“What? When You Read A CBC You Only Look At The Numbers?”

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My Patient Is Sick But Has A Normal White Count: Should I Worry?

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Disclosure

- I am an internist and oncologist, not a clinical pathologist
- I am a consultant with Idexx
- I have used Idexx hematology equipment for 20 years
- Thanks to Dr. DeNicola, Dr. Peta, and Dr. Yore, and to RACC

Today's Program

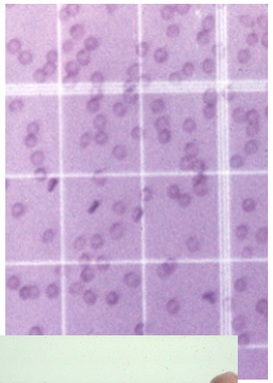
- Leukocytes
- Analyzers
- Total WBC versus differential count
- Case discussions

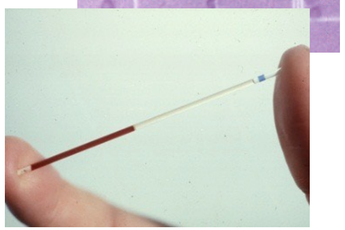
Do you interpret CBC results the same way in a healthy than in a sick pet?

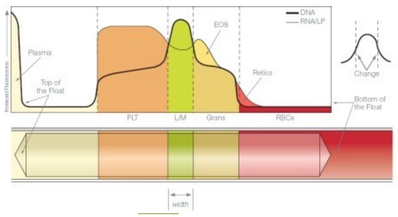
Do you look at <u>all</u> the blood smears?

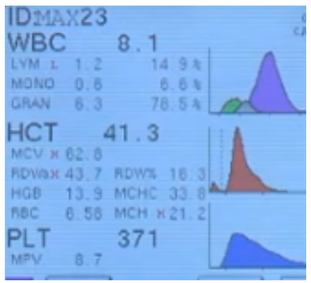
In-House Hematology Analyzers

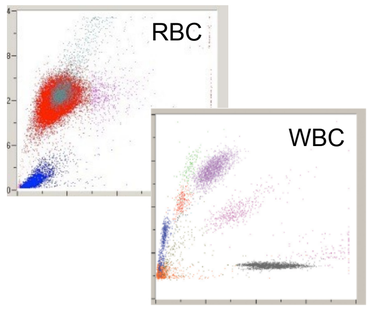
pre1980s	1980s	1990s	2003	2010	2021
Manual	Quantitative Buffy coat (QBC)	Impedance	LaserCyte	ProCyte Dx	ProCyte One

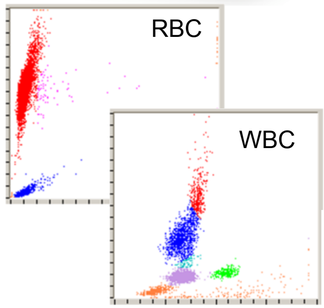


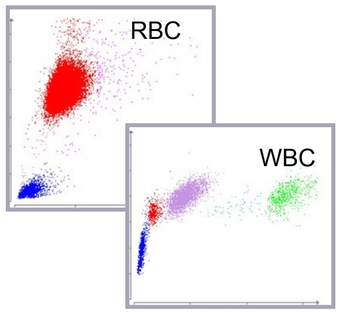




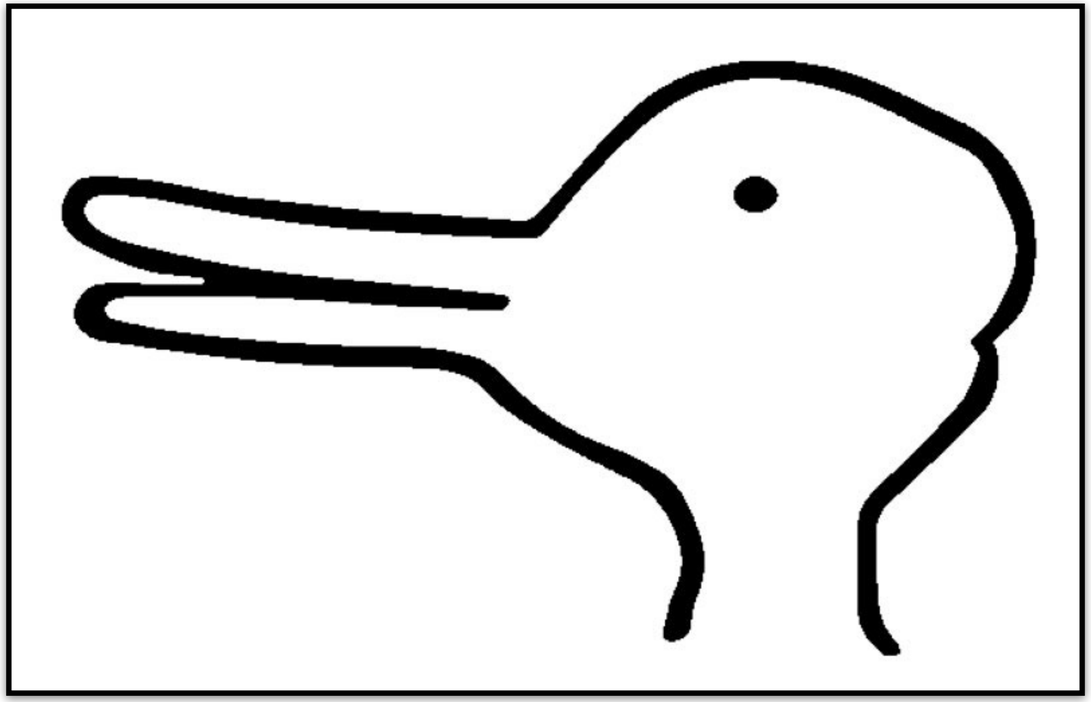






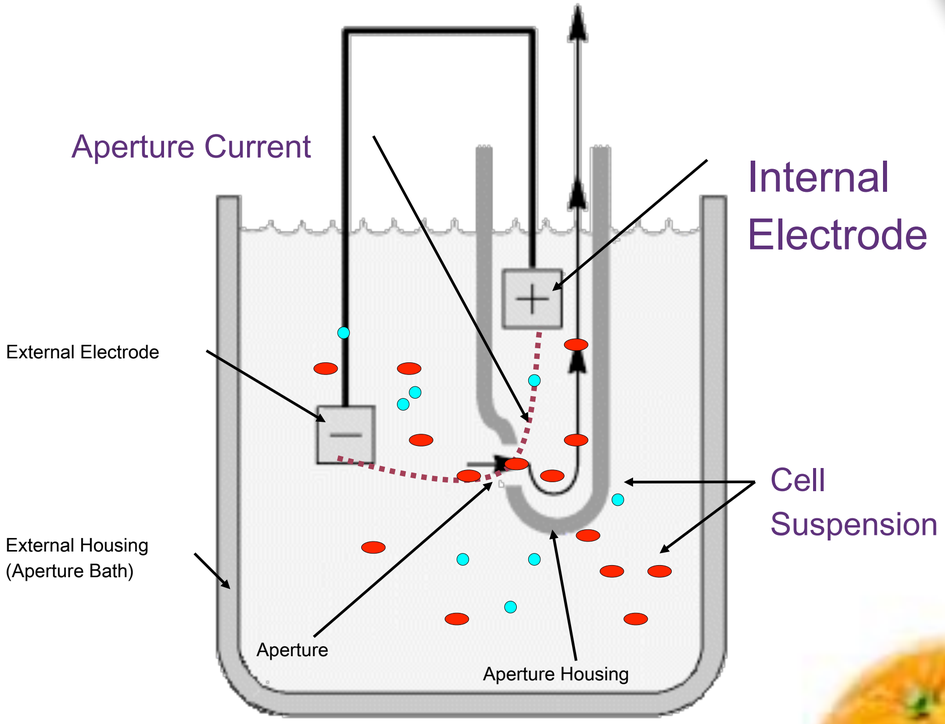


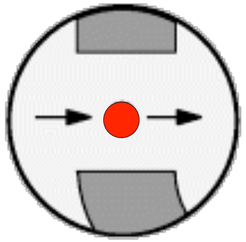
Do you look at the graphics from the analyzer?



