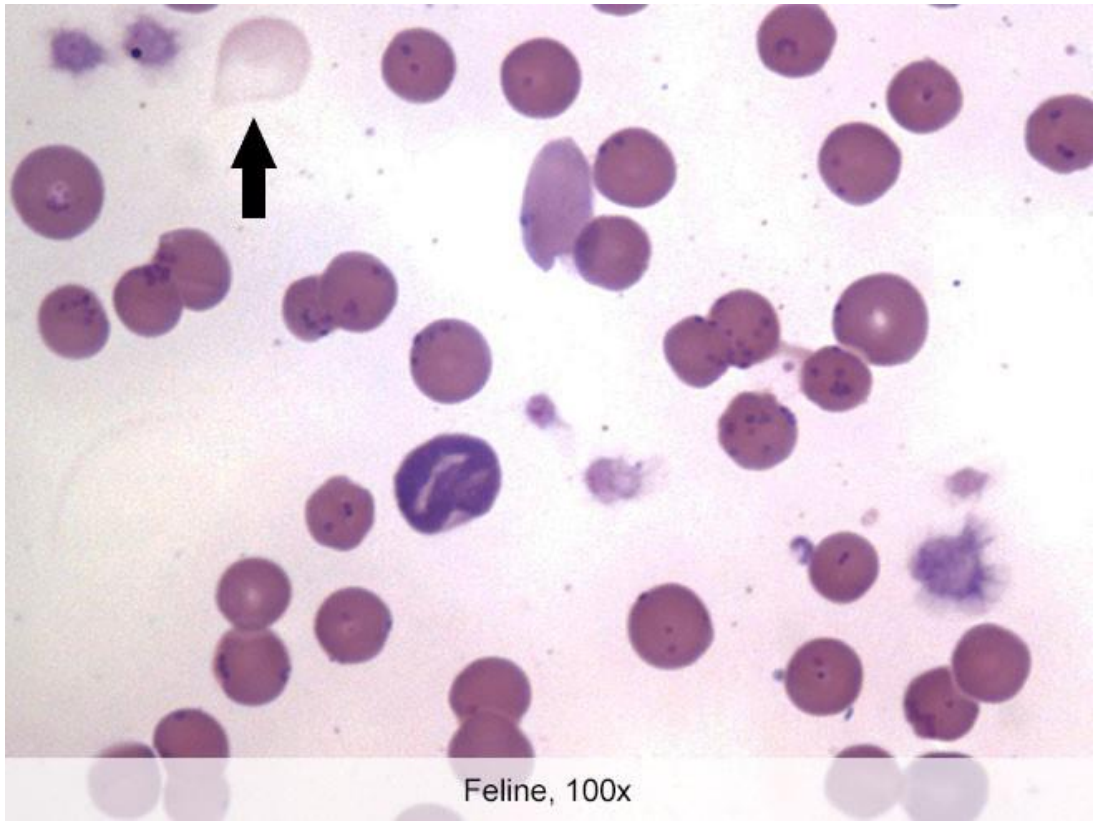
Coombs Test

+ Not required if agglutination positive
+ Detects Ab or complement on surface of rbc
+ Positive result supports diagnosis of IMHA



Spherocytes & Ghost Cells





IMHA in Dogs

- Associative or non-associative

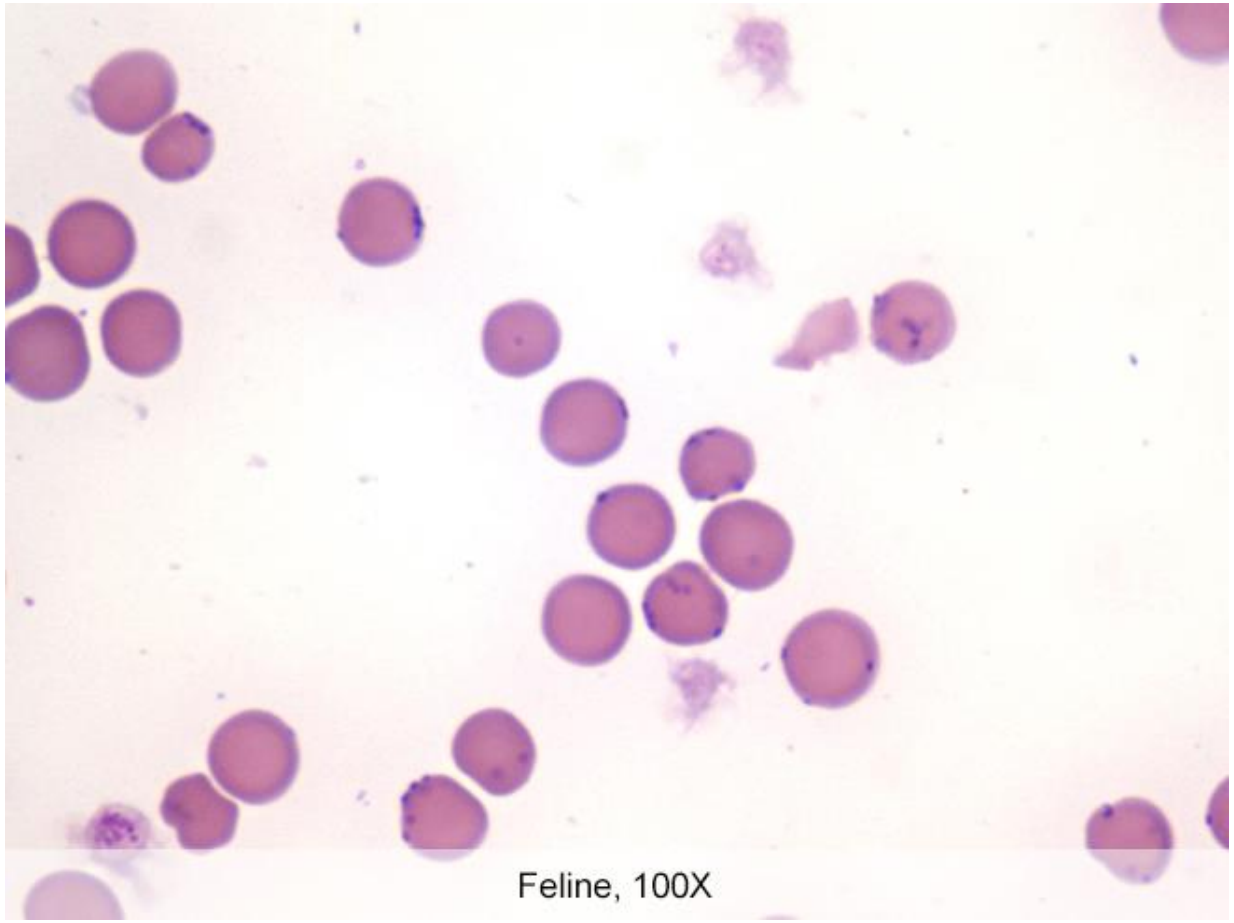
- Non-associative
  - Underlying cause not identified
  - Young adults
  - Cocker Sp, Springer Sp, OES

- Associative
  - Secondary to infectious/inflammatory/neoplastic cause
  - Drug reactions
  - RBC parasites

IMHA in cats

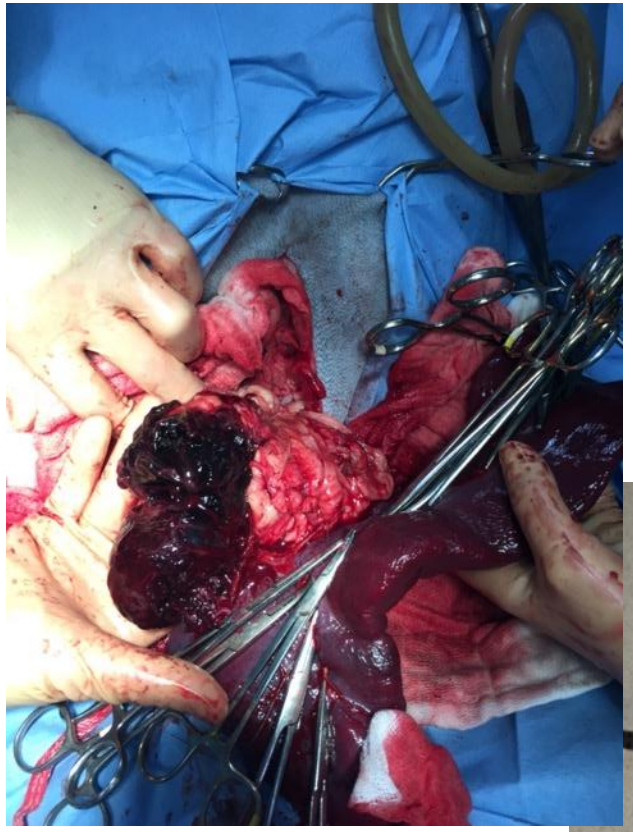
- Associative or non-associative

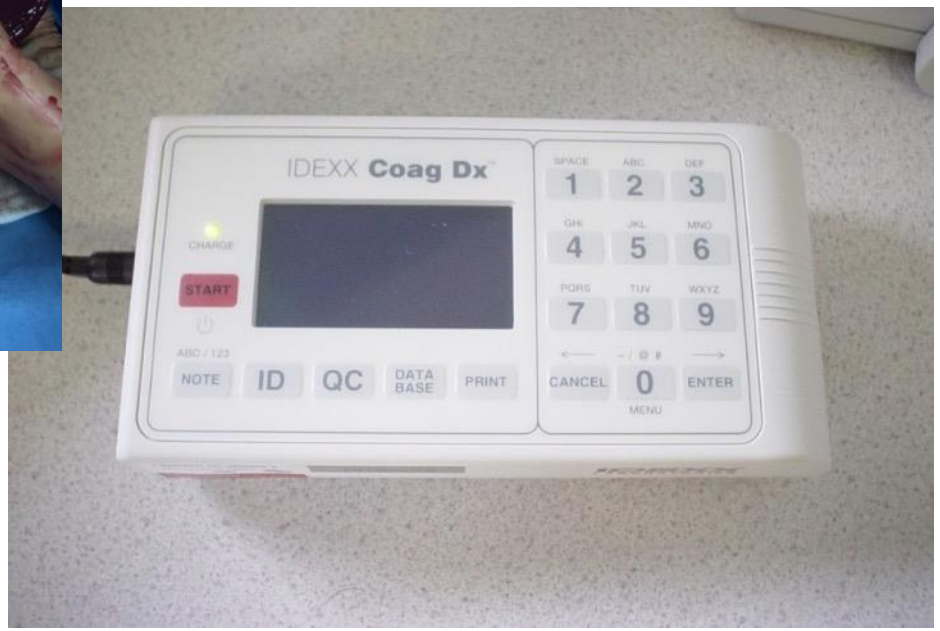
- Associative
  - *Mycoplasma haemofelis sp*
  - FeLV


Feline, 100X

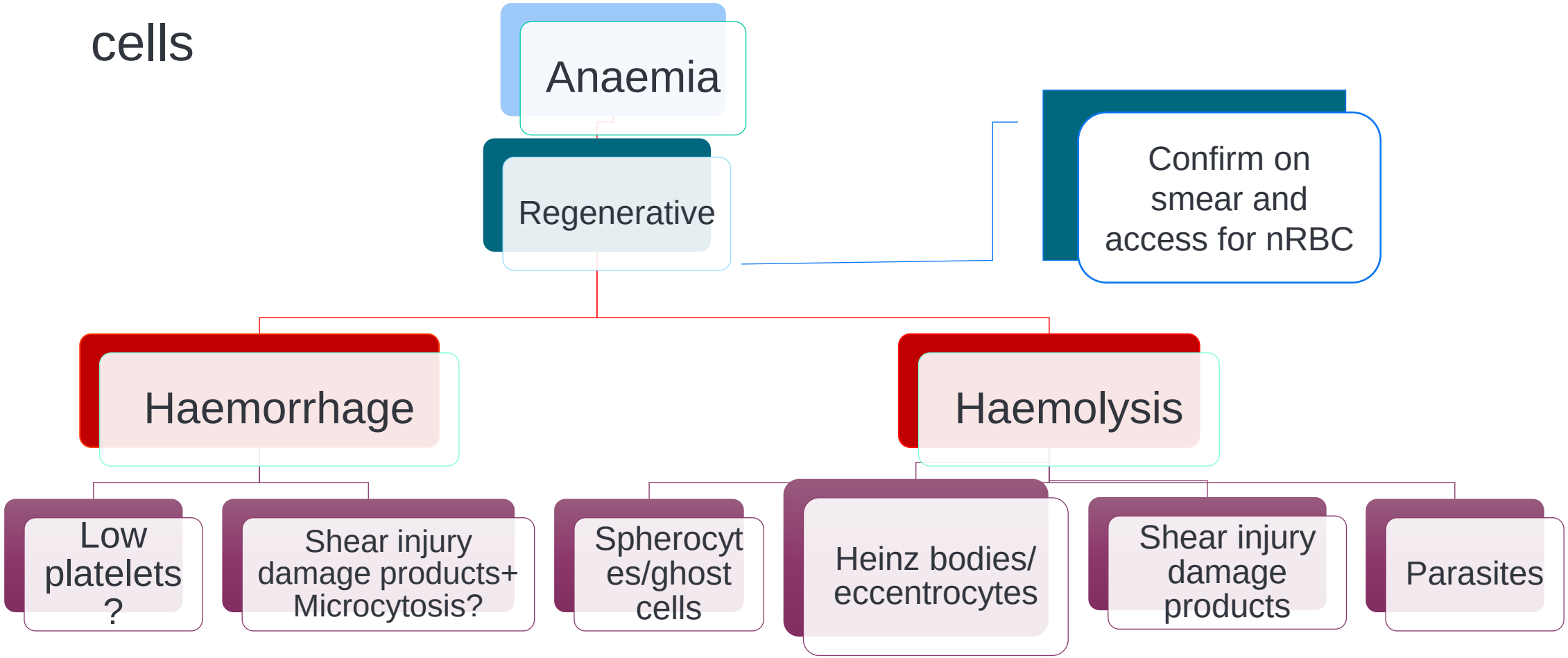
Haemorrhage

+ Trauma
+ Neoplasia
+ Acquired coagulopathy
  + Rat bait ingestion
  + DIC
  + Liver dysfunction
+ Congenital coagulopathy
  + Haemophilia

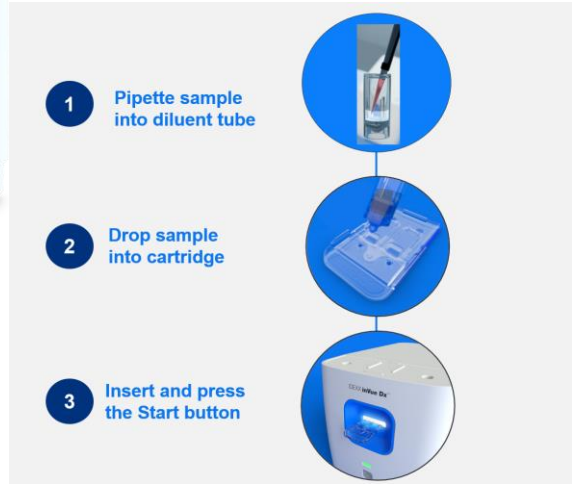




Morphological evaluation of blood cells



Morphological evaluation of blood cells



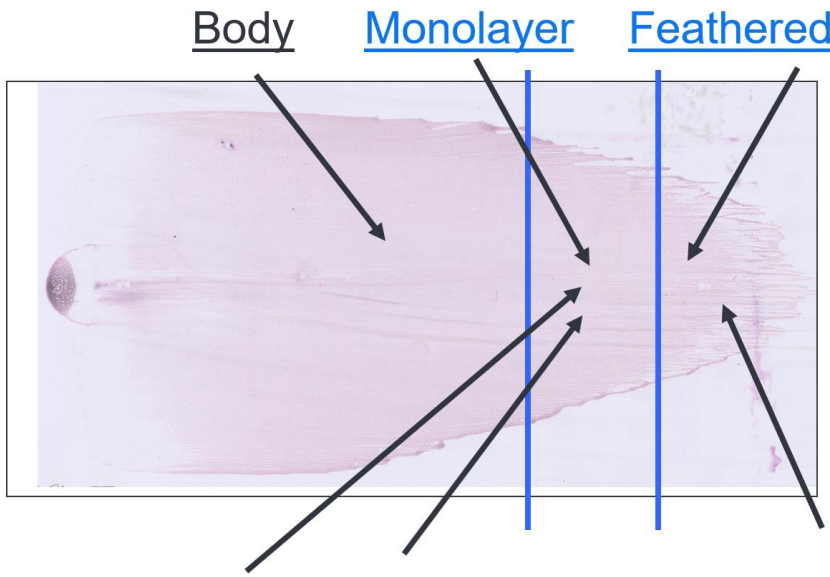
ASVCP guidelines

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

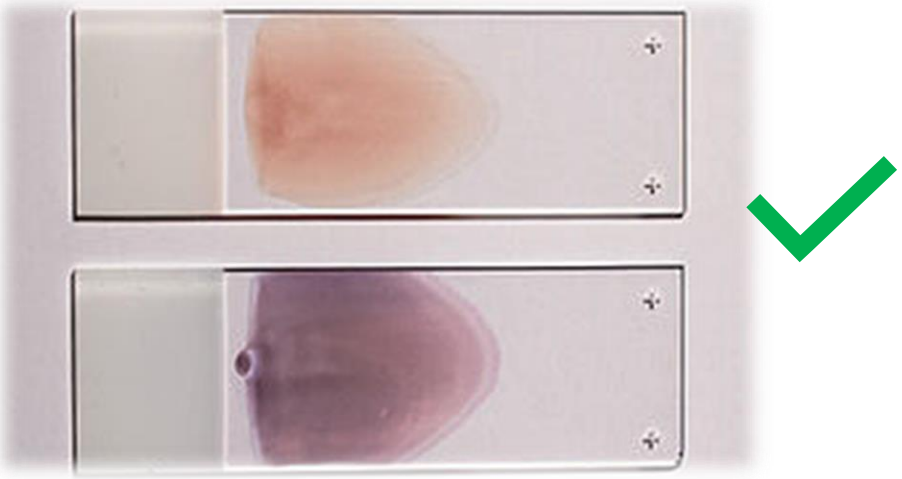
	CRITERIA
WBC	Leukopenia < 3 x10e9/L
	Leukocytosis > 30 x10e9/L
	Lymphocytosis > 10 x10e9/L
	Any unclassified cells
Platelets	Thrombocytopenia < 100 x10e9/L
	Thrombocytosis > 900 x10e9/L
	Abnormal MPV (if reported by instrument)
RBC	Moderate to severe anaemia
	>5 nRBC/100WBC
	Abnormal MCV

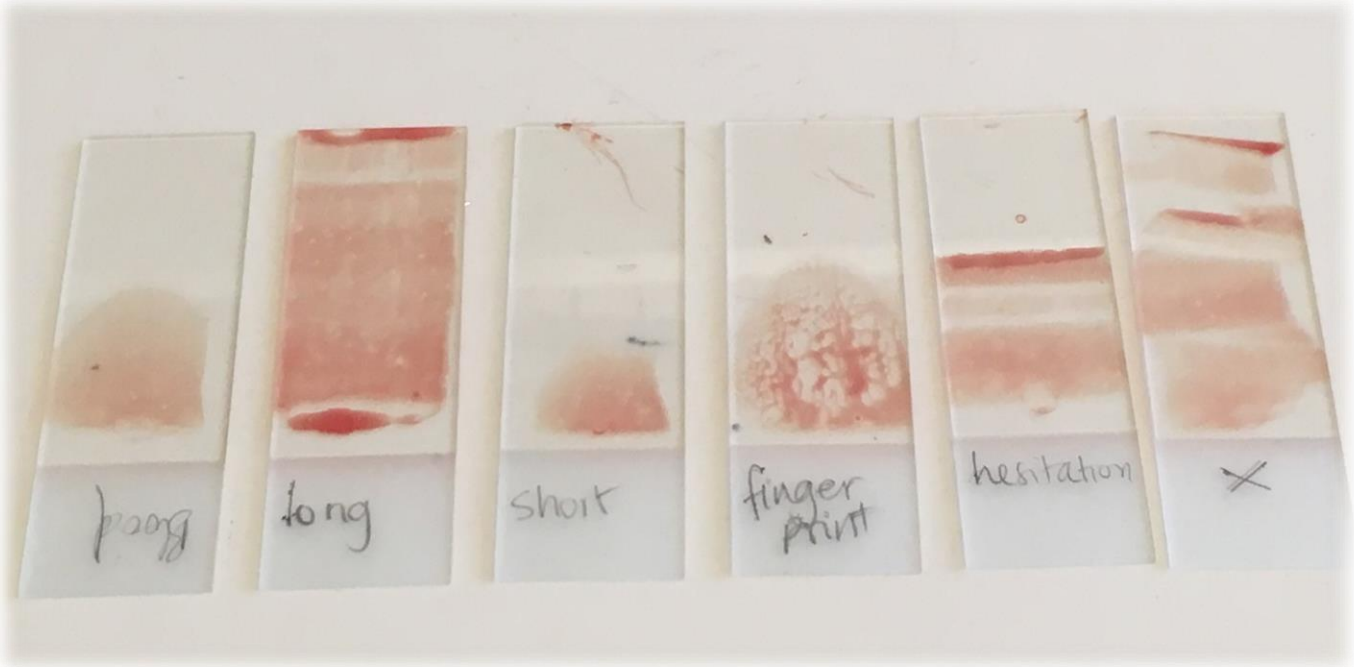
Modified from ASVCP guidelines: quality assurance for point-of-care testing in veterinary medicine. ASVCP, 2013.

Blood smear



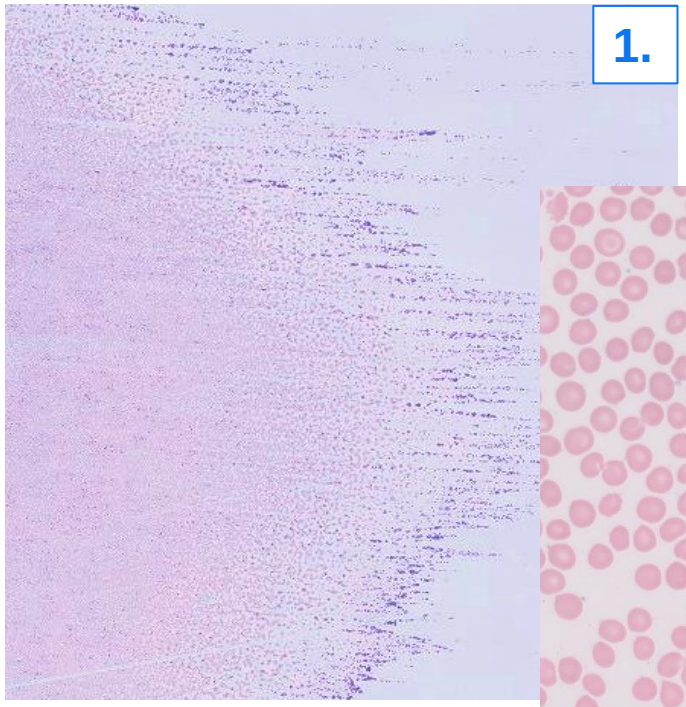
- Rouleaux
- Agglutination
- Estimate numbers
- Morphology
- Platelet clumps
- Large cells
- Microfilaria