Impedance Analyzer

Change in resistance is proportional to cell volume

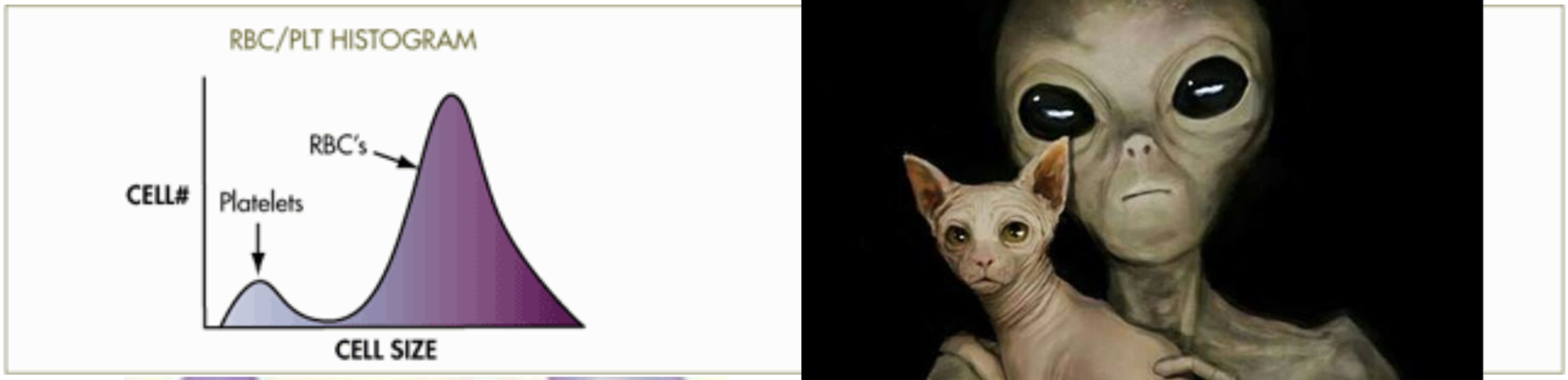


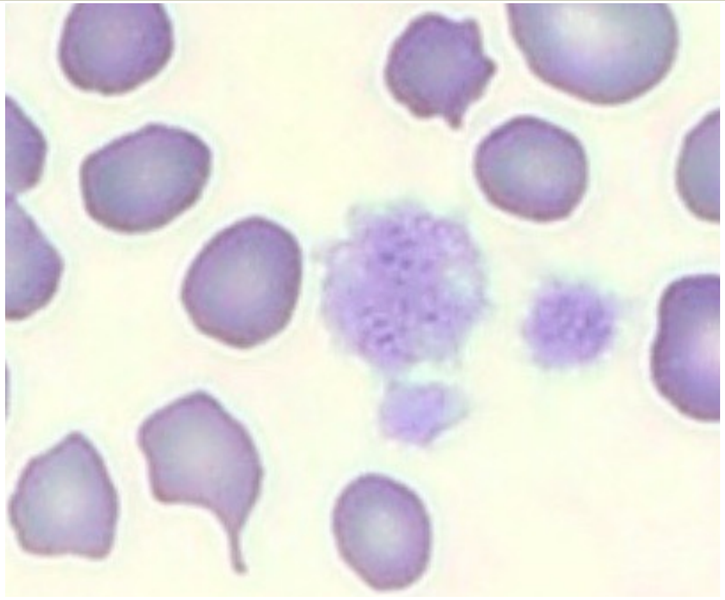


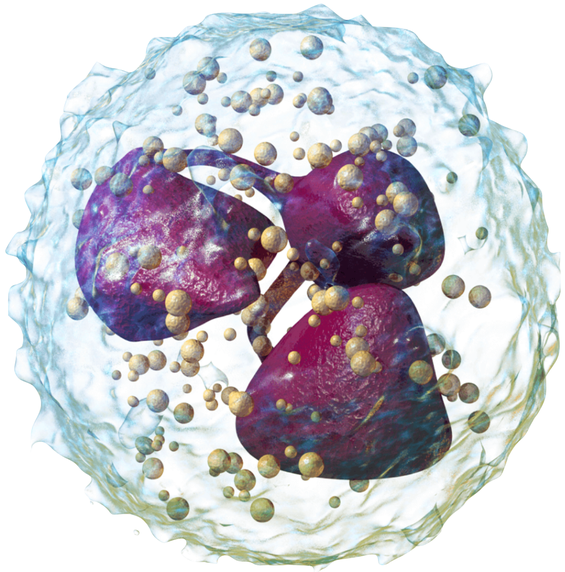
Detail of Aperture

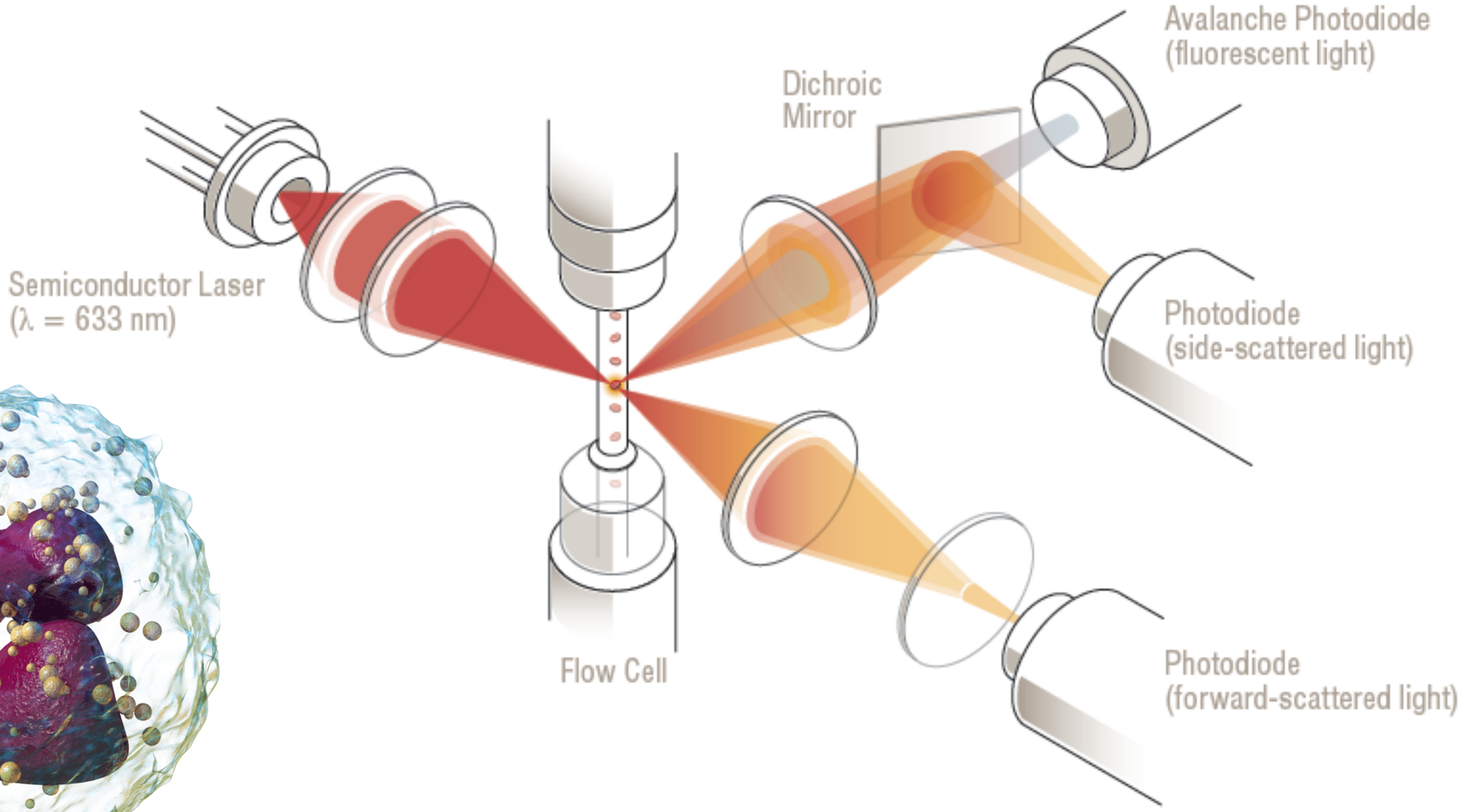
Courtesy Dr. Bill Saxon

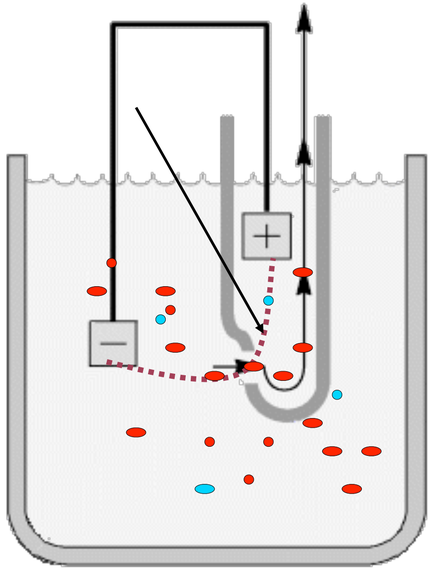
Impedance Analyzer

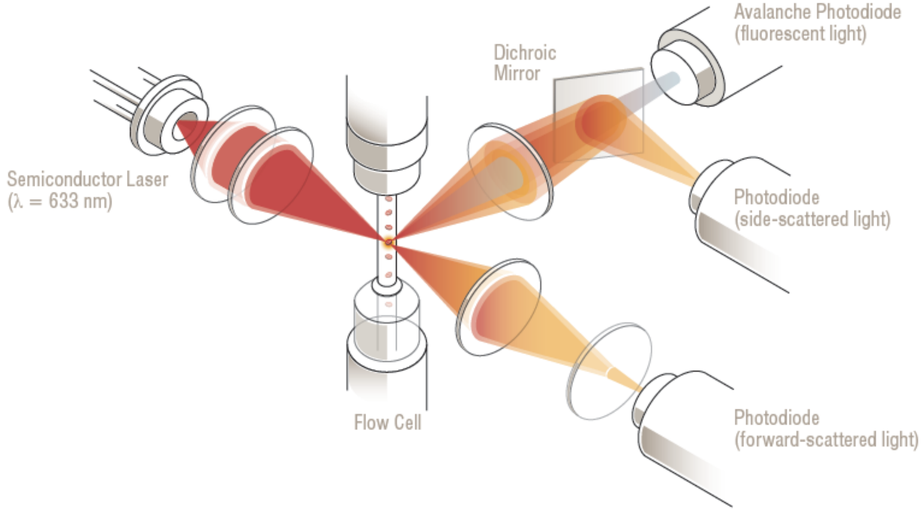




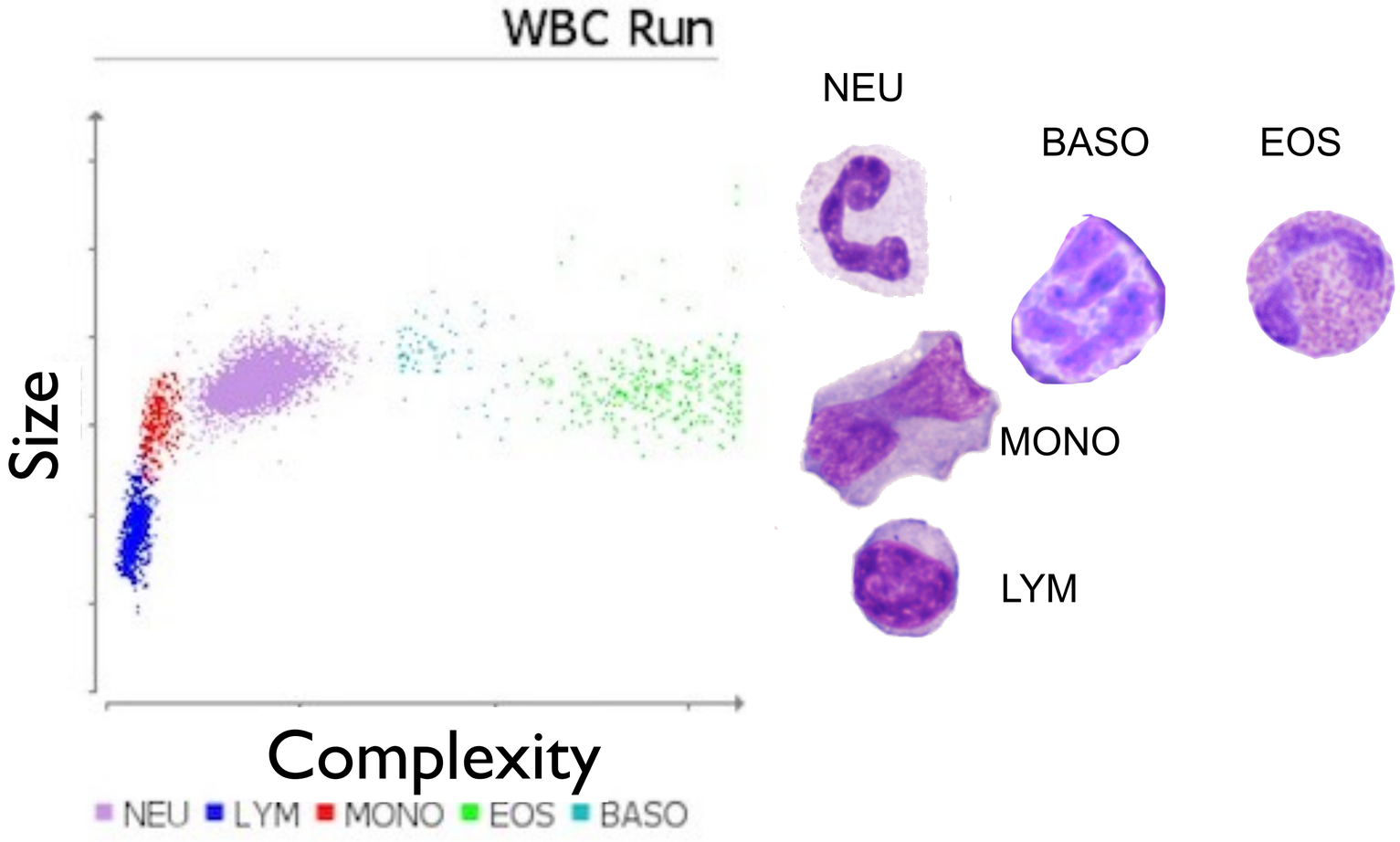



Avalanche Photodiode
(fluorescent light)
Dichroic
Mirror
Semiconductor Laser
(λ = 633 nm)
Photodiode
(side-scattered light)
Flow Cell
Photodiode
(forward-scattered light)

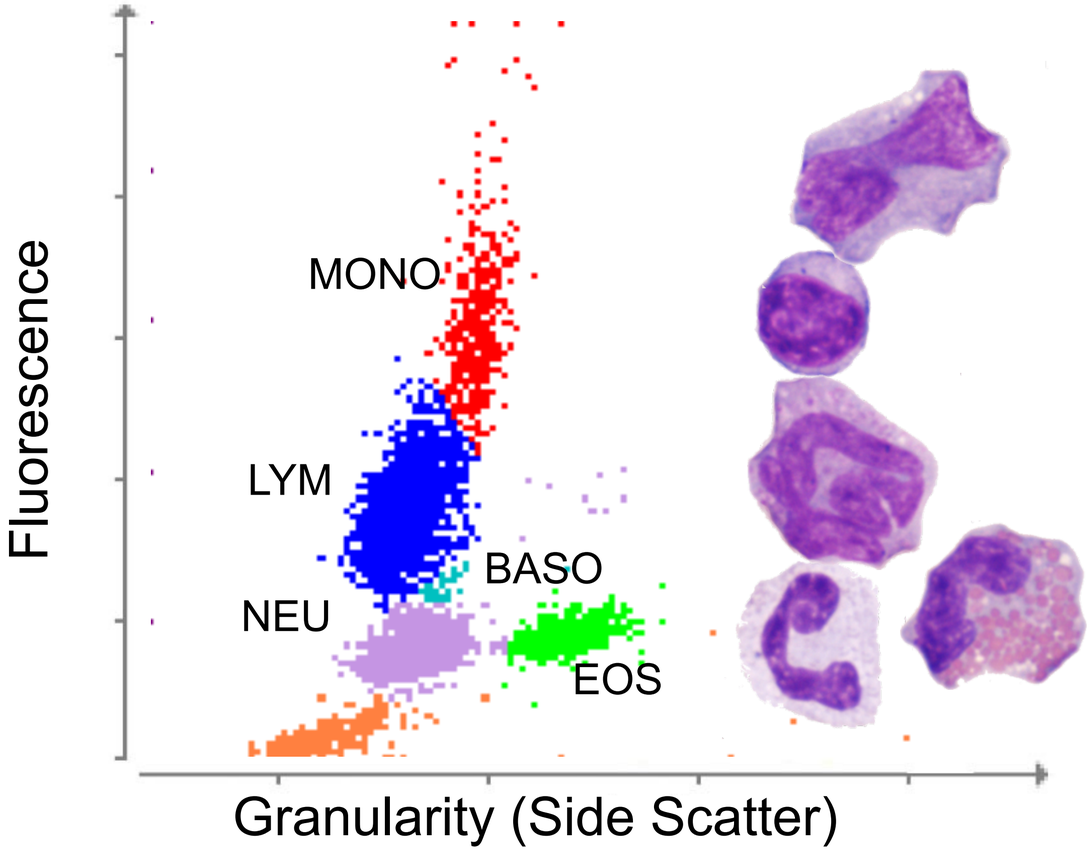




Courtesy Dr. Bill Saxon


WBC Run
Size
Complexity
NEU
LYM
MONO
EOS
BASO

NEU
BASO
EOS
MONO
LYM


Fluorescence
MONO
LYM
BASO
NEU
EOS
Granularity (Side Scatter)


IDEXX ProCyte Dx
IDEXX

Total and Differential WBC Counts

- Hand count
  - ***100 cells***
- Flow cytometer
  - ***12,000-15,000 cells***

Common Leukogram Patterns

Leukocyte Type	Moderate Inflammation	Glucocorticoids ("Stress")	Epinephrine ("Excitement")
Mature Neutrophil	↑ - ↑↑	↑ - ↑↑	N - ↑
Band Neutrophil	↑ - ↑↑	N	N
Lymphocyte	↓ - ↓↓	↓↓	N - ↑
Monocyte	N - ↑↑	N - ↑	N
Eosinophil	↓	↓	N
Basophil	N - ↑	N	N

N=normal

IDEXX LABORATORIES

Stress leukogram

- Neutrophilia
- Lymphopenia
- Eosinopenia
- (Monocytosis)

Stress leukogram

- Neutrophilia
- Lymphopenia
- Eosinopenia
- (Monocytosis)

J Vet Intern Med 2011;25:1351–1356

White Blood Cell Count and the Sodium to Potassium Ratio to Screen for Hypoadrenocorticism in Dogs

M. Seth, K.J. Drobatz, D.B. Church, and R.S. Hess

Variable	Chronic Disease	
Na : K ratio	33.1 (20.5–61.6)	<.001
Hematocrit (%) (reference range: 40.3–60.3%)	42.2 (14.1–61.5)	.006
White blood cells count (cells $\times 10^3/\mu L$) (reference range: 5.3–19.8)	12.6 (0.9–64.2)	.87
Neutrophils (cells $\times 10^3/\mu L$) (reference range: 3.1–14.6)	9.87 (0.68–53.93)	.007
Lymphocytes (cells $\times 10^3/\mu L$) (reference range: 0.9–5.5)	1.07 (0–6.00)	<.001
Eosinophils (cells $\times 10^3/\mu L$) (reference range: 0–1.6)	0.12 (0–7.00)	<.001
Monocytes (cells $\times 10^3/\mu L$) (reference range: 0.1–1.4)	0.65 (0–9.63)	.174
Neutrophil: lymphocyte ratio	9.51 (1.23–95.15)	<.001

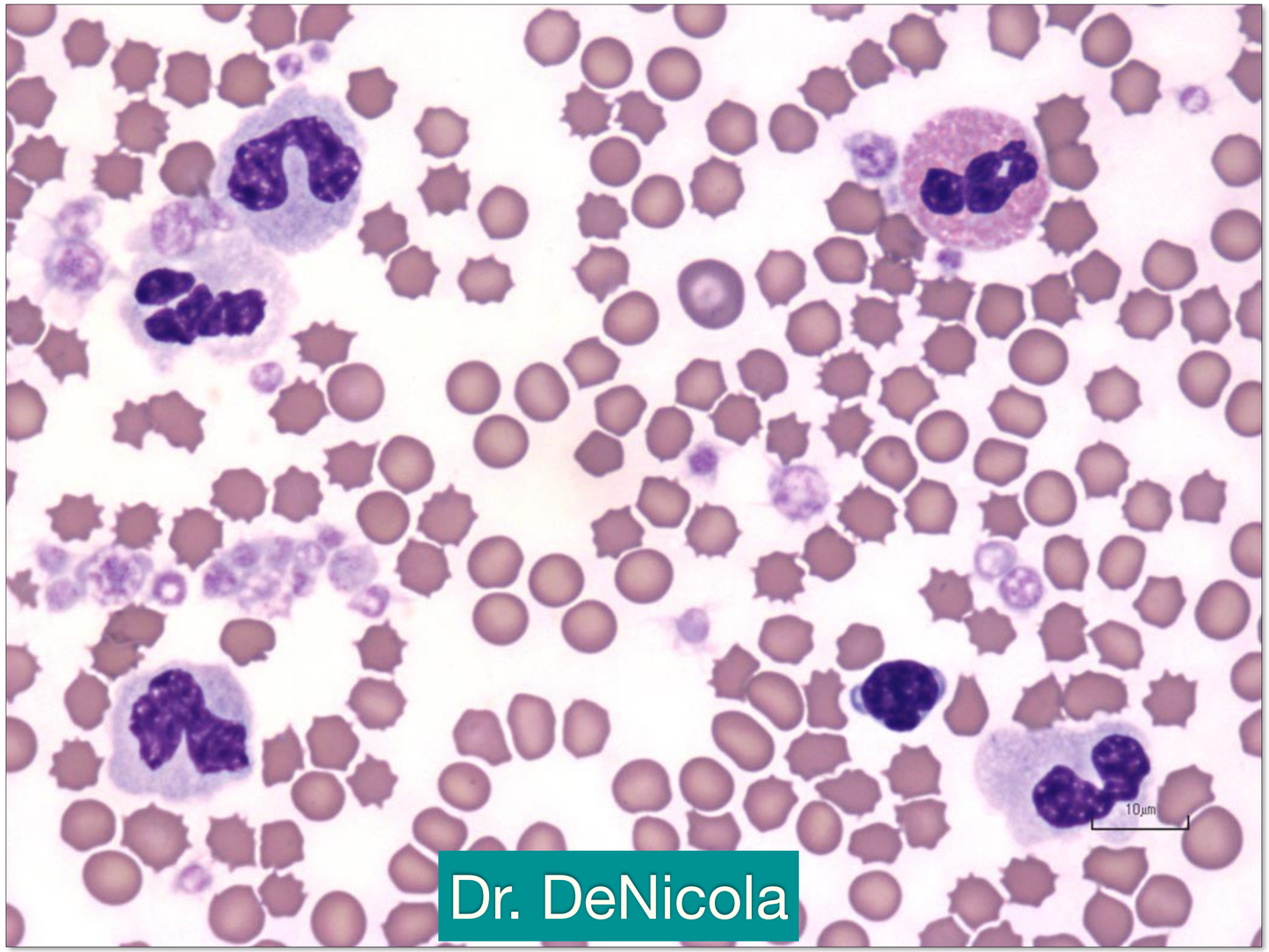
Sick dogs/cats should have < 1,000 lymphs

Stress leukogram

- *A sick dog or cat SHOULD NOT have a high lymphocyte count!*
- Unless:
  - Angry cat
  - Addison's
  - VBDs
  - Leukemia/lymphoma
  - They are not lymphs…

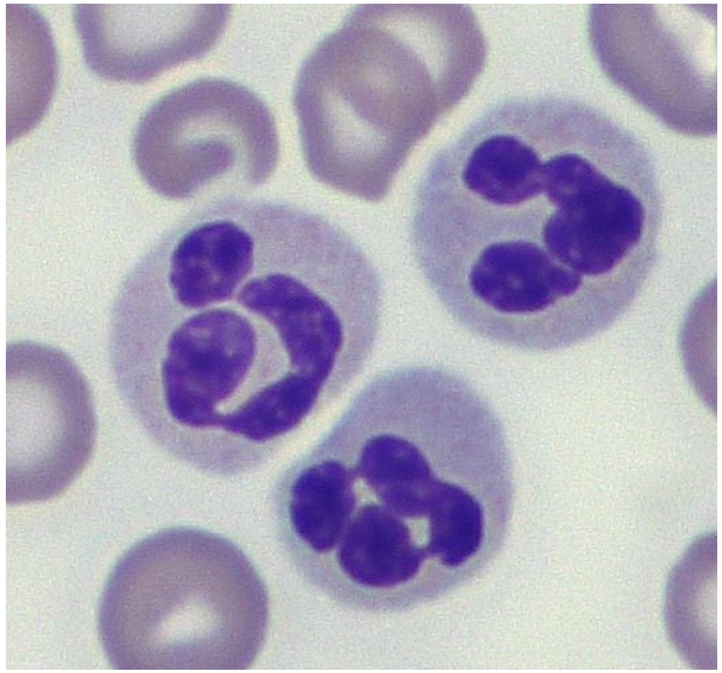
Leukocyte Morphology

- Left shift and toxic changes



My Experience

- *If you do not use CRP, the toxic neutrophil is the best marker of systemic inflammation*



Leukocytes

- Most dogs and cats with severe inflammation have high WBC
  - True
  - False

Leukocytes

- Most dogs and cats with severe inflammation have high WBC
  - True
  - False

JAVMA

AVMA

Clinical features, concurrent disorders, and survival time in cats with suppurative cholangitis-cholangiohepatitis syndrome

Sharon A. Center, DVM*; John F. Randolph, DVM; Karen L. Warner, BS; James A. Flanders, DVM; H. Jay Harvey, DVM

Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY

*Corresponding author: Dr. Center (sac6@cornell.edu)

https://doi.org/10.2460/javma.20.10.0555

Neutrophil count

37% high

59% normal

4% low

Table 2—Clinicopathologic data for the cats of Table 1.

Analyte	No. of cats	Median (range) value	No. (%) with results above RI	No. (%) with results below RI	RI
PCV (%)	160	33 (11–54)	6 (4)	17 (11)	25–45
MCV (fL)	128	45 (35–62)	8 (6)	13 (10)	41–51
WBCs (X 10^3/µL)	160	14.6 (0.6–71.7)	38 (24)	10 (6)	6.1–21.1
Neutrophils (X 10^3/µL)	155	10.9 (0.5–64.4)	57 (37)	6 (4)	2.6–13.6
BUN (mg/dL)	154	20 (4–104)	22 (14)	51 (33)	17–35
Creatinine (mg/dL)	147	1.2 (0.3–2.9)	6 (4)	2 (1)	0.6–2.3
Glucose (mg/dL)	152	127 (68–891)	66 (43)	0 (0)	63–140
Total protein (g/dL)	145	7.4 (4.7–10.8)	10 (7)	26 (18)	6.5–8.9
Albumin (g/dL)	152	3.1 (1.4–4.3)	0 (0)	76 (50)	3.2–4.7
Globulin (g/dL)	150	4.3 (1.9–8.2)	36 (24)	7 (5)	2.8–4.8
Cholesterol (mg/dL)	140	202 (39–494)	36 (26)	6 (4)	73–265

MCV = Mean corpuscular volume. RI = Reference interval.

DOI: 10.1111/jvim.16374

STANDARD ARTICLE

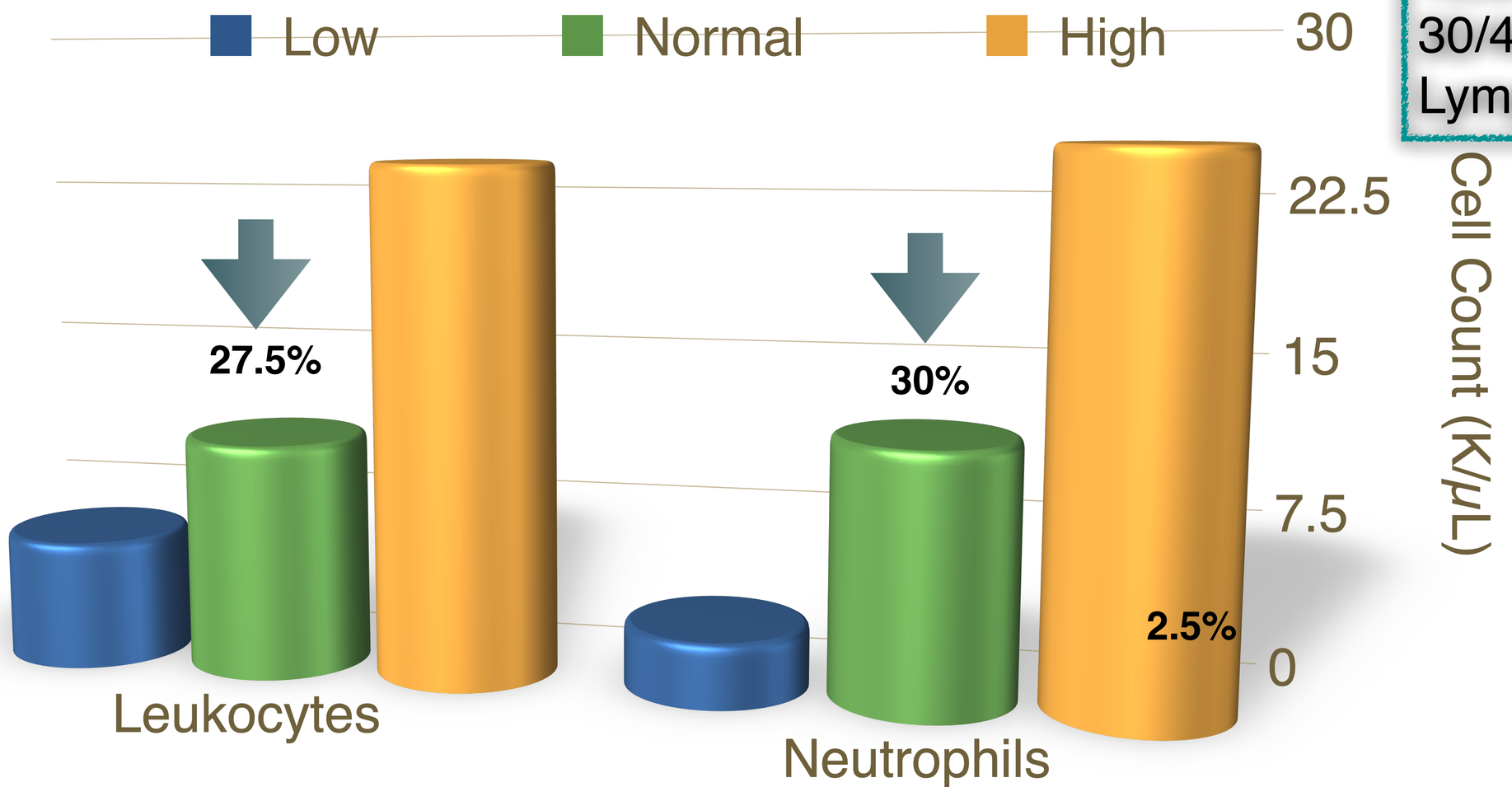
Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Serial analysis of blood biomarker concentrations in dogs with pneumonia, septic peritonitis, and pyometra

Robert Goggs[1] | Sarah N. Robbins[1] | Denise M. LaLonde-Paul[1] | Julie M. Menard[2]

Mean Lymph count:
1,500 K/μL
30/40 (75%)
Lymphs <2,000 K/μL



Clinical, laboratory, and hemostatic findings in cats with naturally occurring sepsis

Sigal Klainbart DVM
Limor Agi DVM
Tali Bdolah-Abram MSc
Efrat Kelmer DVM, MSc
Itamar Aroch DVM

From the Departments of Small Animal Emergency and Critical Care (Klainbart, Agi, Kelmer) and Small Animal Internal Medicine (Aroch) and the Robert H. Smith Faculty of Agricultural, Food, and Environmental Quality Sciences (Bdolah-Abram), Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot 761001, Israel.

Address correspondence to Dr. Klainbart (klainbart@gmail.com).

OBJECTIVE
To characterize clinical and laboratory findings in cats with naturally occurring sepsis, emphasizing hemostasis-related findings, and evaluate these variables for associations with patient outcomes.

DESIGN
Prospective, observational, clinical study.

ANIMALS
31 cats with sepsis and 33 healthy control cats.

PROCEDURES
Data collected included history; clinical signs; results of hematologic, serum biochemical, and hemostatic tests; diagnosis; and outcome (survival vs death during hospitalization or ≤ 30 days after hospital discharge). Differences between cats with and without sepsis and associations between variables of interest and death were analyzed statistically.

RESULTS
The sepsis group included cats with pyothorax (n = 10), septic peritonitis (7), panleukopenia virus infection (5), bite wounds (5), abscesses and diffuse cellulitis (3), and pyometra (1). Common clinical abnormalities included dehydration (21 cats), lethargy (21), anorexia (18), pale mucous membranes (15), and dullness (15). Numerous clinicopathologic abnormalities were identified in cats with sepsis; novel findings included metarubricytosis, hypertriglyceridemia, and high circulating muscle enzyme activities. Median activated partial thromboplastin time and plasma D-dimer concentrations were significantly higher, and total protein C and antithrombin activities were significantly lower, in the sepsis group than in healthy control cats. Disseminated intravascular coagulopathy was uncommon (4/22 [18%] cats with sepsis). None of the clinicopathologic abnormalities were significantly associated with death on multivariate analysis.

WBC count
39% leukopenia
22% normal
39% leukocytosis

Neutrophil Counts and Morphology in Cats: A Retrospective Case-Control Study of 517 Cases

Nivy, R., Itkin, Y., Bdolah-Abram, T., Segev, G. and Aroch, I.*

Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Israel, P.O. Box 12, Rehovot, 76100, Israel.