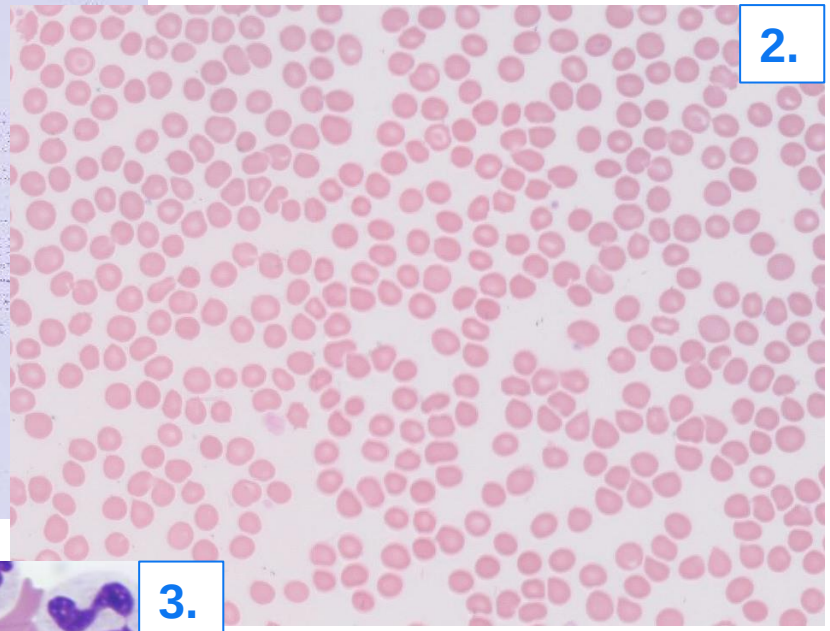


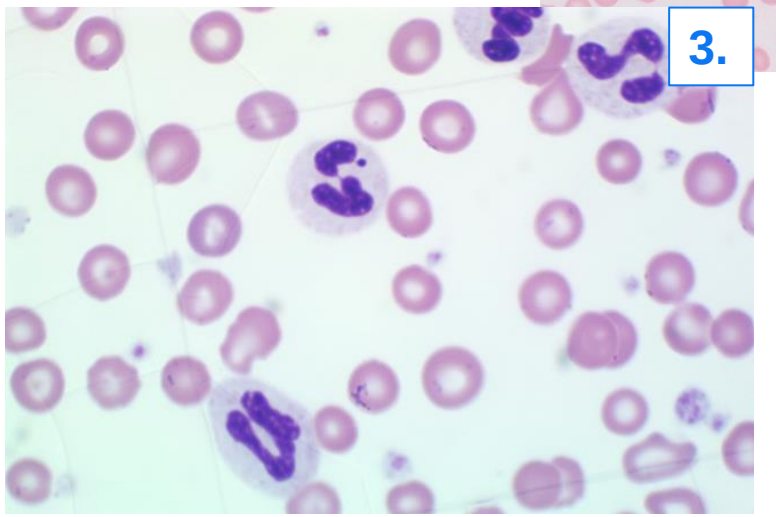


Systematic approach to blood smear review

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

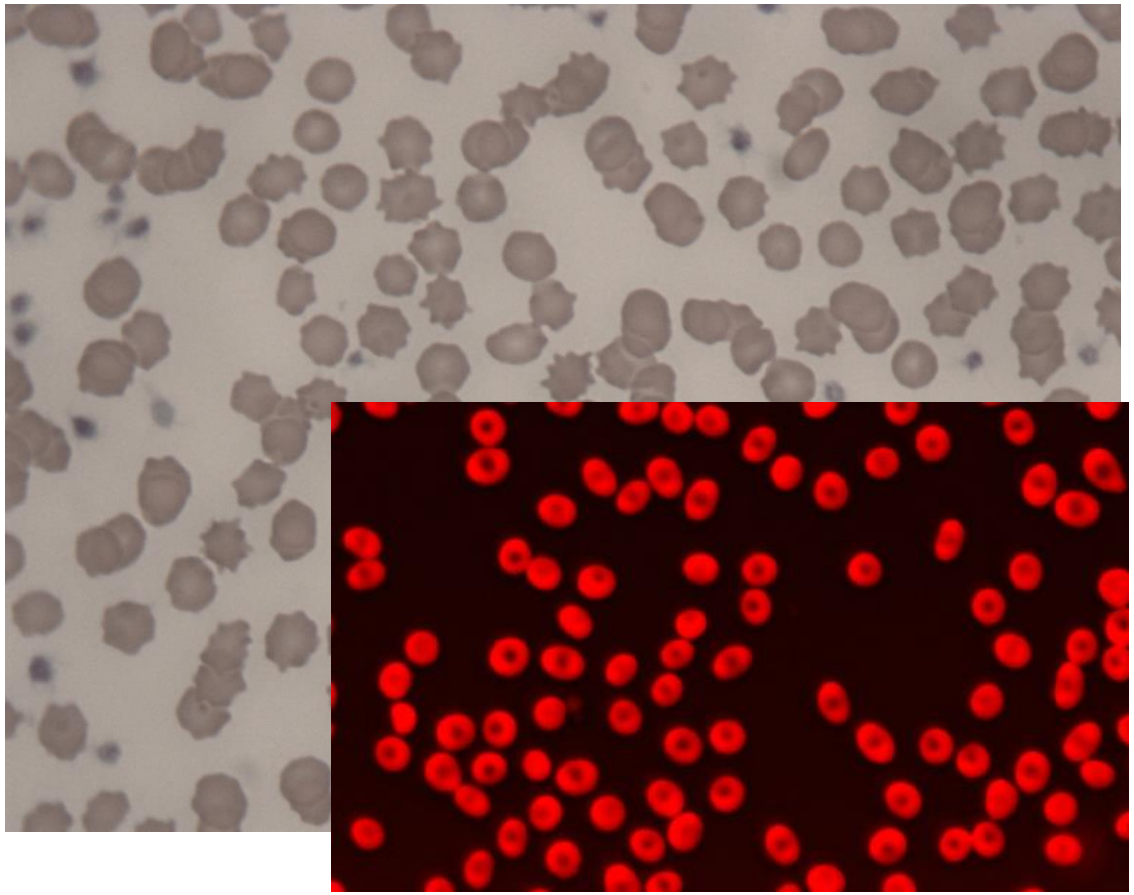




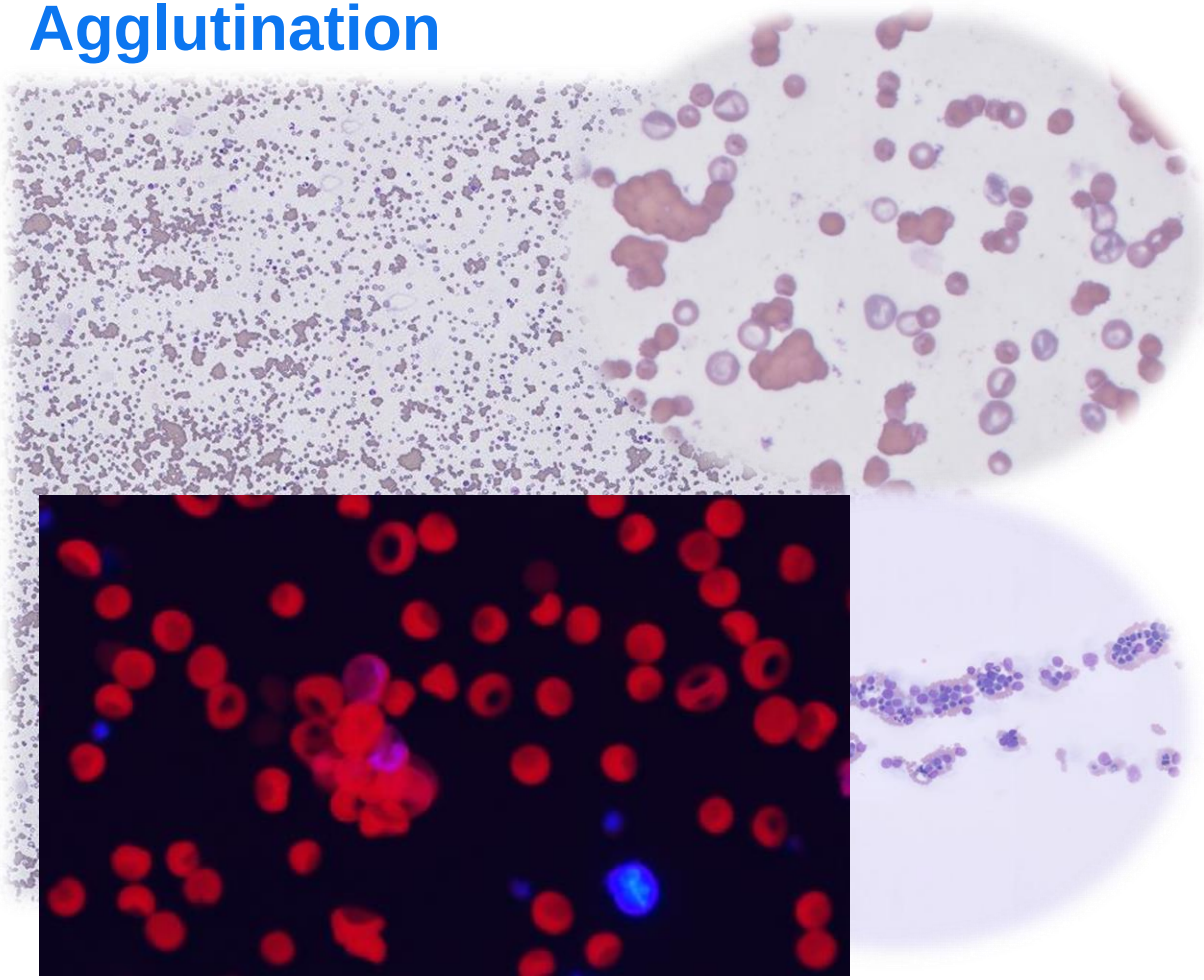


Cell distribution

Rouleaux

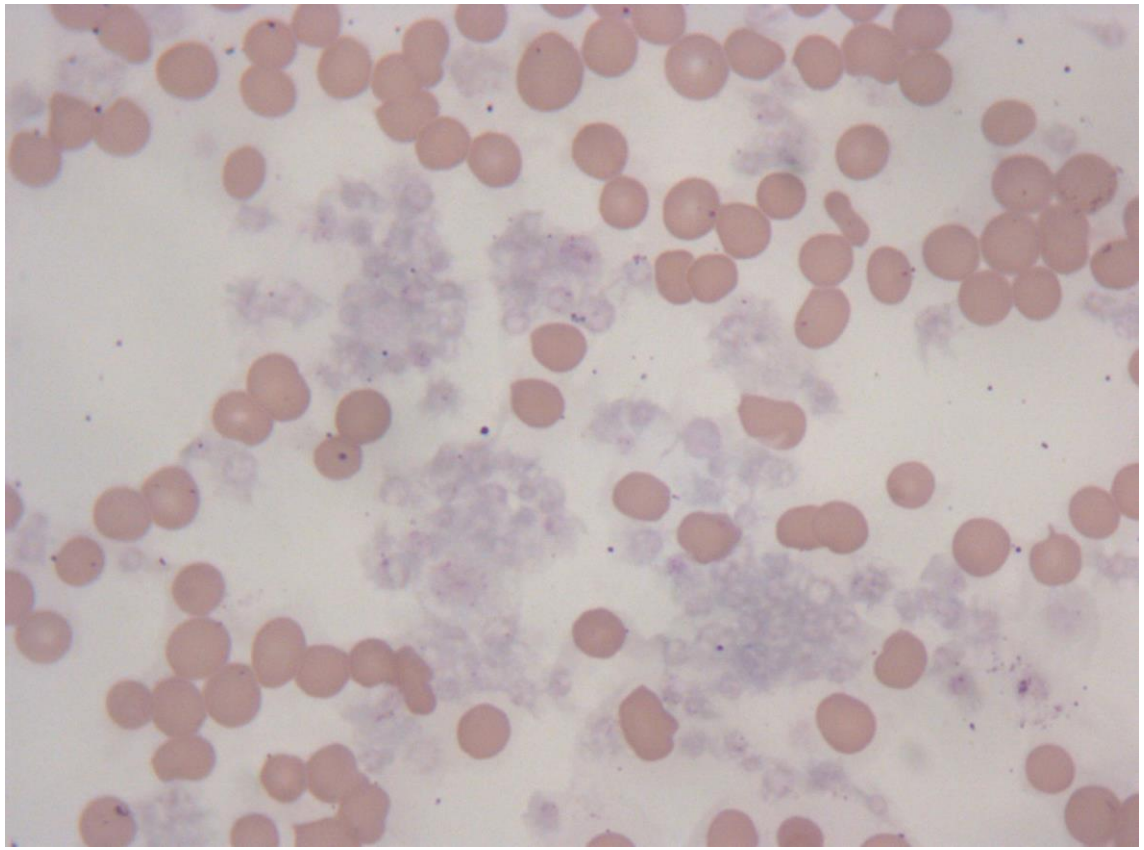


Agglutination

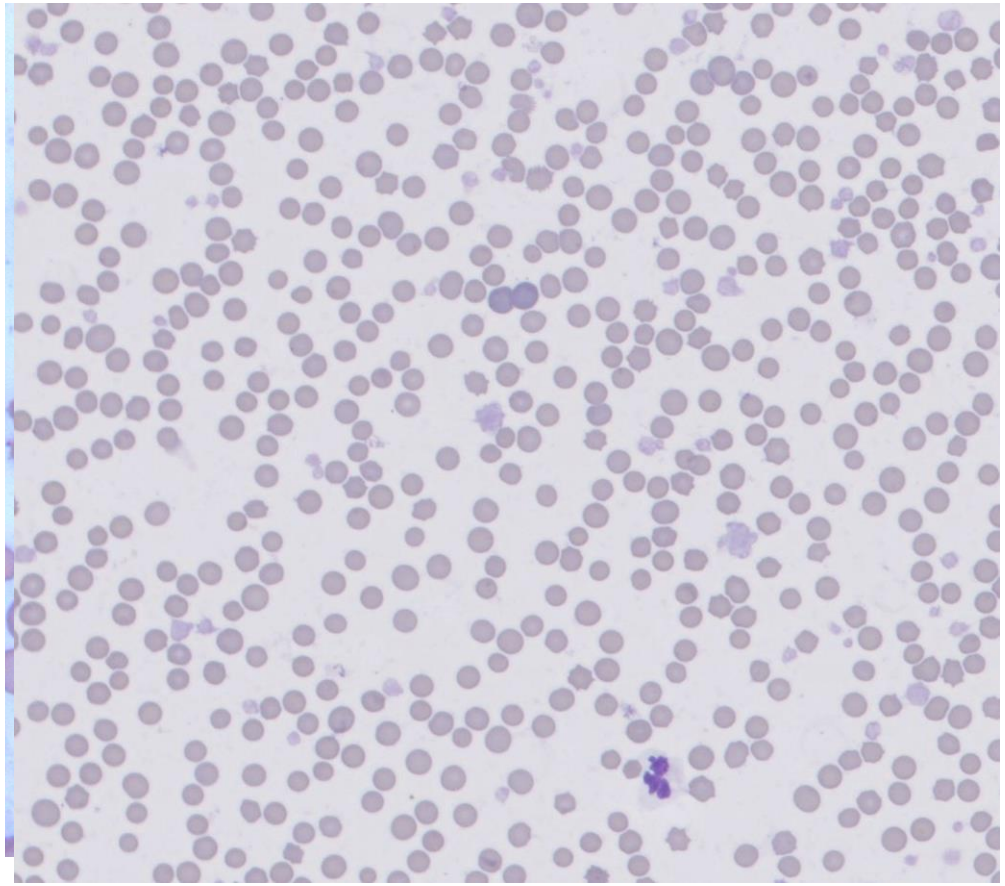


Platelets

Platelet clumps



Macroplatelets



Platelet estimates

- ✓ Assuming NO PLT CLUMPS in feathered edge and NO CLOTS!

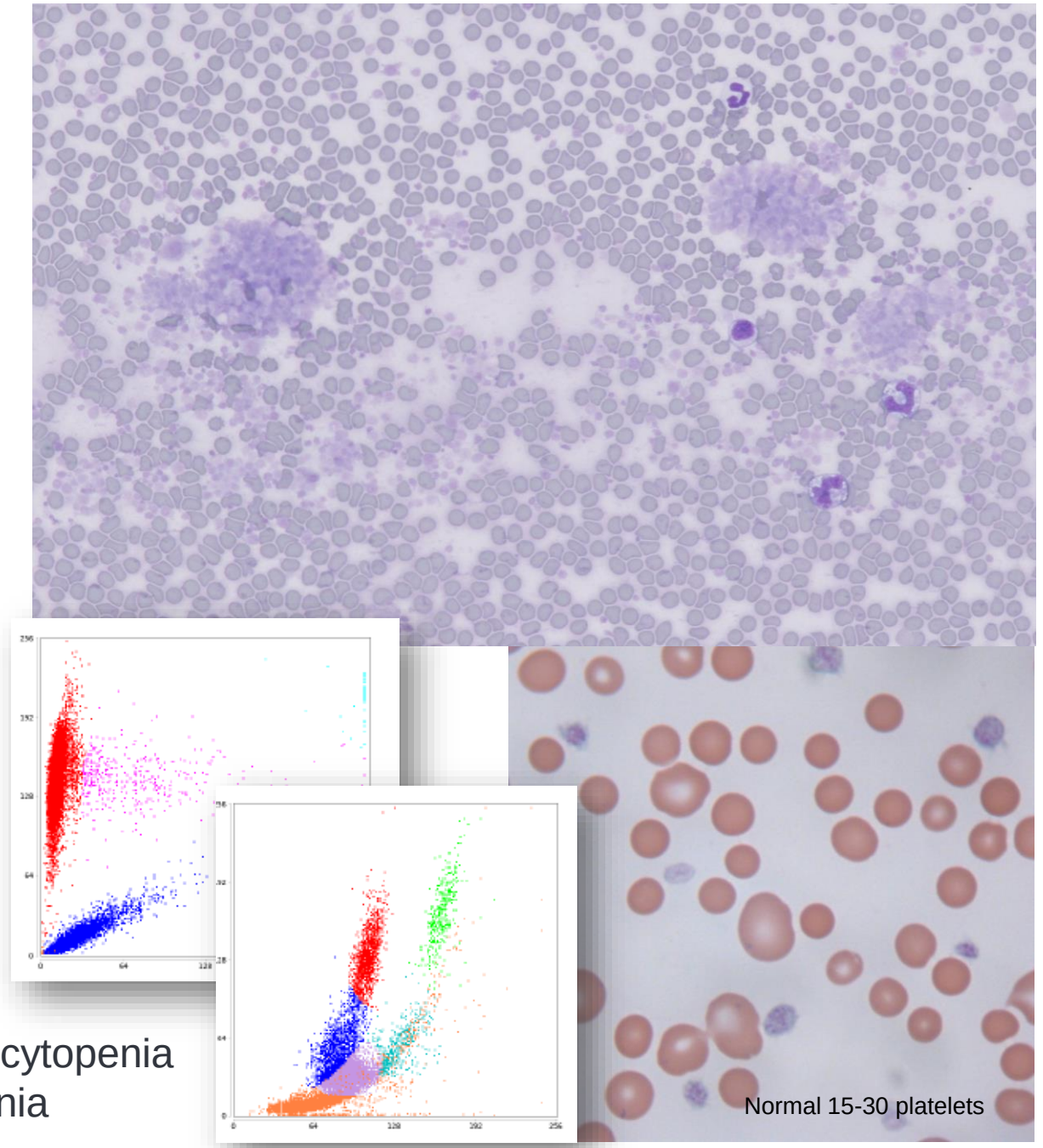
1. Count number of platelets in 10 fields oil immersion in monolayer

2. Do the average (Σ /10)

3. Multiply by 15 or 20

4. This is the ***estimated*** number

   (x 10^9/L)