* **Corresponding author:** Prof. Itamar Aroch. Tel: +97239688556, Fax:

50% of cats with toxic NEUTS have a normal count

Table 3: Occurrence of neutrophil cytoplasmic toxic [illegible] ped by their absolute neutrophil cou[illegible]

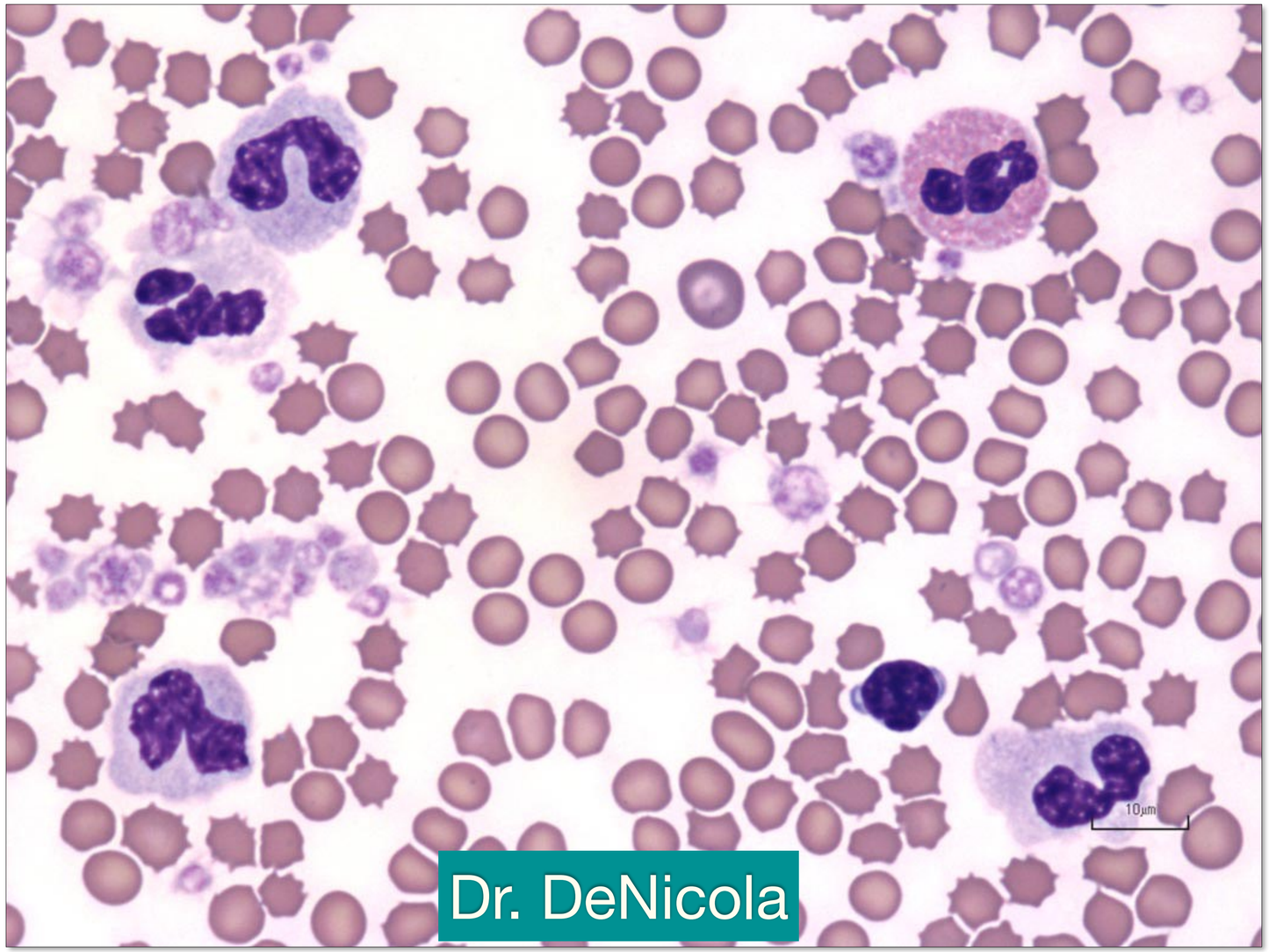
Group	Neutropenia n (%)	Neutrophils WRI[1] n (%)	Neutrophilia n (%)	All cats n (%)	*P* value
Toxicity[2]	18 (69.2%)	155 (49.5%)	124 (69.7%)	297 (100.0%)	
No Toxicity[2]	8 (30.8%)	158 (50.5%)	54(30.3%)	220 (100.0%)	
Left Shift[3]	6 (23.1%)	16 (5.1%)	32 (18.0%)	54 (100.0%)	<0.0001
No Left Shift[3]	20 (76.9%)	297 (94.9%)	146 (82.0%)	463 (100.0%)	
All cats	26 (100.0%)	313 (100.0%)	178 (100.0%)	517 (100.0%)	

Leukocytes and Inflammation

- Repeat with me:
  - *As many as half of the dogs and cats with severe systemic inflammation have normal WBC and neutrophil counts!!*

Why do we care?

- Left shift and toxic changes



Toxic Neutrophils

J Vet Intern Med 2005;19:64–73

Clinical, Biochemical, and Hematological Characteristics, Disease Prevalence, and Prognosis of Dogs Presenting with Neutrophil Cytoplasmic Toxicity

Itamar Aroch, Eyal Klement, and Gilad Segev

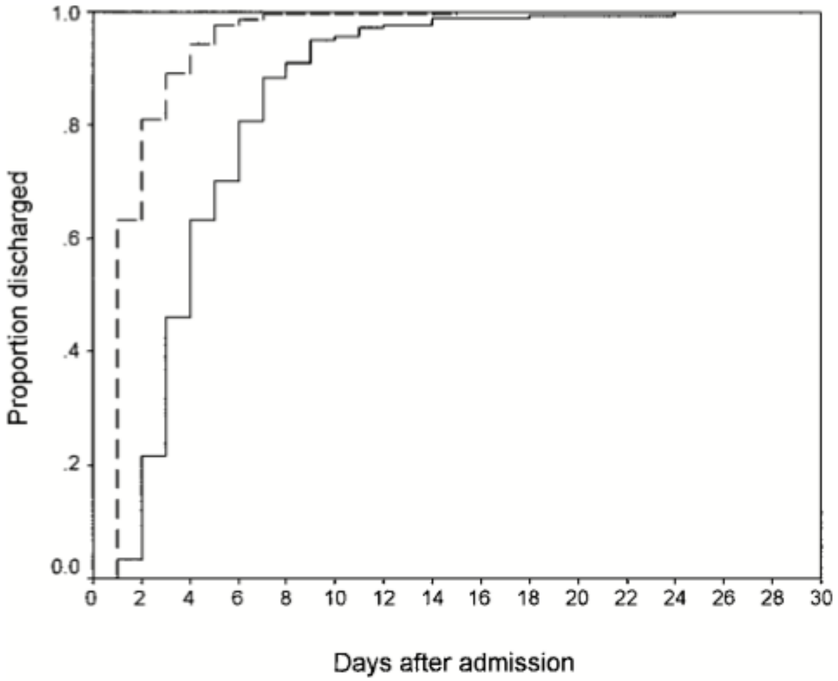


Fig 3. Comparison of hospitalization duration between dogs with neutrophil toxicity (———) and controls (– – –). Proportion of dogs discharged is depicted as a function of days passed from admission.

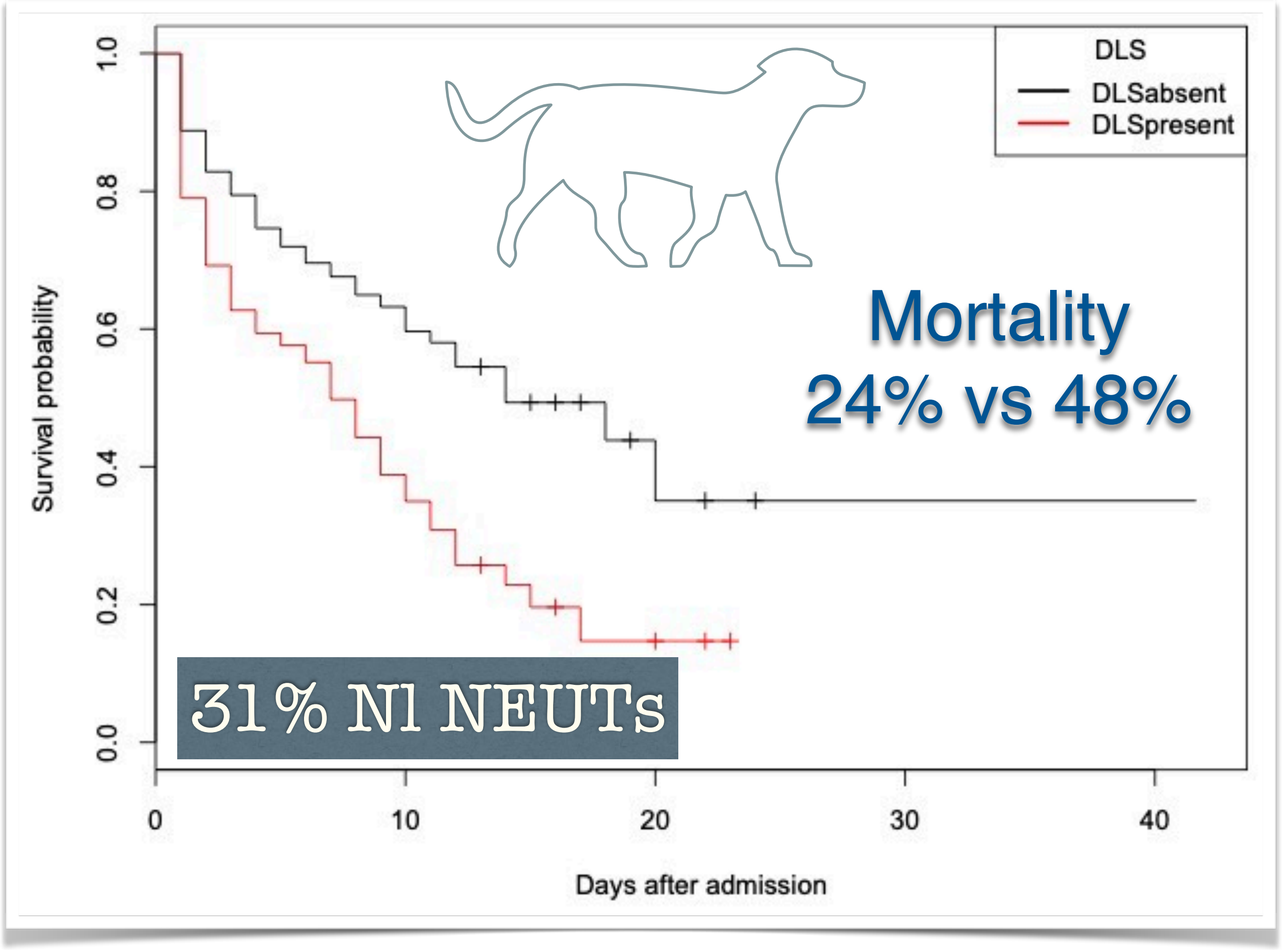
Mortality
11.7 vs
24%

Degenerative LS

J Vet Intern Med 2013;27:1517–1522

The Prognostic Utility of Degenerative Left Shifts in Dogs

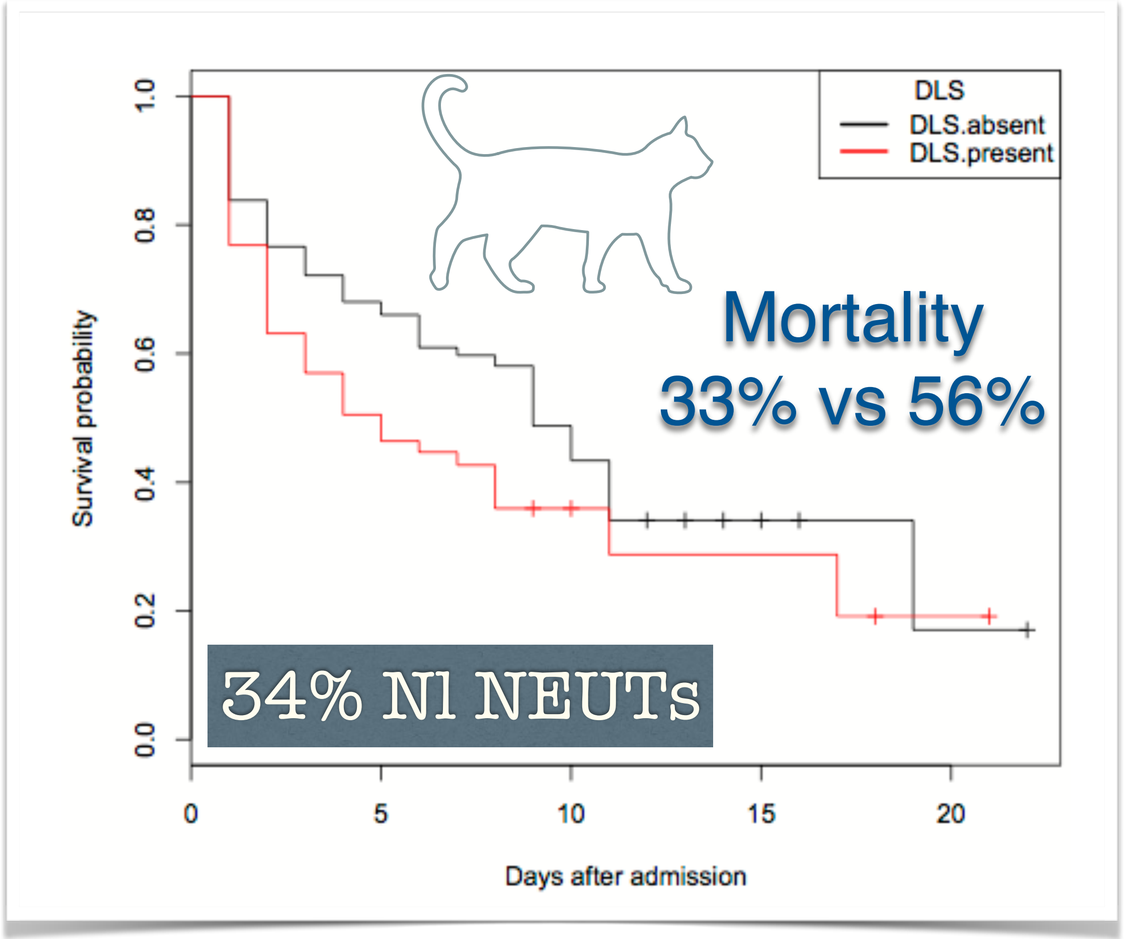
A.G. Burton, L.A. Harris, S.D. Owens, and K.E. Jandrey



J Vet Intern Med 2014

Degenerative Left Shift as a Prognostic Tool in Cats

A.G. Burton, L.A. Harris, S.D. Owens, and K.E. Jandrey



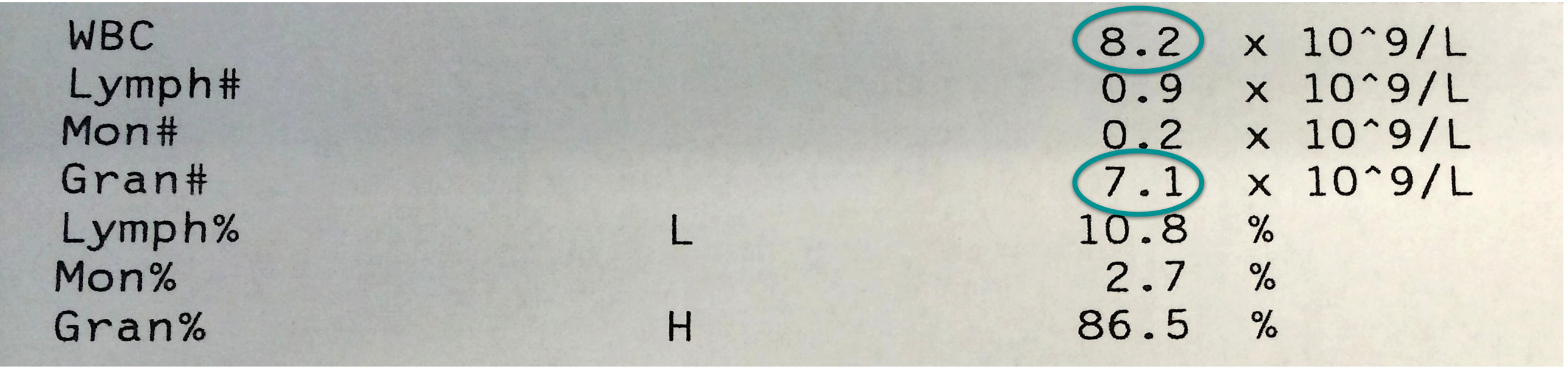
Case 1

- I have an impedance counter and I do/do not look at all the blood smears

“Guantes”

- 5 month old, M, DSH
- Acutely ill
- PE: fever, depression, swollen LR leg, lateral recumbency, open mouth breathing

“Guantes”

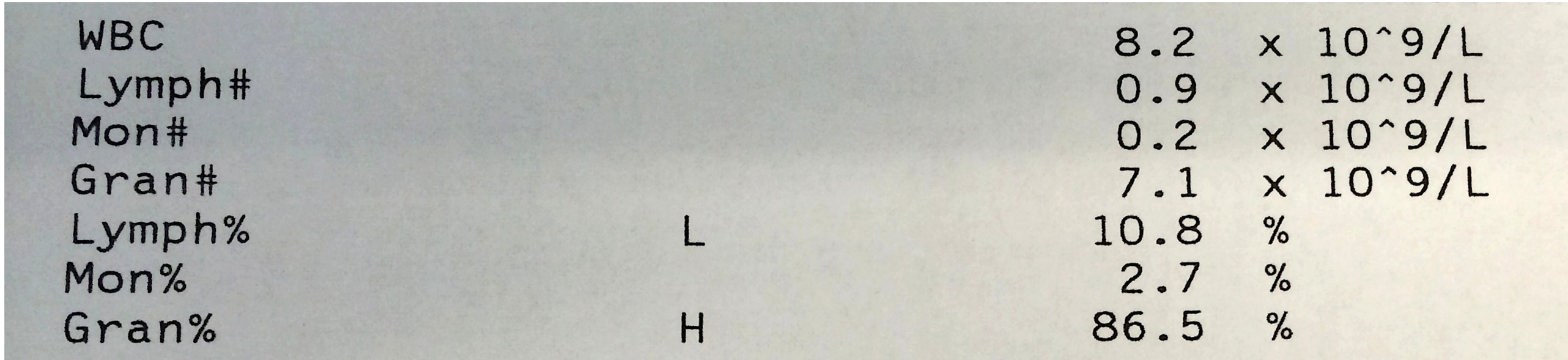


WBC		8.2	x 10^9/L
Lymph#		0.9	x 10^9/L
Mon#		0.2	x 10^9/L
Gran#		7.1	x 10^9/L
Lymph%	L	10.8	%
Mon%		2.7	%
Gran%	H	86.5	%

Do the numbers worry you?

Case 1 - “Guantes”

- I have an impedance counter and I <u>do not</u> look at blood smears
- I conclude that all is good…



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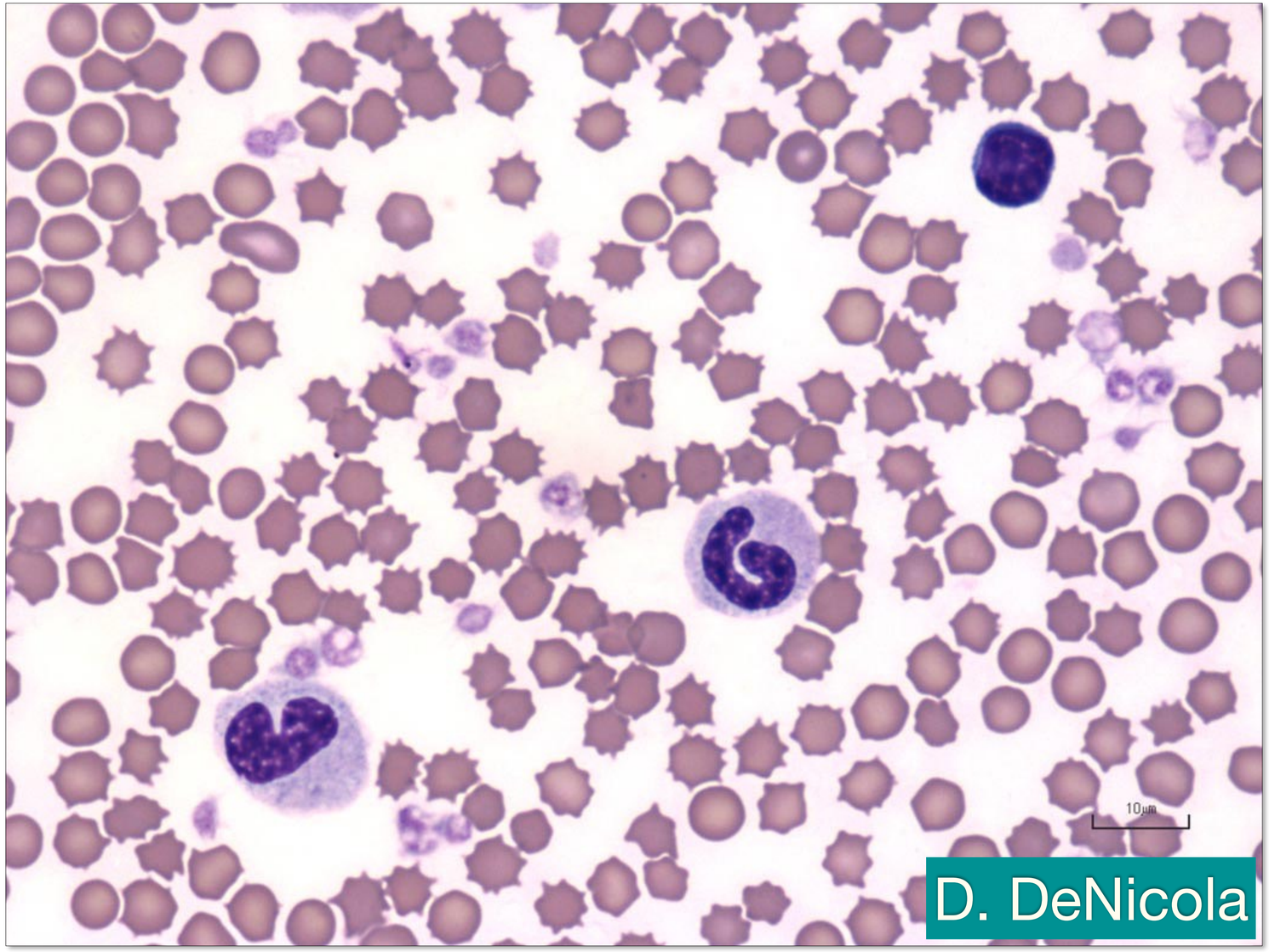
Lymph%	L	10.8	%
Mon%		2.7	%
Gran%	H	86.5	%

Case 1 - “Guantes”

- But wait! Maybe I <u>should</u> look at a blood smear…

“Guantes”



Case 1 - “Guantes”

- I have an impedance counter and I did look at a blood smear
- I conclude that…
- He is likely septic
- And, of course, he doesn’t have a high WBC ☹️

“Guantes”

- Final Dx: *E. coli* osteomyelitis and sepsis
- Died 1 hour after doing CBC

Clinical, laboratory, and hemostatic findings in cats with naturally occurring sepsis

REMEMBER!

Sigal Klainbart DVM
Limor Agi DVM
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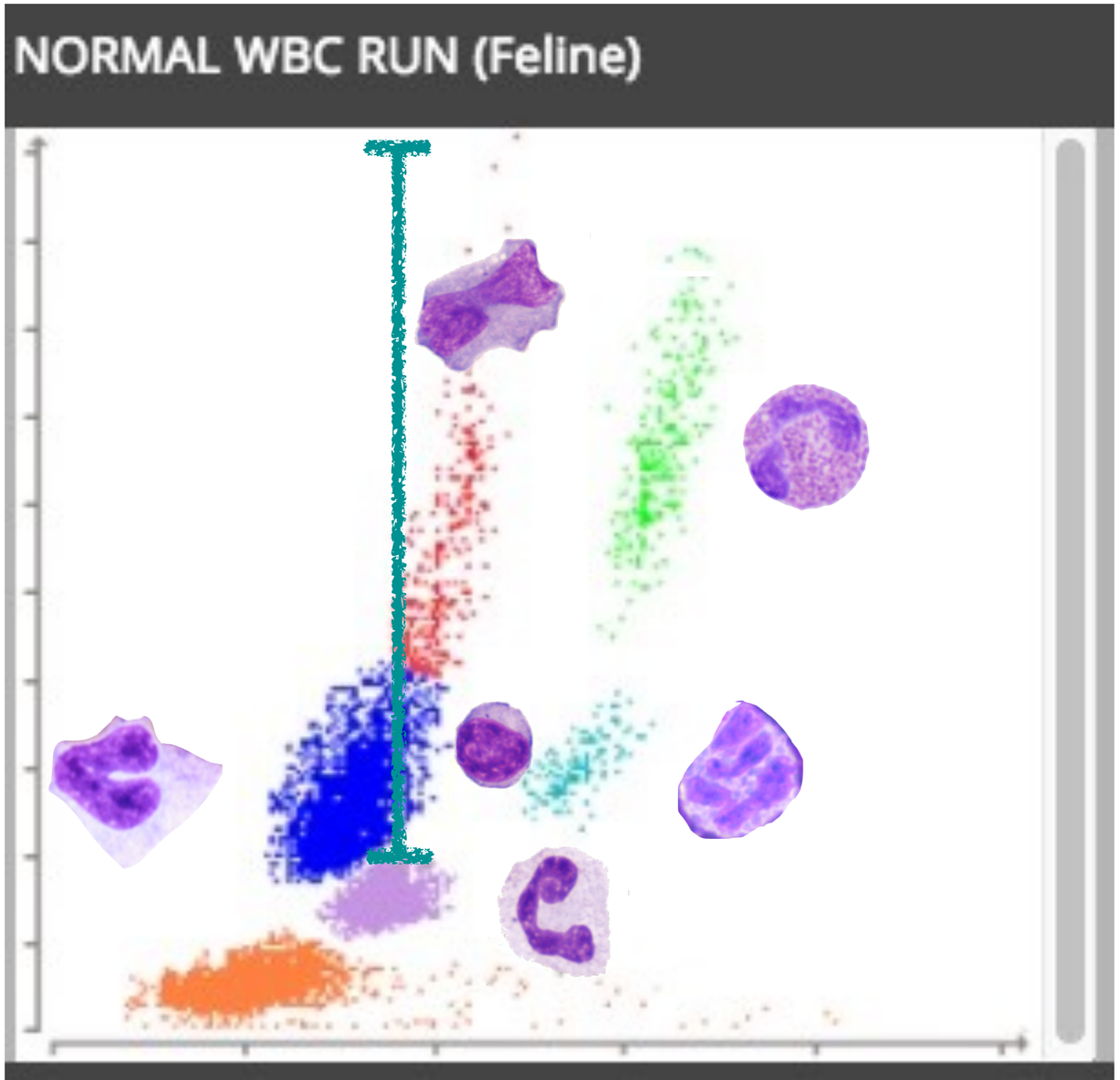
Case 2

- I have a ProCyte Dx and use the dotplots

Where do bands (TNs) live?



Case 2-“Casper”

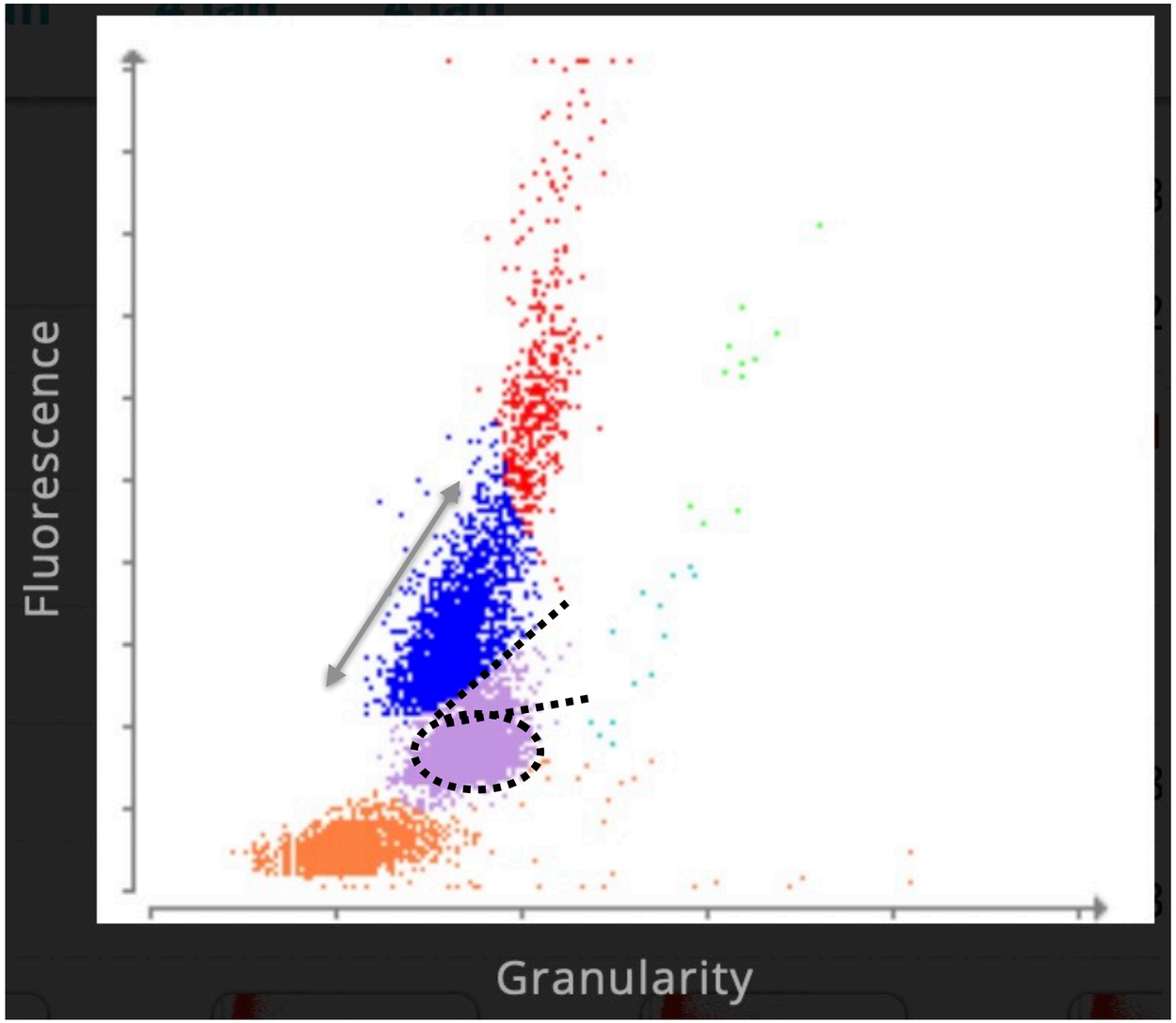
- “Casper”, 16 week-old, MC, Maine Coon
- Recently obtained from a breeder
- After questioning, has had diarrhea since D1
- “ADR”, febrile, abdominal pain/discomfort
- CBC, chem (ALT: 553 U/L)