Normal 15-30 platelets

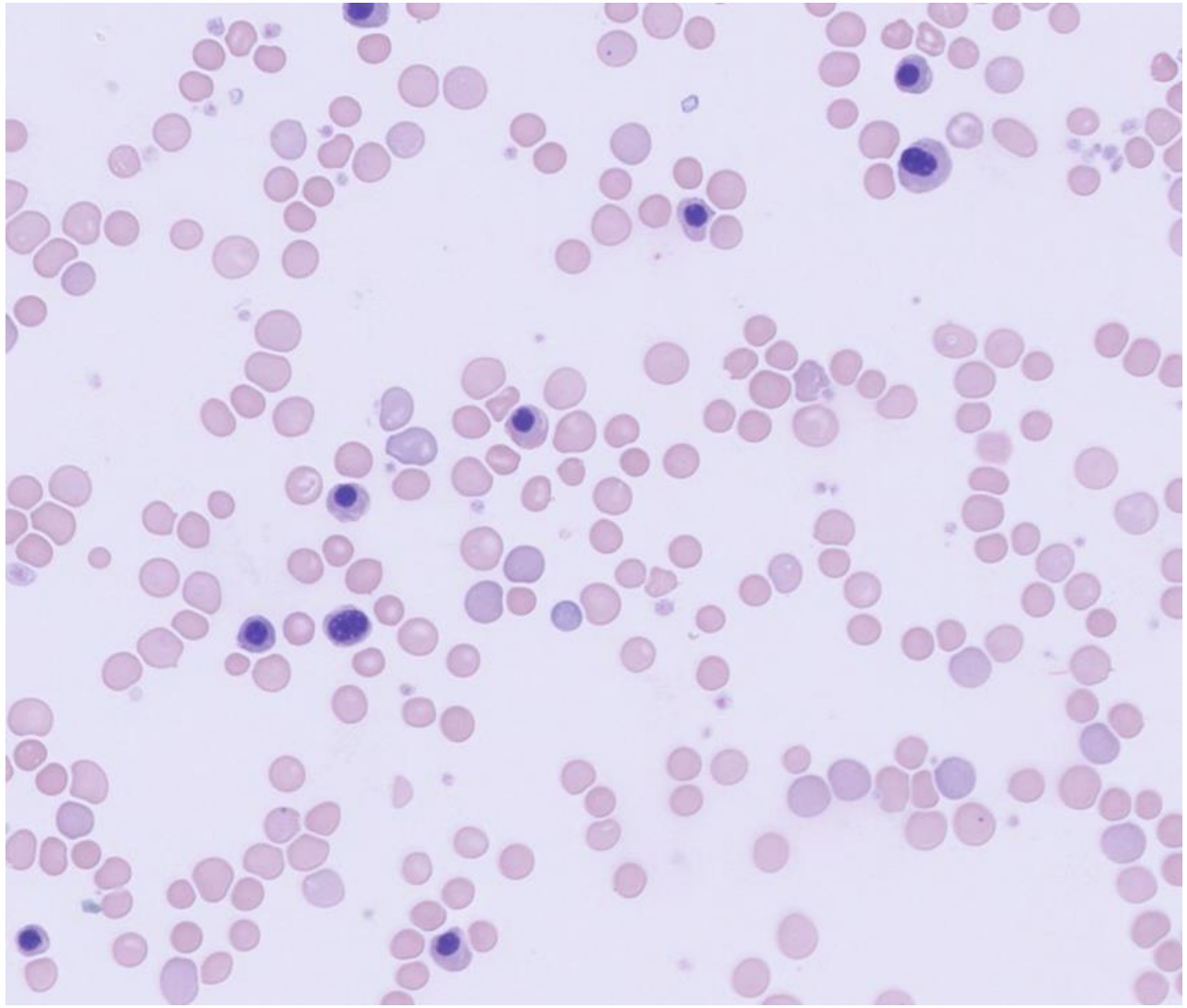
>10 per HPF = no significant thrombocytopenia
<2 per HPF = marked thrombocytopenia

For the RBC we are evaluating 3 main things…

+ Density and spread
  + Agglutination

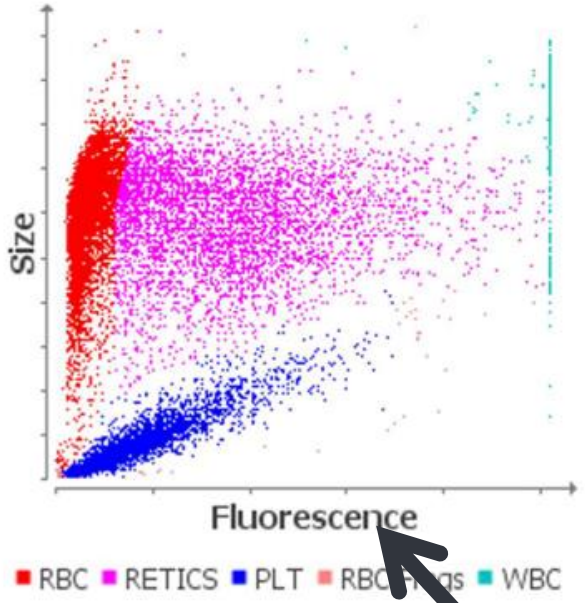
+ Colour
  + Polychromasia
  + Hypochromasia

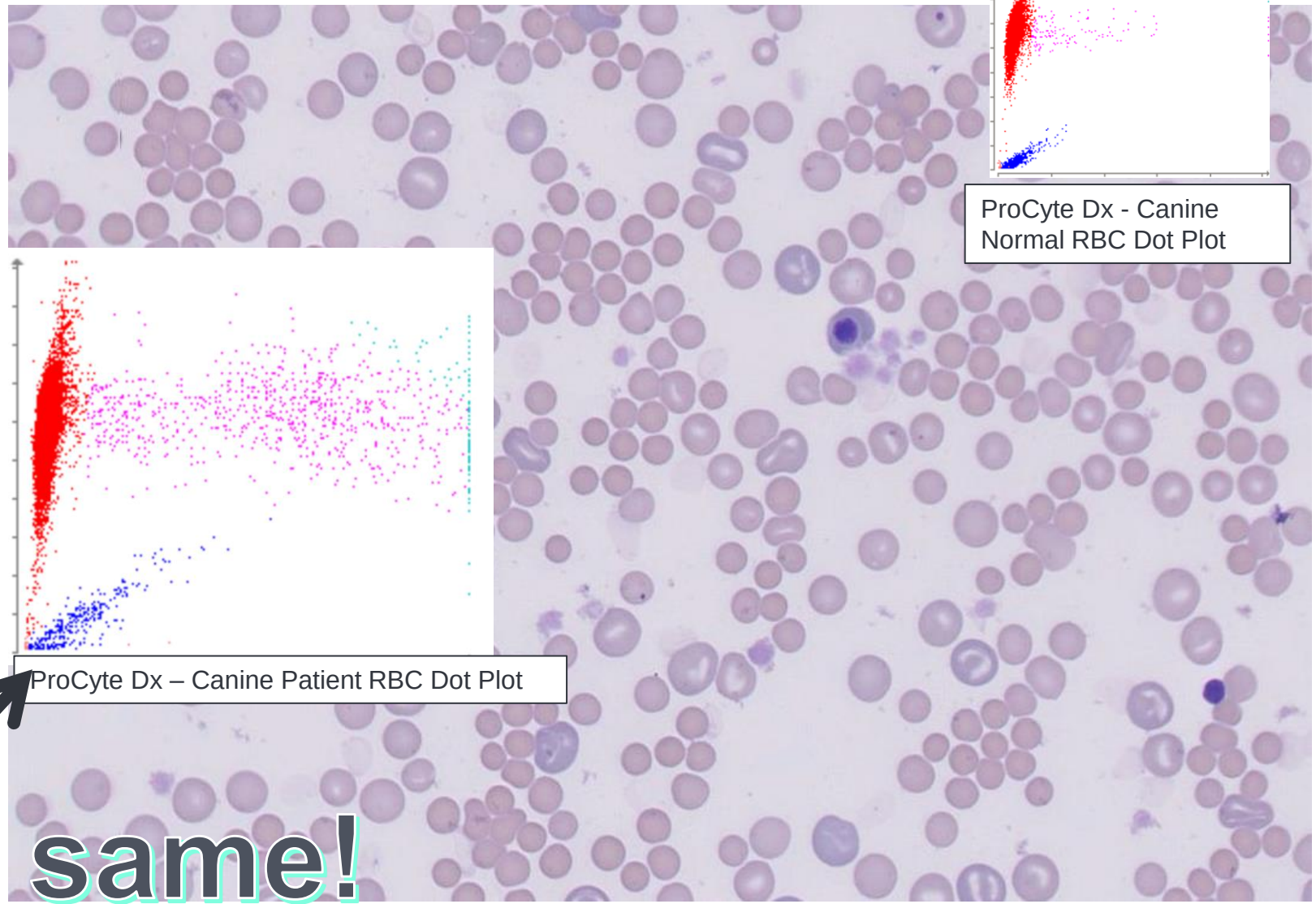
+ Size, shapes and inclusions
  + nRBC
  + Heinz bodies
  + Spherocytes and ghost cells
  + Poikilocytes



Red blood cell abnormalities

+ Polychromasia





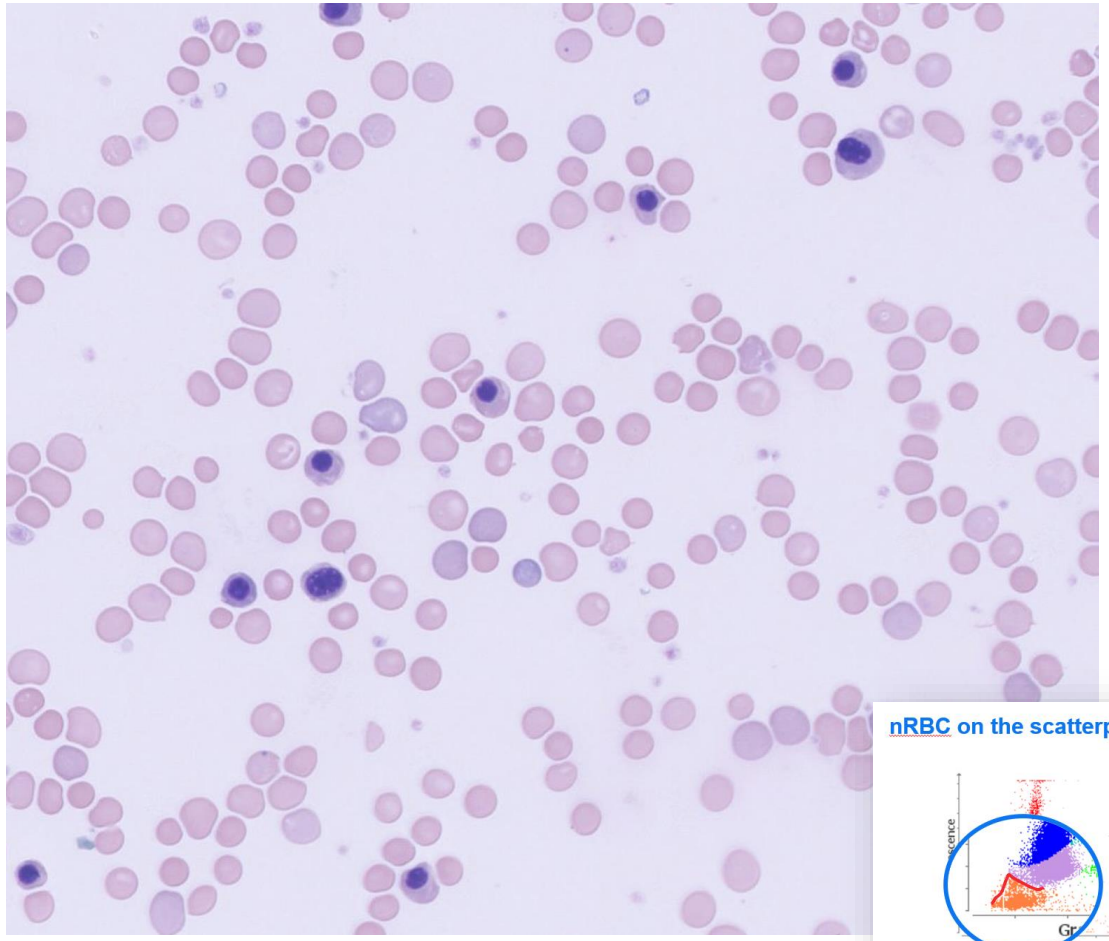
ProCyte Dx - Canine
Normal RBC Dot Plot

ProCyte Dx – Canine Patient RBC Dot Plot

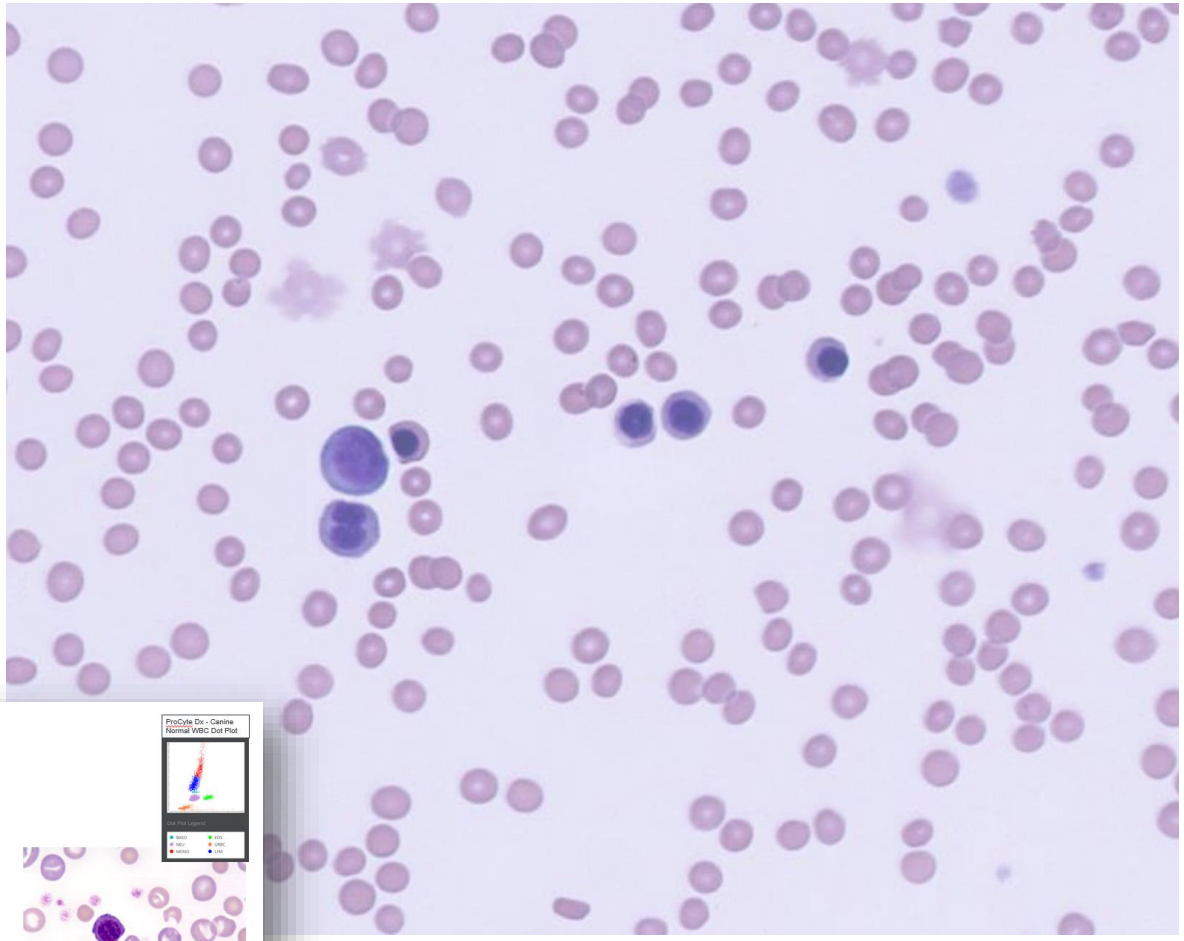
Not the same!