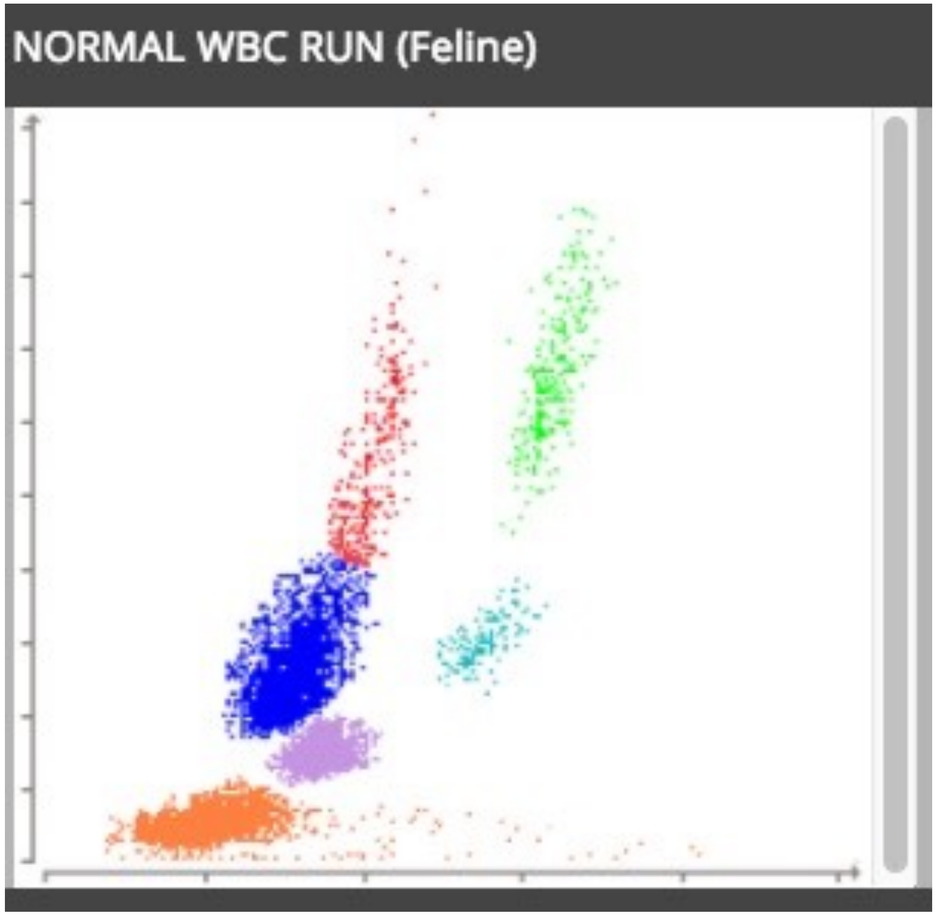
Case 2-“Casper”-WBC

WBC	9.35	2.87 - 17.02 K/µL	
% Neutrophils	62.9	%	
% Lymphocytes	31.3	%	
% Monocytes	5.6	%	
% Eosinophils	0.1	%	
% Basophils	0.1	%	
Neutrophils	5.88	2.30 - 10.29 K/µL	
Lymphocytes	2.93	0.92 - 6.88 K/µL	
Monocytes	0.52	0.05 - 0.67 K/µL	
Eosinophils	**0.01**	0.17 - 1.57 K/µL	
Basophils	0.01	0.01 - 0.26 K/µL	

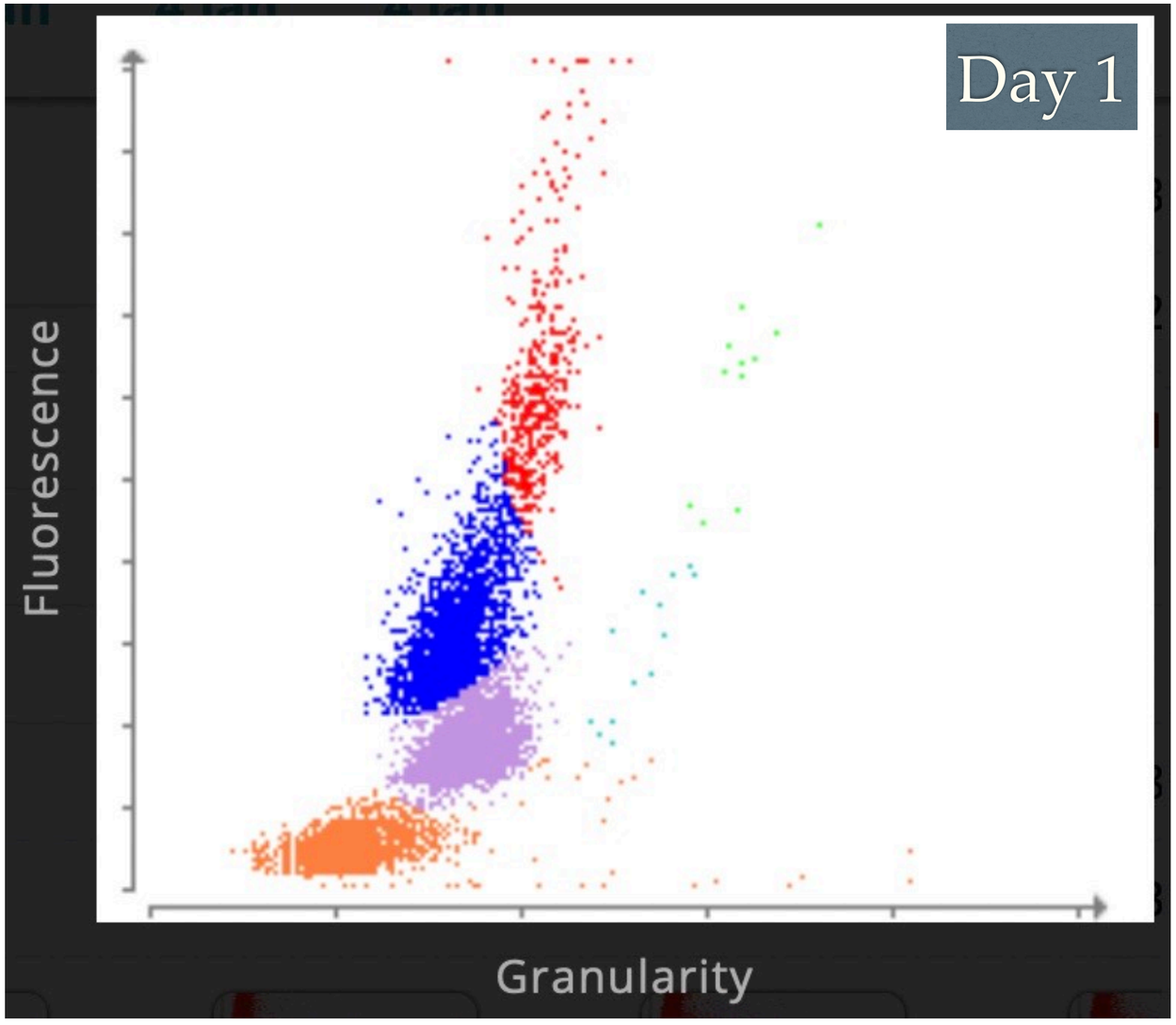
How concerned are we about the leukogram?

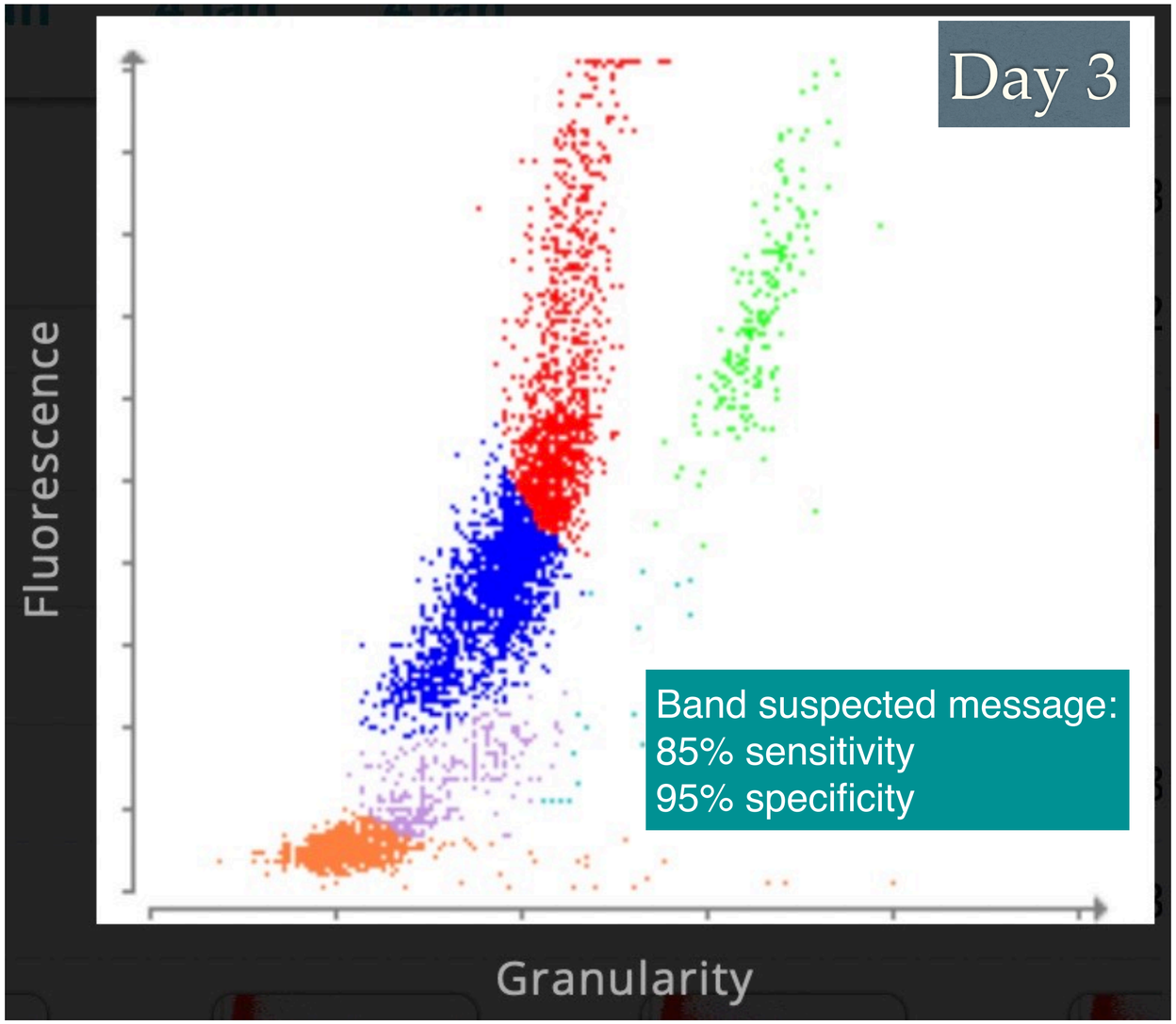
Case 2-“Casper”-Dotplots



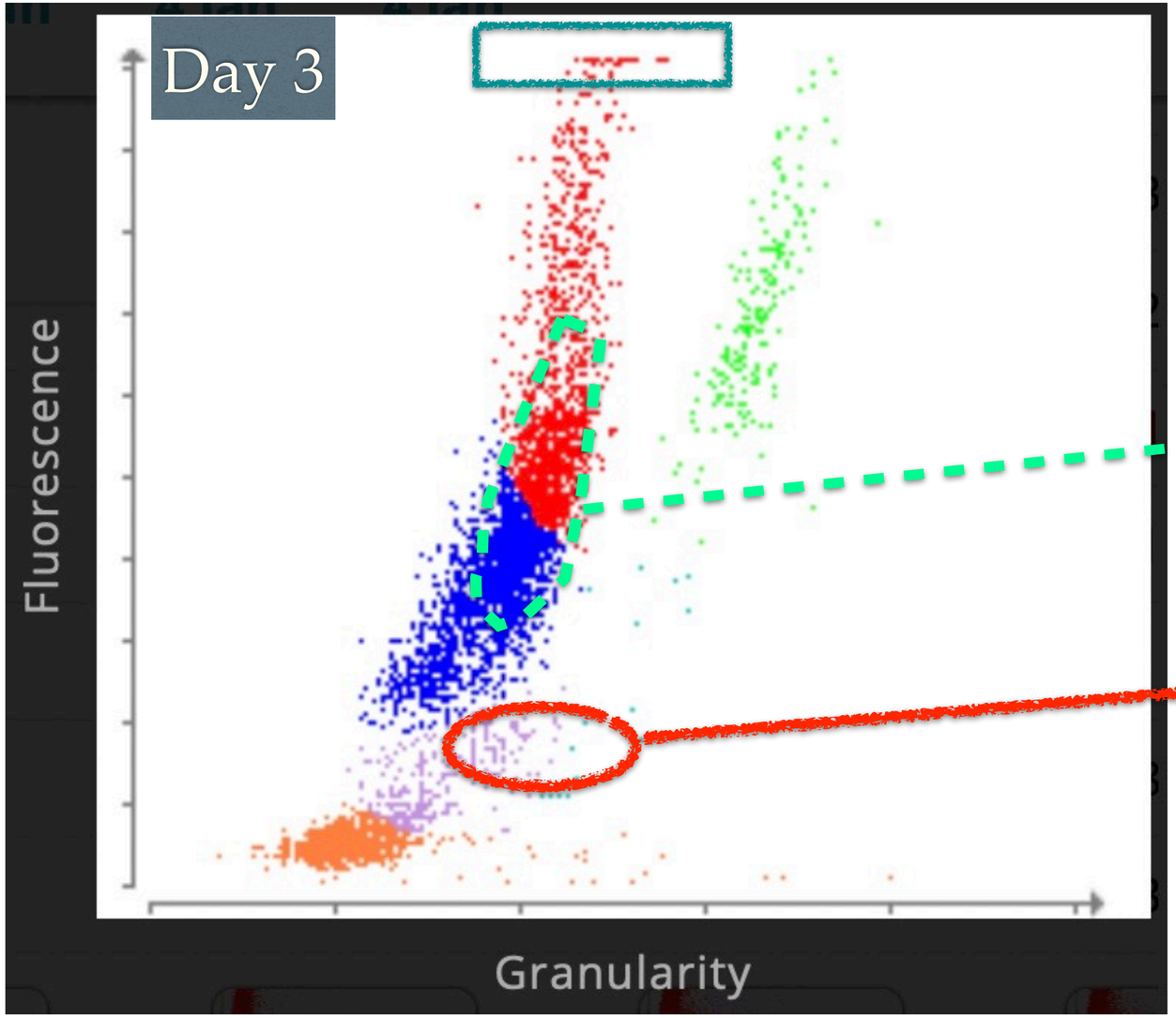


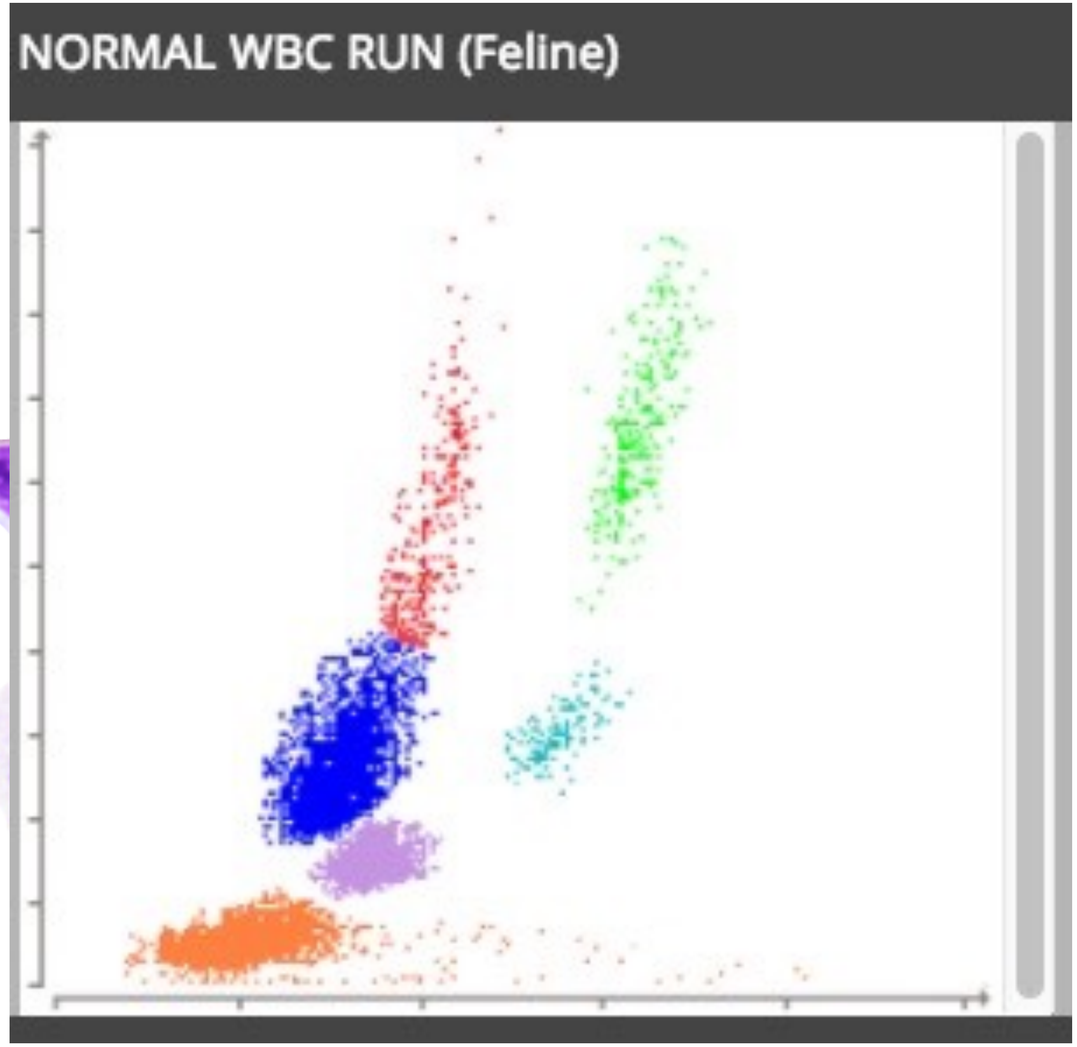
Case 2-“Casper”-Dotplots

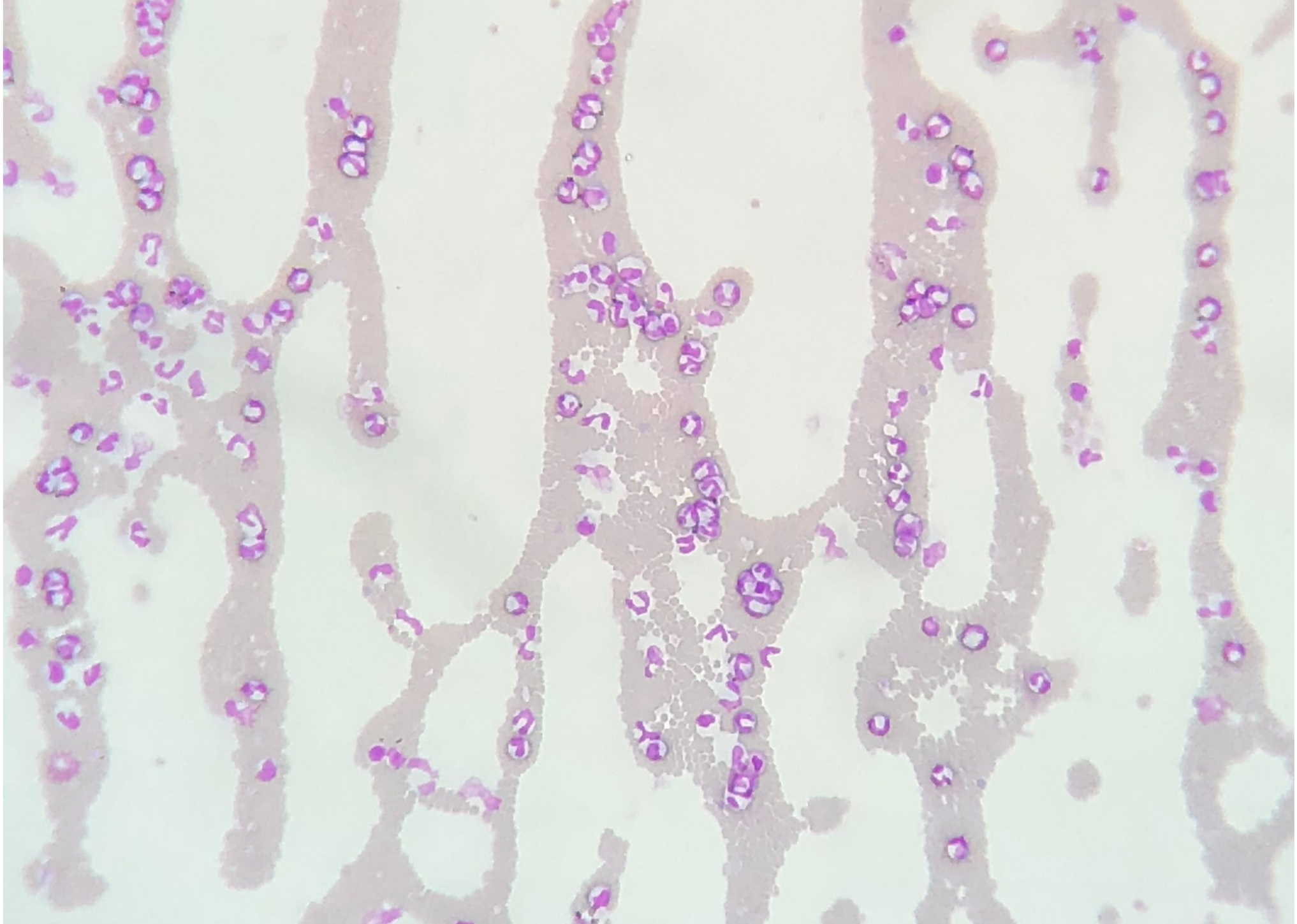




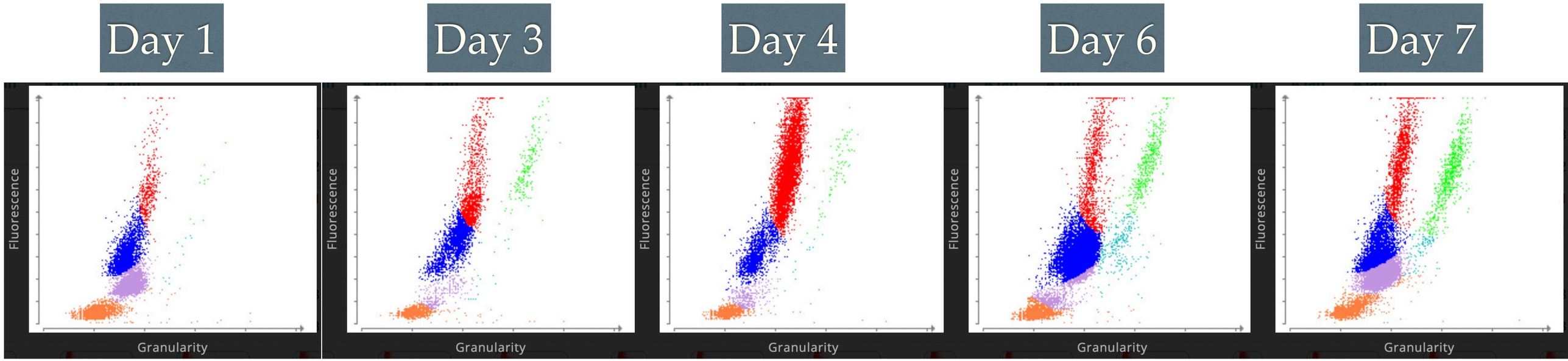
Case 2-“Casper”-Dotplots







Case 2-“Casper”-Serial Dotplots

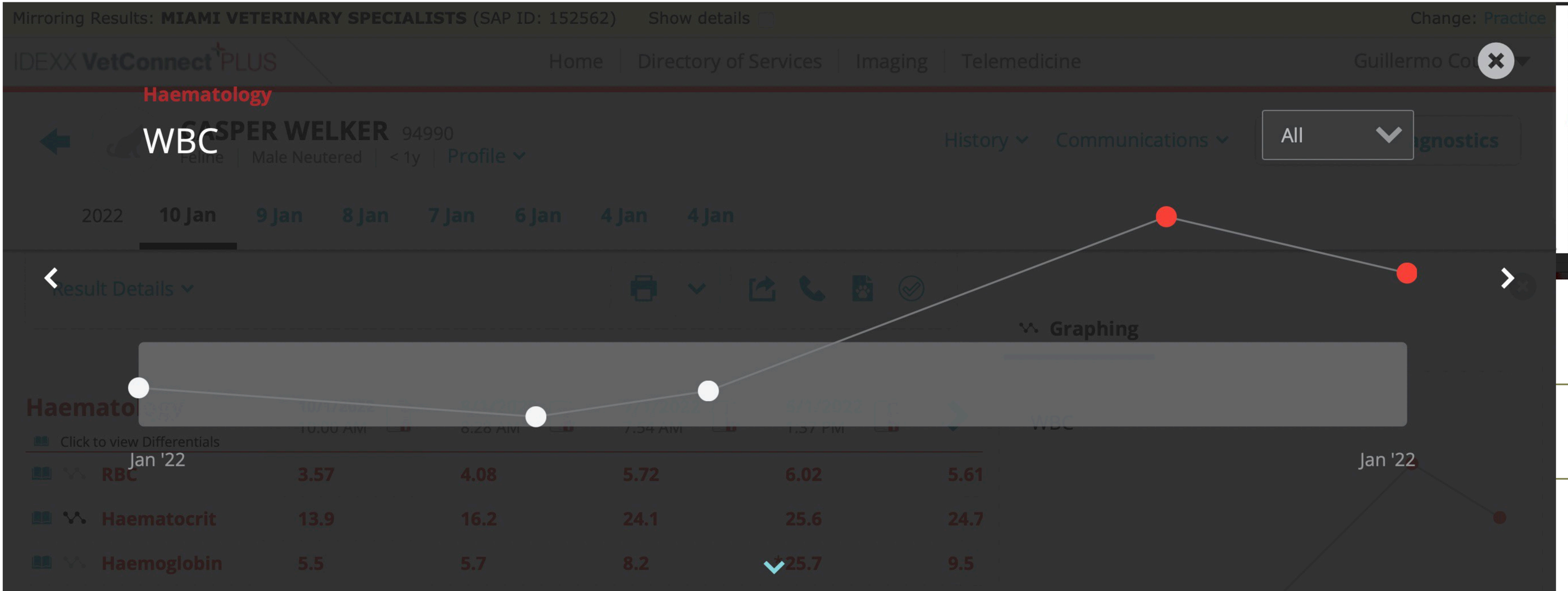


Total WBC

9.35	4.51	8.83	38.06	28.61

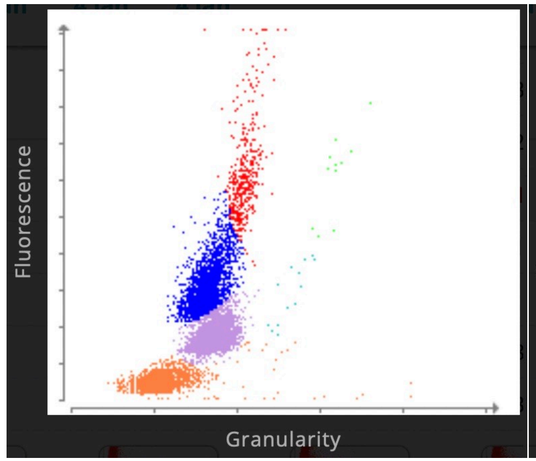
Case 2-“Casper”-Serial Dotplots

Day 1 Day 3 Day 4 Day 6 Day 7

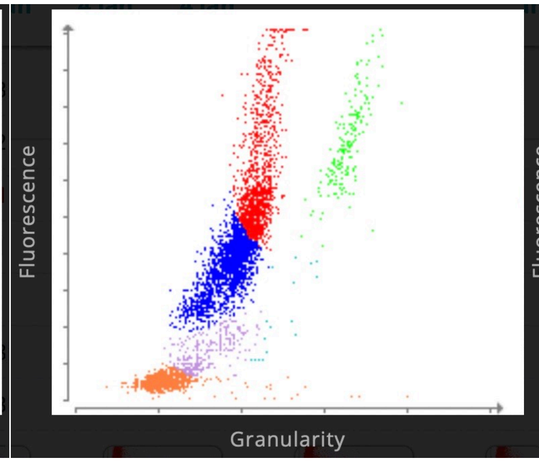


Case 2-“Casper”-Serial Dotplots

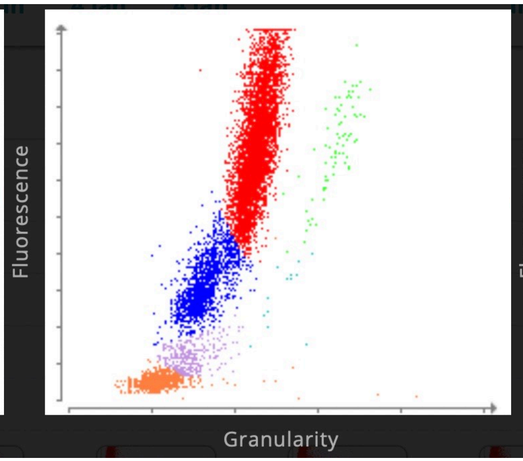
Day 1



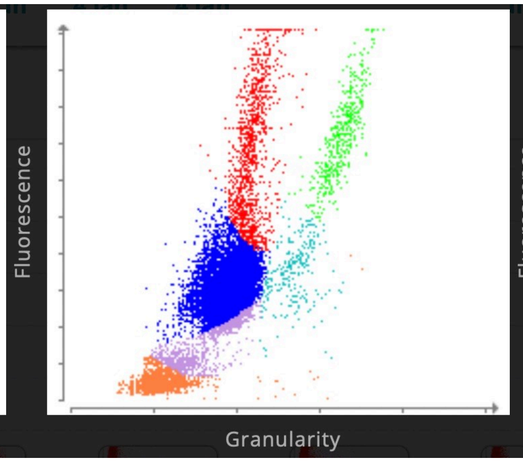
Day 3



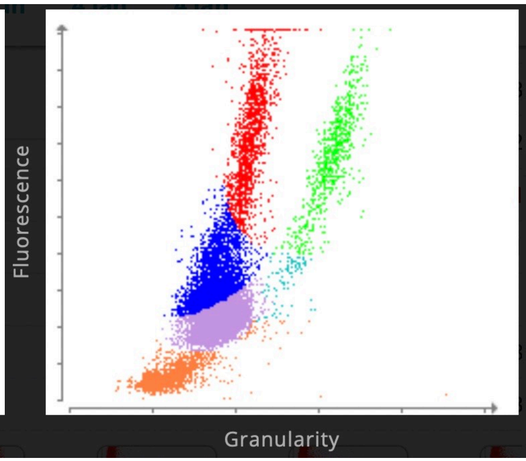
Day 4

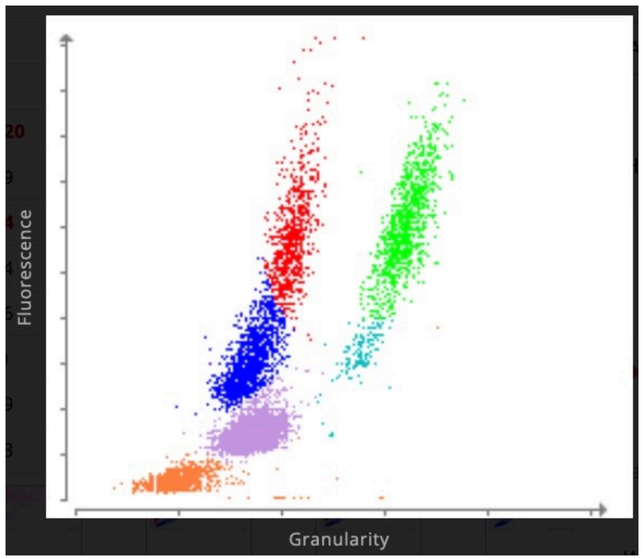


Day 6



Day 7





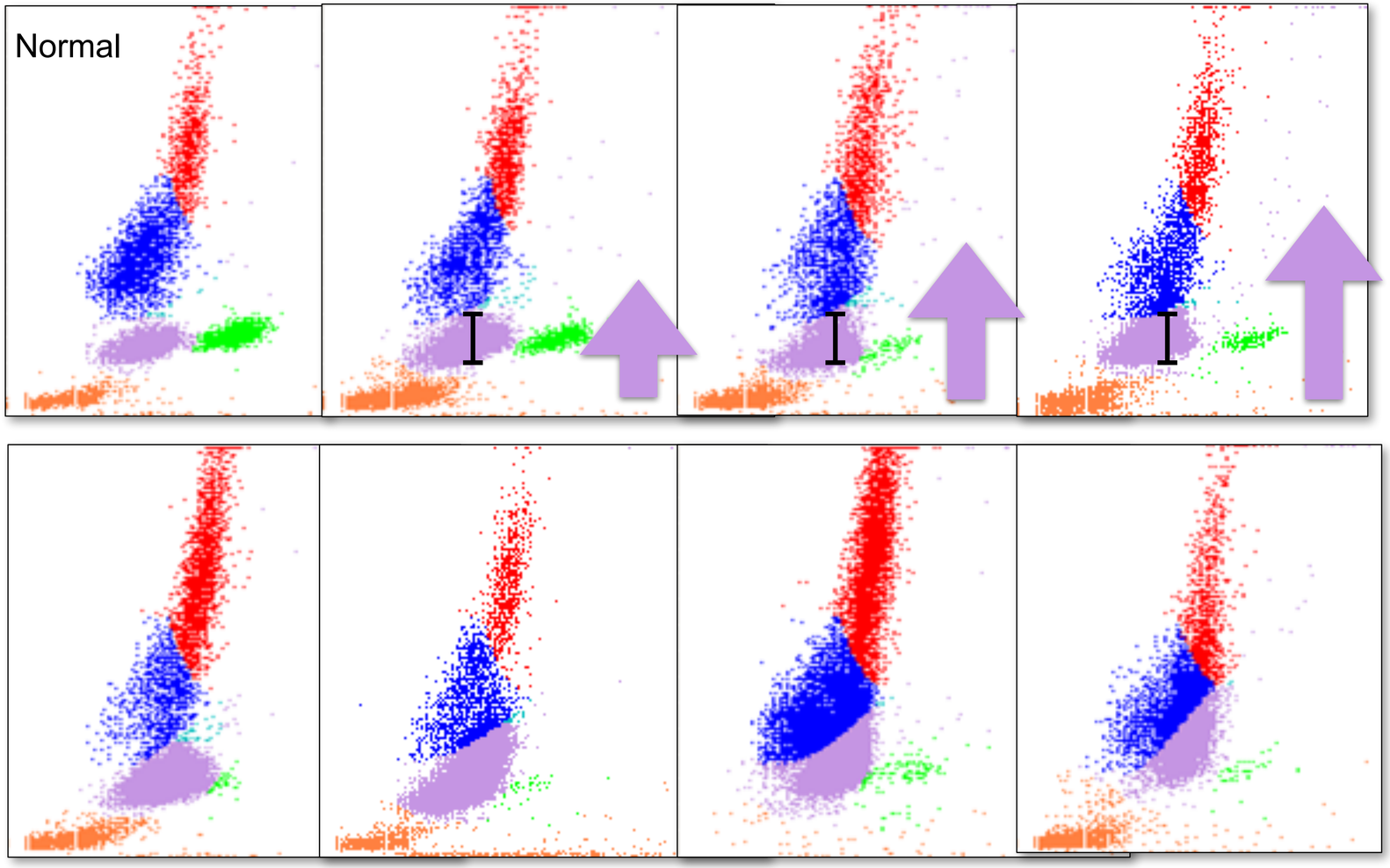
Day 17

Total WBC: 13.6

Case 2-“Casper”

- **Diagnosis:**
  - Sepsis (Salmonella?)
  - Went home on D8 on oral antibiotics
  - Back to normal on D17

Dot Plots – Immature and/or toxic neutrophils



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Case 3

- I have a ProCyte One and use the dot plots