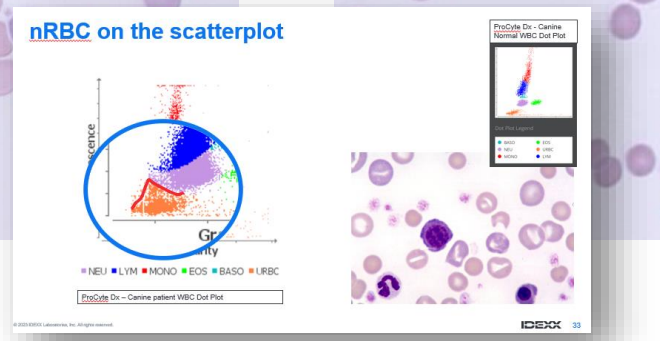
Nucleated RBC

As part of regeneration

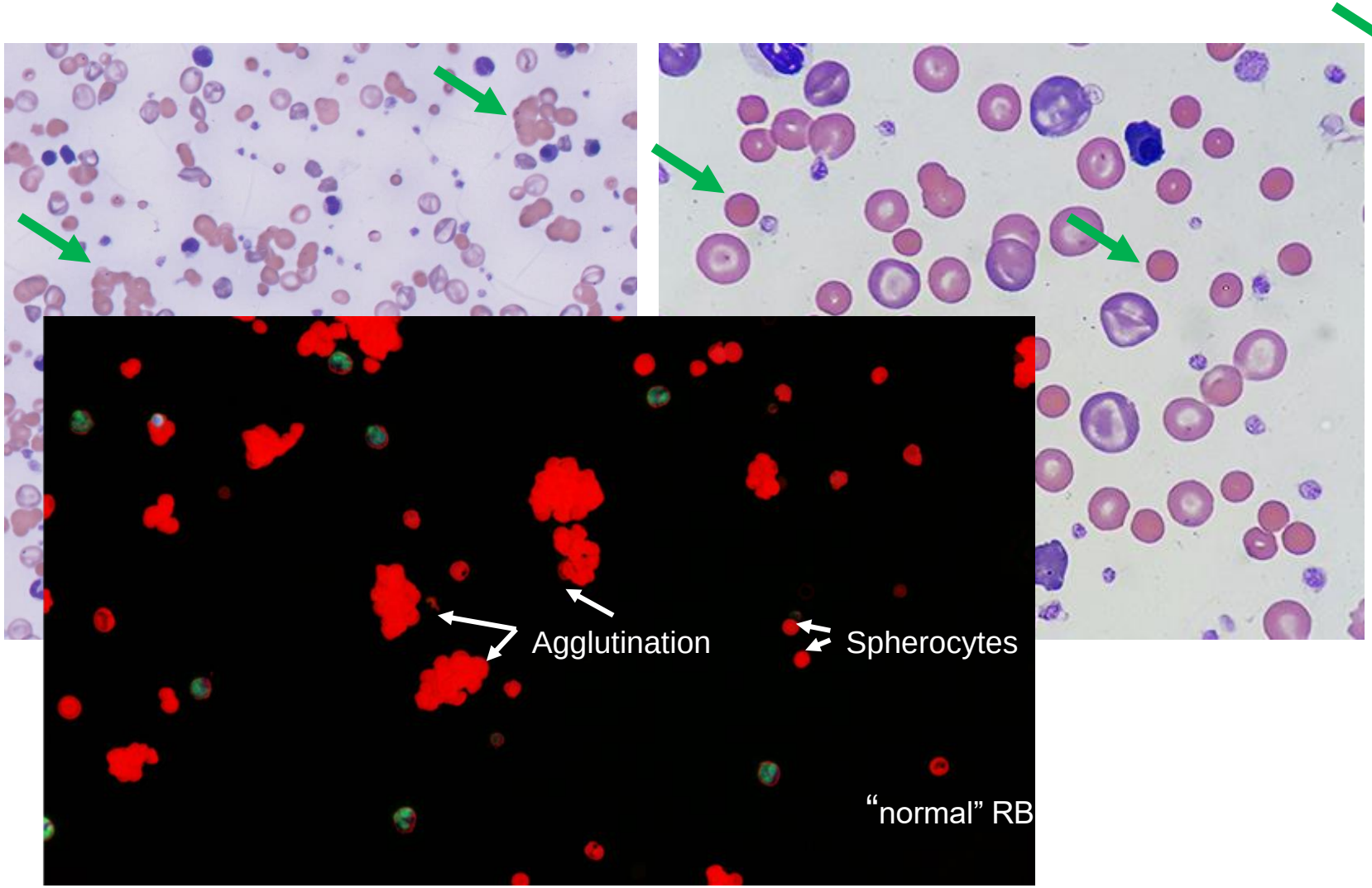


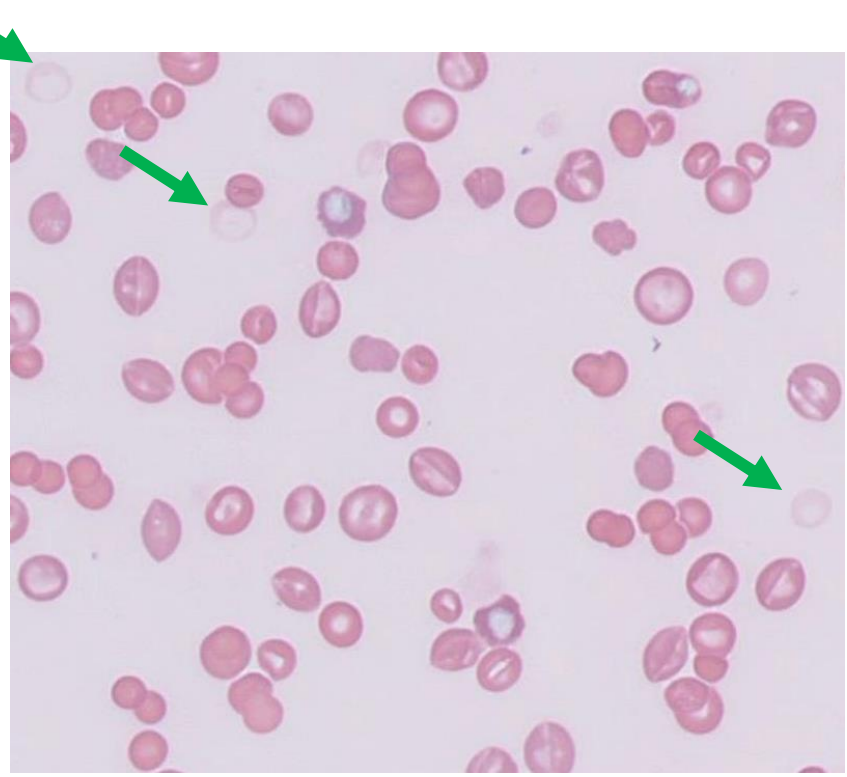
Inappropriate rubricytosis





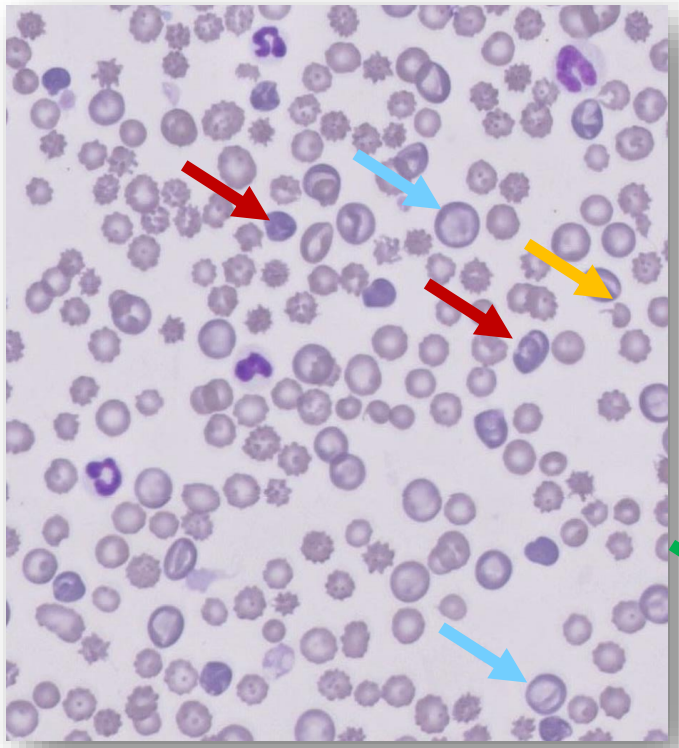
Features suggestive of **immune mediated haemolytic anaemia**



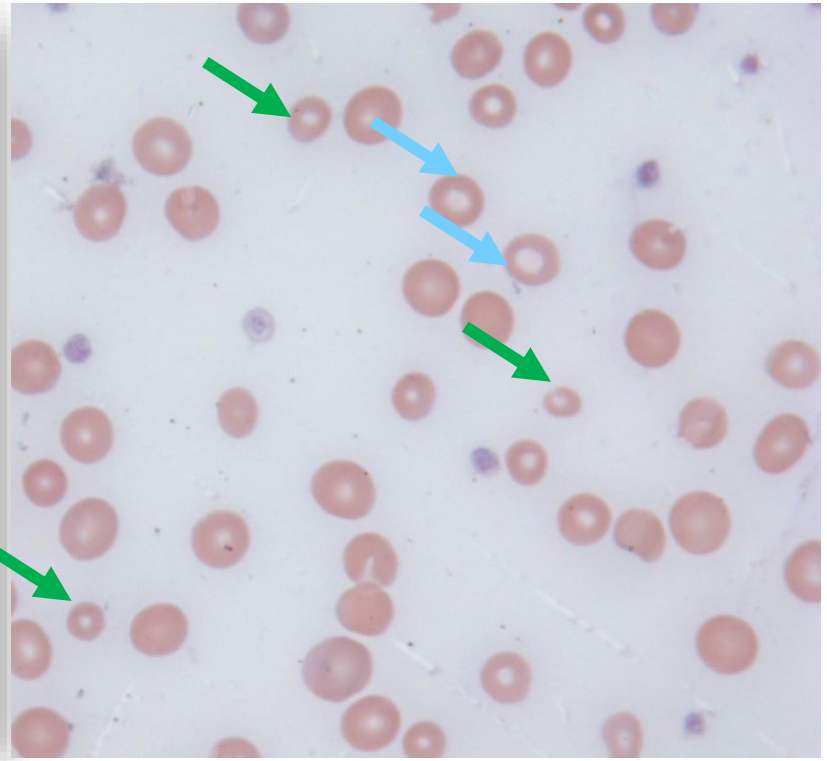


Ghost cells (fresh smear)

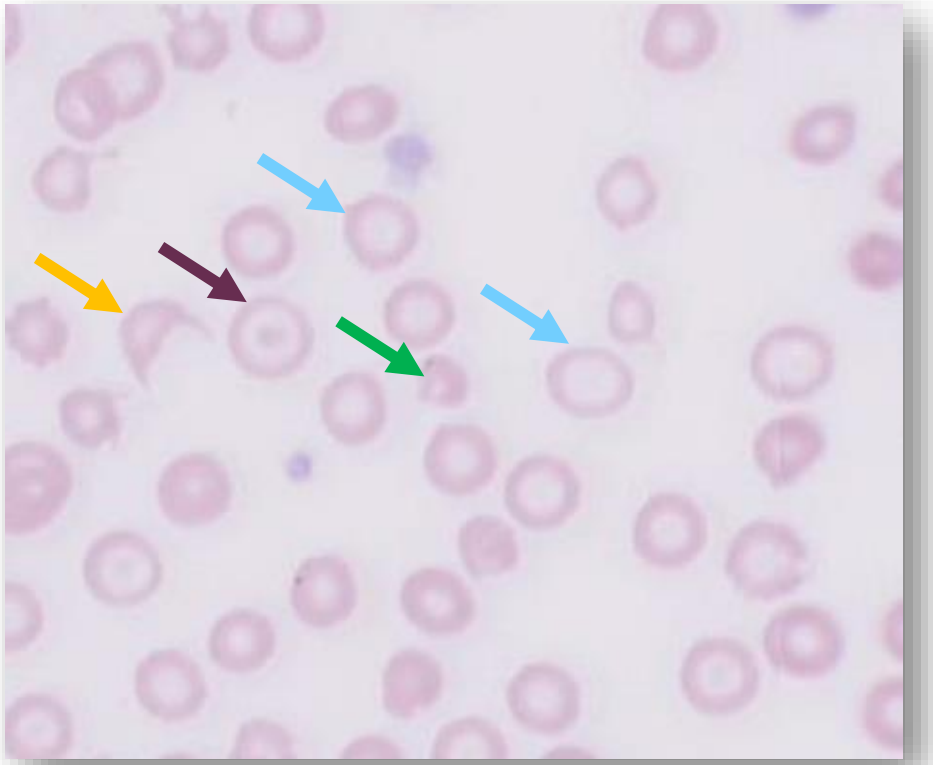
Features seen with **iron deficiency anaemia**



Regeneration variable
Anisocytosis present

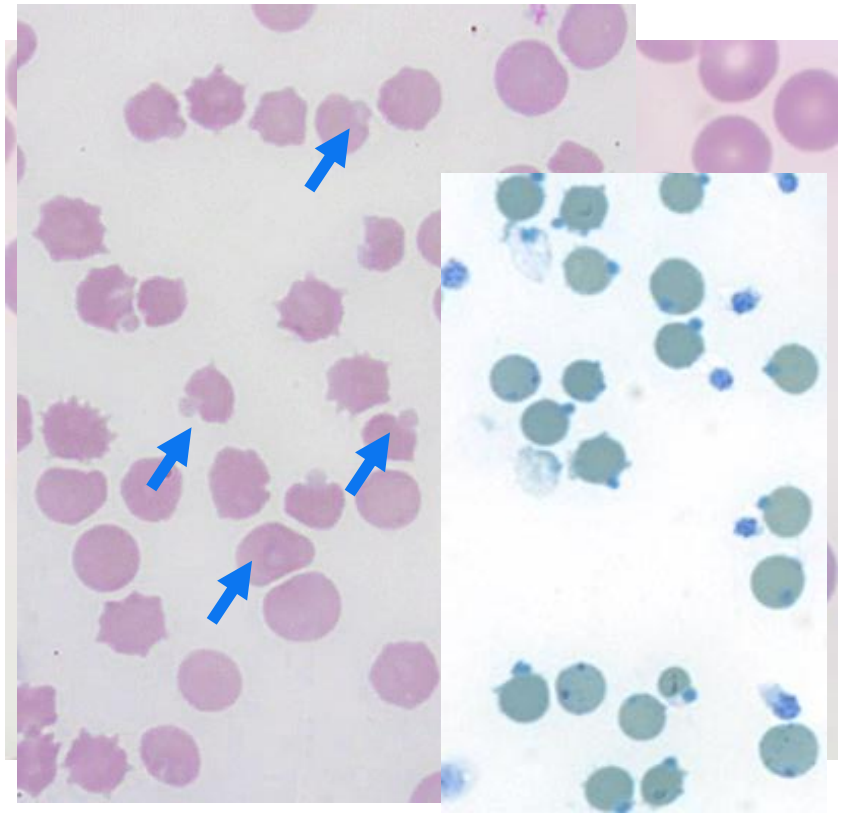


Microcytosis and
hypocromasia

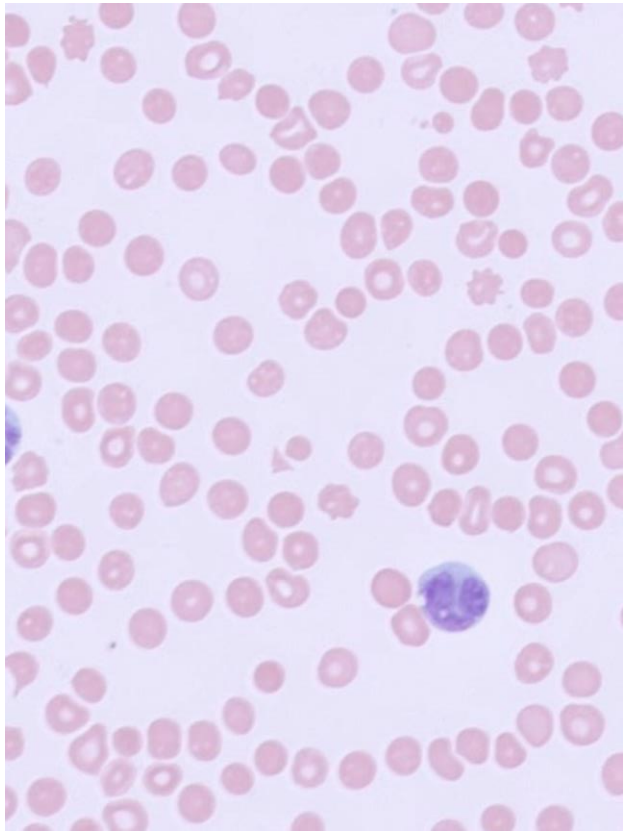


Poikilocytosis
codocytes
schistocyes

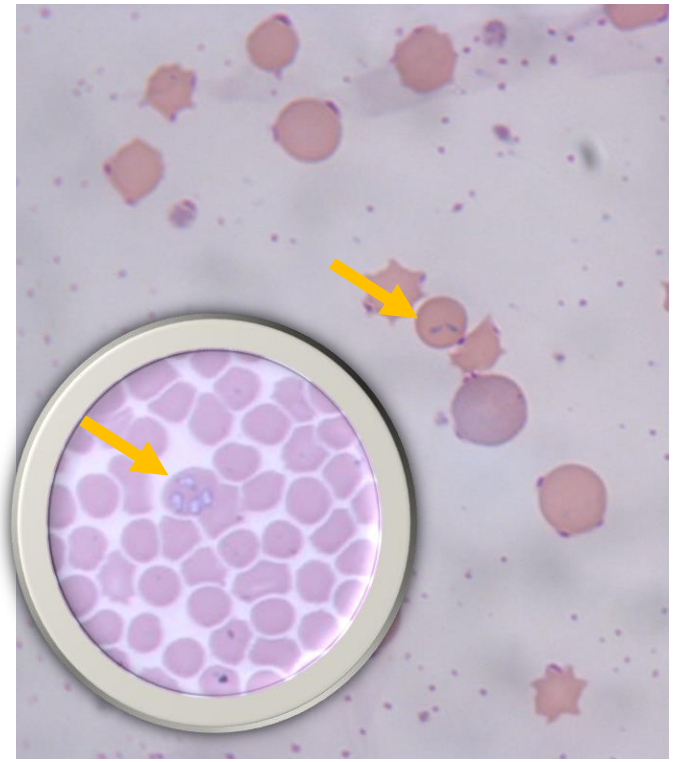
Other interesting features in regenerative **anaemias**



Heinz bodies
Eccentrocytes



Shear injury and spherocytes

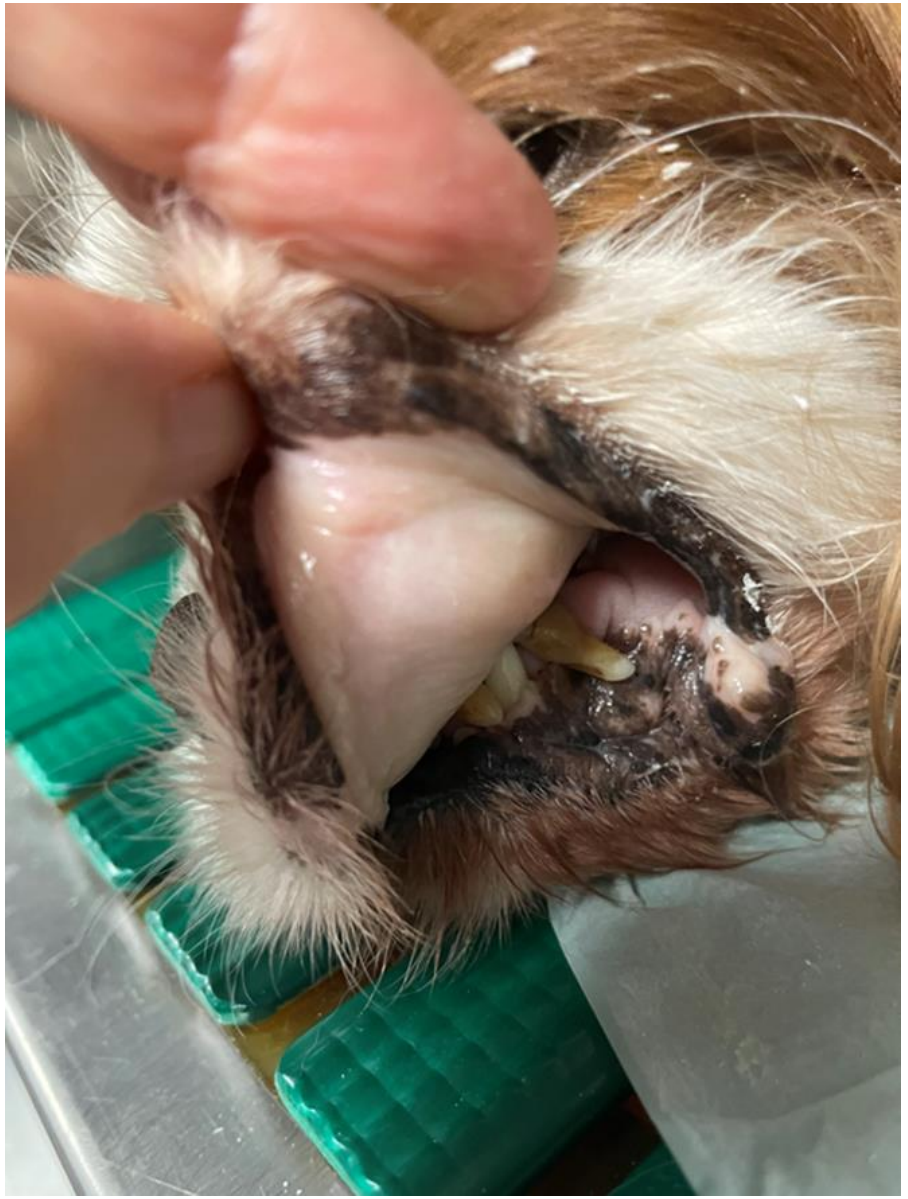


Intraerythrocytic parasites

Non-Regenerative Anaemia

Non-regenerative Anaemia

- Peracute haemorrhage
  - Pre-regenerative
- Inflammatory disease
  - Mild non-regen anaemia
- Chronic kidney disease
  - Can be severe anaemia
- Chronic GI blood loss
- Bone marrow disease
- Vector borne disease
  - *Ehrlichia/Anaplasma/Babesia*



First steps for non-regenerative anaemia

+ Consider if acute onset
  + Pre regenerative

+ Full CBC with film exam
  + Concurrent cytopenias?
  + Abnormal cells?
  + Reticulocyte haemoglobin

+ Check biochemistry
  + Azotaemia?

+ FeLV and FIV testing in cats

+ Vector borne disease testing in dogs
  + *Ehrlichia/Anaplasma/Babesia*

RBC	**4.10**	6.54 - 12.20 x10^12/L
Haematocrit	**0.177**	0.303 - 0.523 L/L
Haemoglobin	**59**	98 - 162 g/L
MCV	43.2	35.9 - 53.1 fL
MCH	14.4	11.8 - 17.3 pg
MCHC	333	281 - 358 g/L
RDW	18.1	15.0 - 27.0 %
% Reticulocytes	0.4	%
Reticulocytes	17.6	3.0 - 50.0 K/µL
Reticulocyte Haemoglobin	13.6	13.2 - 20.8 pg

Reticulocyte Haemoglobin

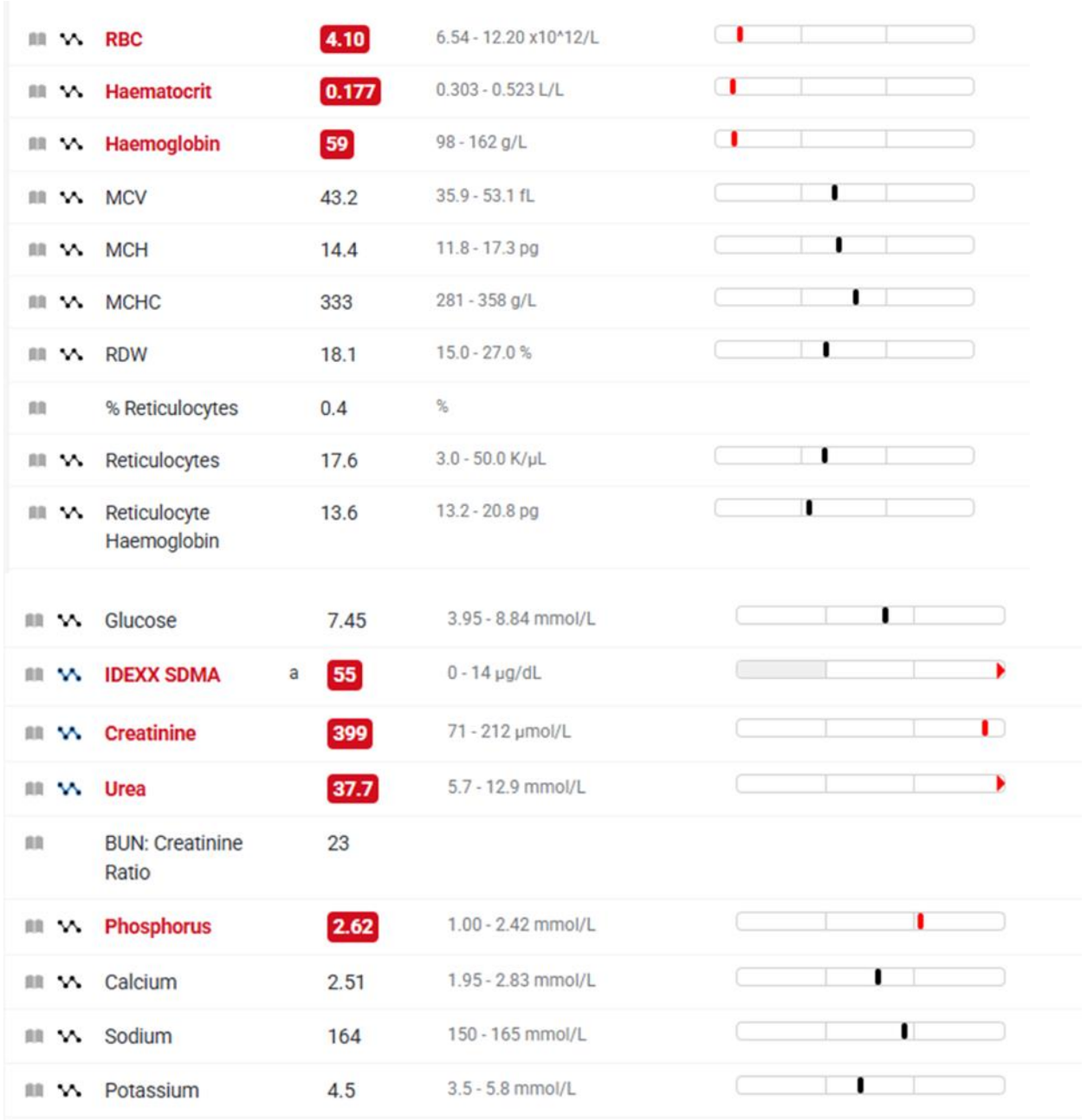
RBC	4.32	5.39 - 8.70 x10^12/L	
Haematocrit	0.289	0.383 - 0.565 L/L	
Haemoglobin	101	134 - 207 g/L	
MCV	66.9	59.0 - 76.0 fL	
MCH	23.4	21.9 - 26.1 pg	
MCHC	349	326 - 392 g/L	
Reticulocytes a	60.0	<= 110.0 K/µL	
Reticulocyte Haemoglobin	20.1	24.5 - 31.8 pg	

+ Sensitive indicator of decreased iron availability

+ DDx
  + Blood loss
    + Haemorrhage
    + Parasitism
  + Chronic Inflammation
    + (iron sequestration)

Anaemia with CKD

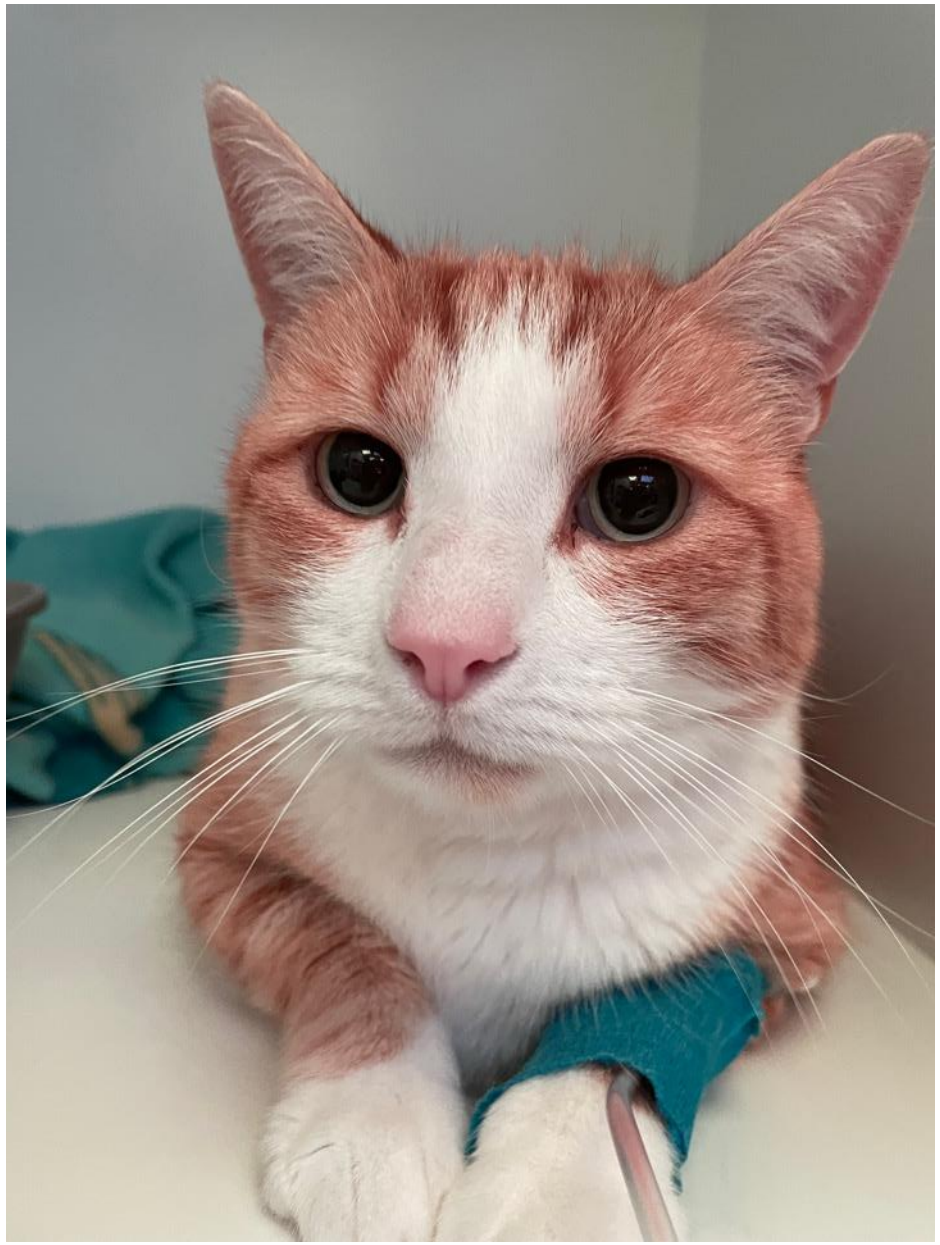
- Can result in severe non regenerative anaemia
- Lack of EPO production
- Treatment
  - Transfusions?
  - rhEPO- Darbopoietin?
  - Varenzin



RBC		4.10	6.54 - 12.20 x10^12/L
Haematocrit		0.177	0.303 - 0.523 L/L
Haemoglobin		59	98 - 162 g/L
MCV		43.2	35.9 - 53.1 fL
MCH		14.4	11.8 - 17.3 pg
MCHC		333	281 - 358 g/L
RDW		18.1	15.0 - 27.0 %
% Reticulocytes		0.4	%
Reticulocytes		17.6	3.0 - 50.0 K/µL
Reticulocyte Haemoglobin		13.6	13.2 - 20.8 pg
Glucose		7.45	3.95 - 8.84 mmol/L
IDEXX SDMA	a	55	0 - 14 µg/dL
Creatinine		399	71 - 212 µmol/L
Urea		37.7	5.7 - 12.9 mmol/L
BUN: Creatinine Ratio		23	
Phosphorus		2.62	1.00 - 2.42 mmol/L
Calcium		2.51	1.95 - 2.83 mmol/L
Sodium		164	150 - 165 mmol/L
Potassium		4.5	3.5 - 5.8 mmol/L

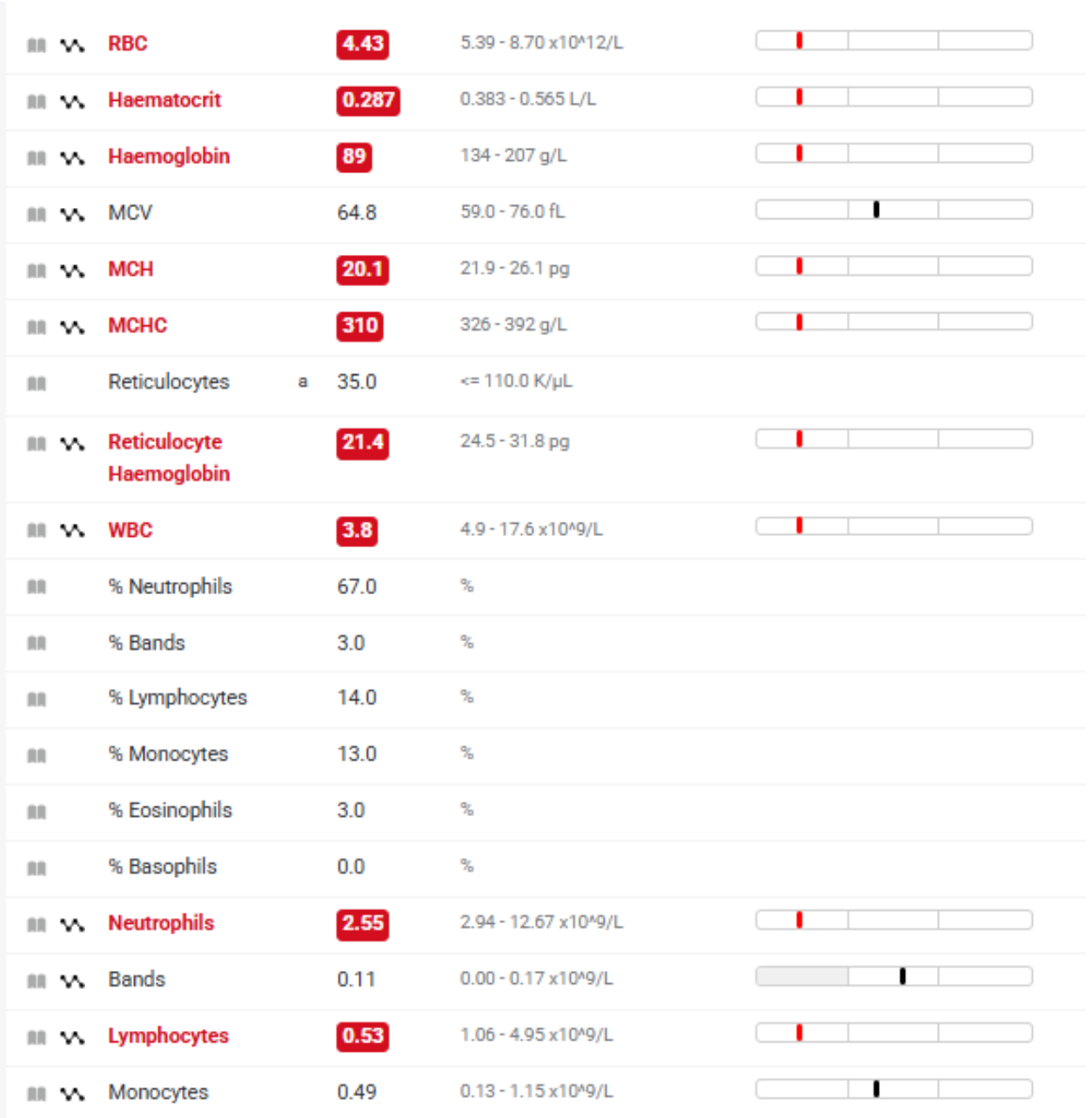
Future Horizons

- Varenzin- CA1
  - Molidustat
  - HIF-PH inhibitor
  - Increases EPO production by kidneys
- Control of non-regenerative anaemia with CKD
  - 5mg/kg orally SID for up to 28 days
  - Can be repeated after 7 day pause
- Side effects
  - Vomiting
  - Hypertension
  - Thromboembolism



Bone Marrow Biopsy Indications

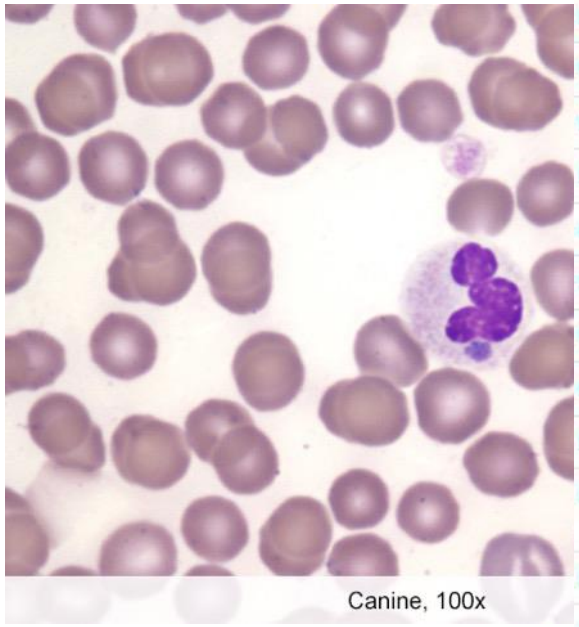
+ Unexplained non regenerative anaemia
  + Having excluded other causes
+ Bi- or pancytopenia
+ Suspicion of non-regenerative IMHA

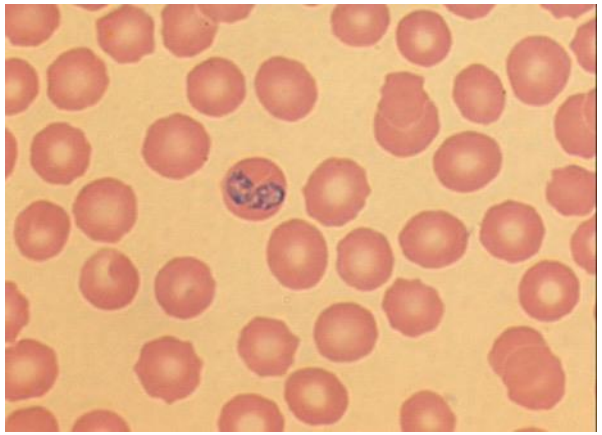


RBC	4.43	5.39 - 8.70 x10^12/L	
Haematocrit	0.287	0.383 - 0.565 L/L	
Haemoglobin	89	134 - 207 g/L	
MCV	64.8	59.0 - 76.0 fL	
MCH	20.1	21.9 - 26.1 pg	
MCHC	310	326 - 392 g/L	
Reticulocytes a	35.0	<= 110.0 K/µL	
Reticulocyte Haemoglobin	21.4	24.5 - 31.8 pg	
WBC	3.8	4.9 - 17.6 x10^9/L	
% Neutrophils	67.0	%	
% Bands	3.0	%	
% Lymphocytes	14.0	%	
% Monocytes	13.0	%	
% Eosinophils	3.0	%	
% Basophils	0.0	%	
Neutrophils	2.55	2.94 - 12.67 x10^9/L	
Bands	0.11	0.00 - 0.17 x10^9/L	
Lymphocytes	0.53	1.06 - 4.95 x10^9/L	
Monocytes	0.49	0.13 - 1.15 x10^9/L	

Vector Borne Disease

- *Ehlichia sp*
- *Anaplasma sp*
- *Babesia sp*


Canine, 100x

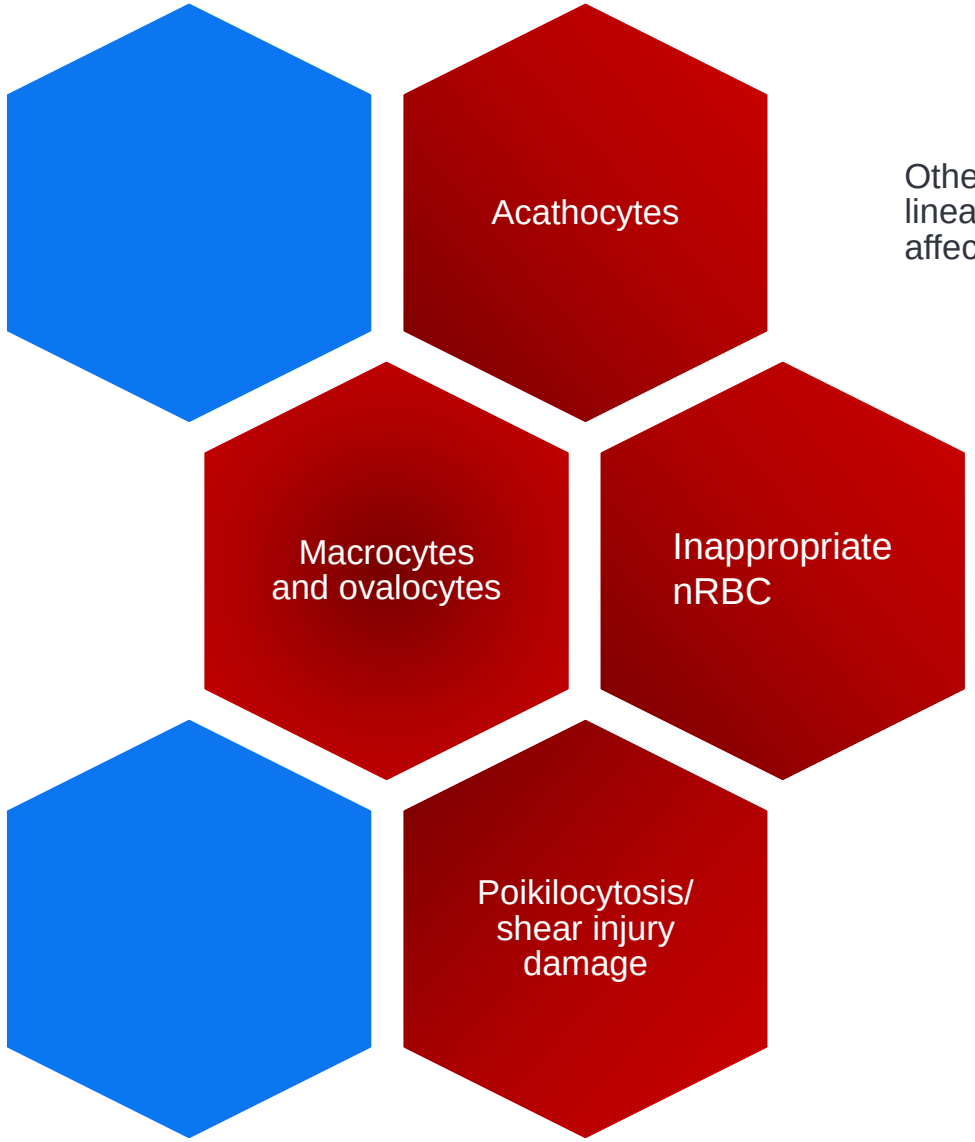


RBC	5.42	5.65 - 8.87 x10^12/L	
Haematocrit	0.379	0.373 - 0.617 L/L	
Haemoglobin	129	131 - 205 g/L	
MCV	69.9	61.6 - 73.5 fL	
MCH	23.8	21.2 - 25.9 pg	
MCHC	340	320 - 379 g/L	
RDW	17.8	13.6 - 21.7 %	
% Reticulocyte	0.5	%	
Reticulocytes	26.0	10.0 - 110.0 K/µL	
Reticulocyte Haemoglobin	25.2	22.3 - 29.6 pg	
WBC	3.01	5.05 - 16.76 x10^9/L	
% Neutrophils	39.9	%	
% Lymphocytes	56.1	%	
% Monocytes	3.0	%	
% Eosinophils	1.0	%	
% Basophils	0.0	%	
Neutrophils	1.20	2.95 - 11.64 x10^9/L	
Lymphocytes	1.69	1.05 - 5.10 x10^9/L	
Monocytes	0.09	0.16 - 1.12 x10^9/L	
Eosinophils	0.03	0.06 - 1.23 x10^9/L	
Basophils	0.00	0.00 - 0.10 x10^9/L	
Platelets	*7	148 - 484 x10^9/L	

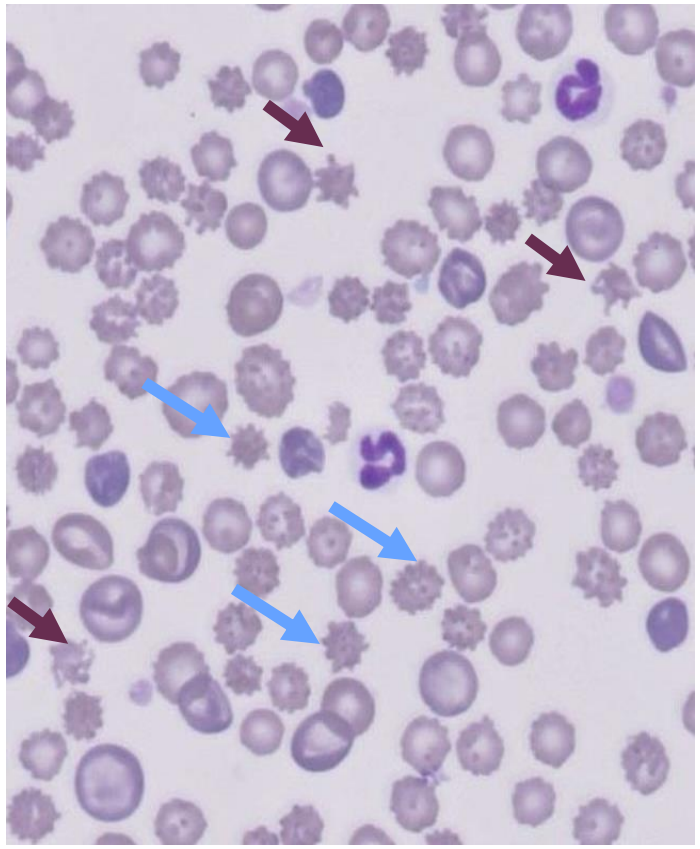
Anaemia

Non-regenerative

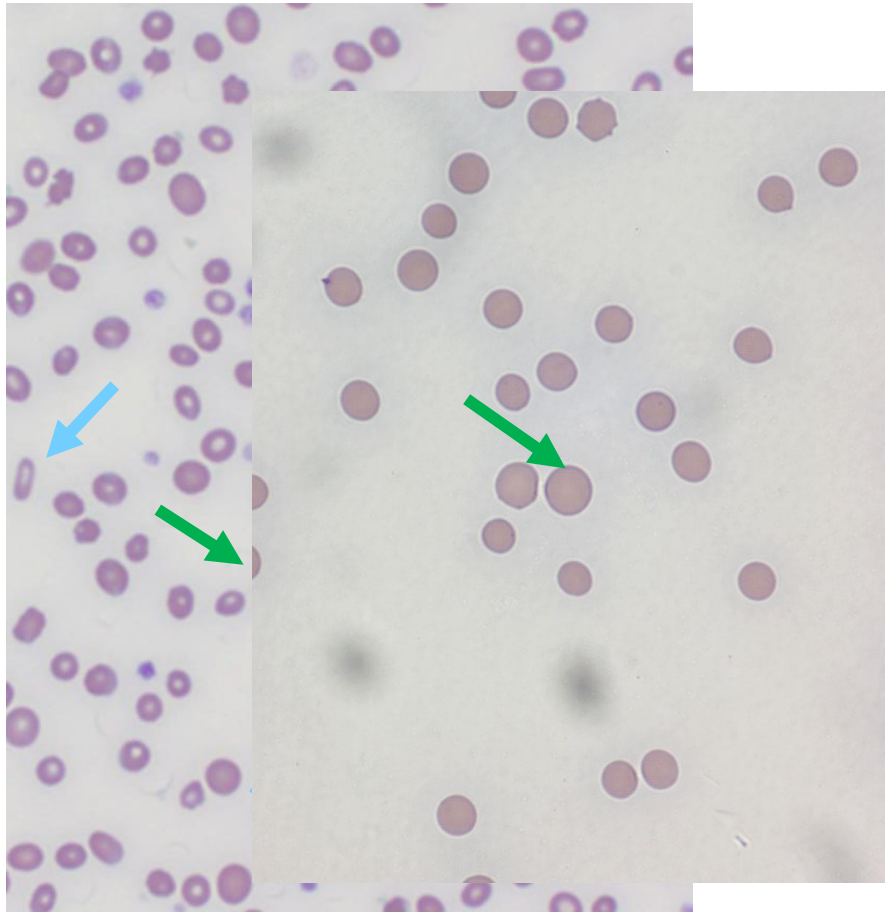
- Chronic Disease
- Bone Marrow Disease
- Renal Disease
- Per-acute blood loss
- Vector borne disease/retroviruses



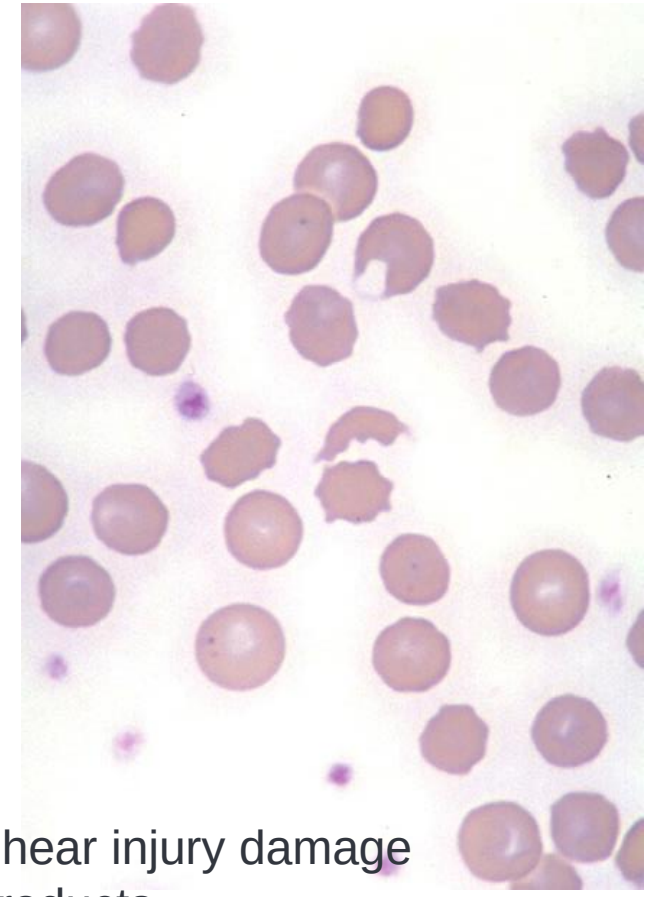
Possible interesting features in **non-regenerative anaemias**



Acanthocytes vs
Echinocytes



Macrocytes /ovalocytes



Shear injury damage products

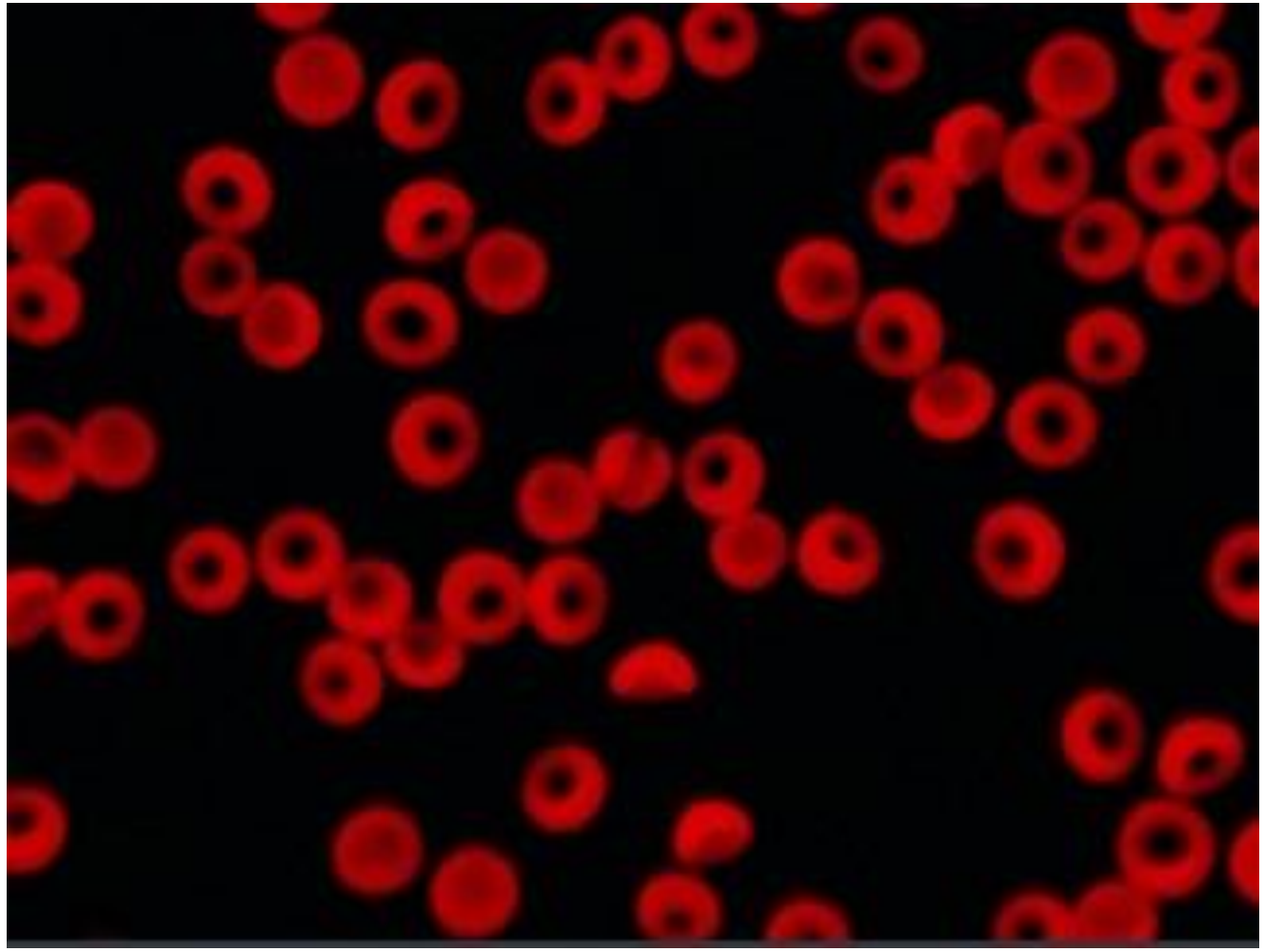
schistocytes
keratocytes

For submission of blood smears

- Blood smears and tubes are labeled with 1-2 unique patient IDs and date of collection.
- Good quality smears.
- Unstained smears are preferred.
- Stored at room temperature and sent in slide carriers
- Accompanied by available instrument derived data and relevant clinical history.

Summary

- Anaemia is a symptom NOT a diagnosis
- Logical work up depends on determining whether anaemia is regenerative or non-regenerative
- Film examination essential!!!



Any Questions?