Case 3

Wasabi: 9-year-old, F, Mixed breed cat

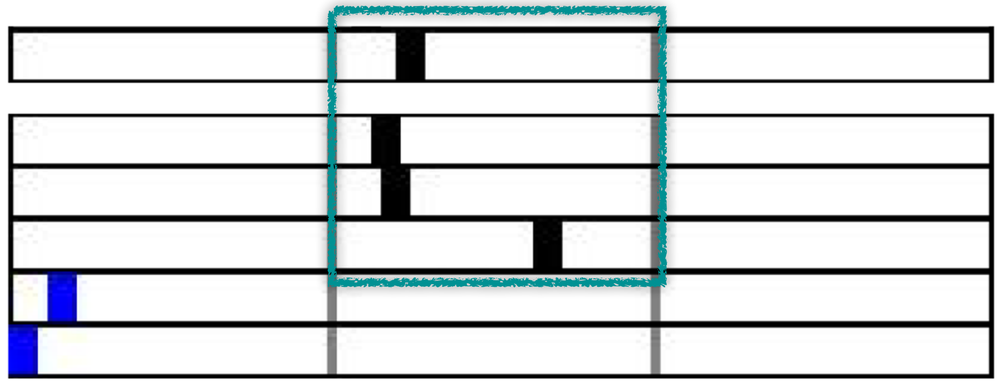
Clinical Presentation

- Owner found blood drops from either the rectum or vulva 3 days ago
- No blood in urine or feces
- Patient is ‘ill’
  - Lethargic and “warm to the touch”
  - Did not eat morning of visit

Thanks to Drs. Kim Yore and Heidi Peta

“Wasabi”-WBC Results

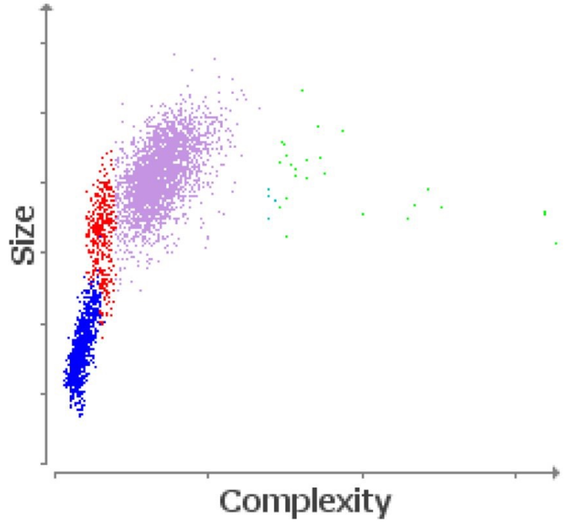
Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte One (October 4, 2021 10:25 AM)					
WBC	6.33 K/µL	2.87 - 17.02			
NEU	3.72 K/µL	2.30 - 10.29			
LYM	2.11 K/µL	0.92 - 6.88			
MONO	0.47 K/µL	0.05 - 0.67			
EOS	0.03 K/µL	0.17 - 1.57	LOW		
BASO	0.00 K/µL	0.01 - 0.26	LOW		



How concerned are we about the leukogram?

“Wasabi”-WBC Dotplots

ProCyte One Numeric Values and Dots



Test	Results	Reference Interval		LOW NORMAL HIGH
ProCyte One (October 4, 2021 10:25 AM)				
WBC	6.33 K/µL	2.87 - 17.02		
NEU	3.72 K/µL	2.30 - 10.29		
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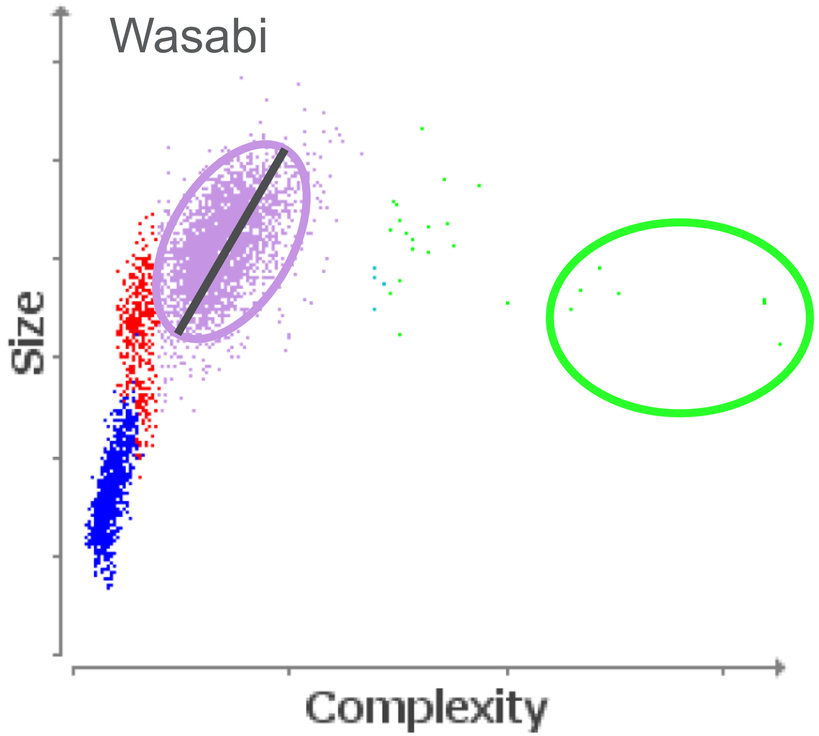
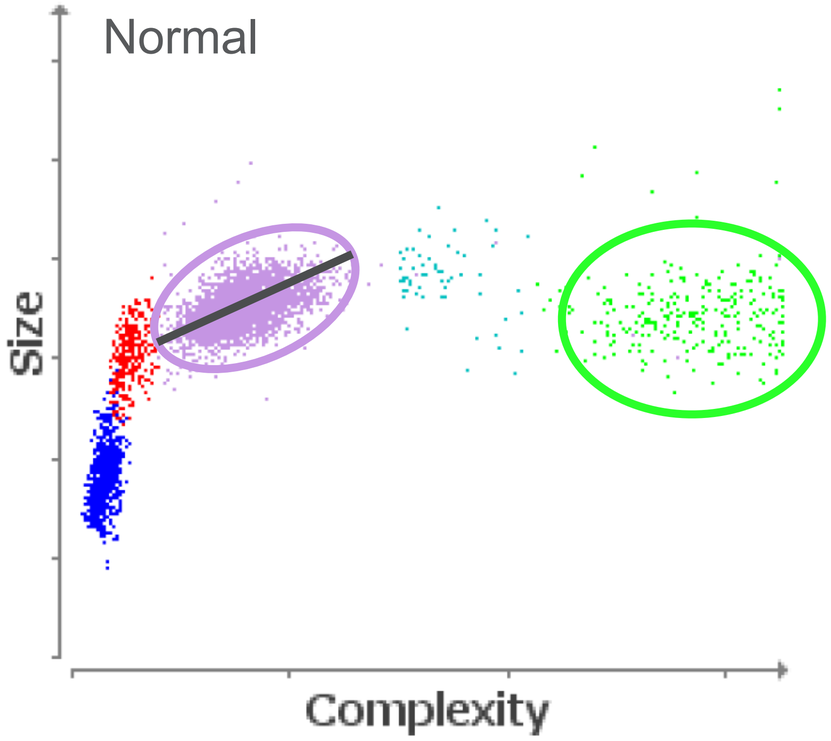
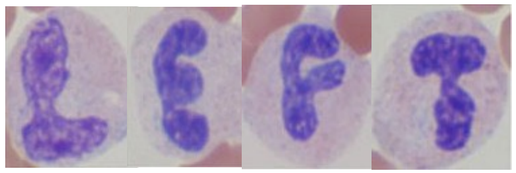
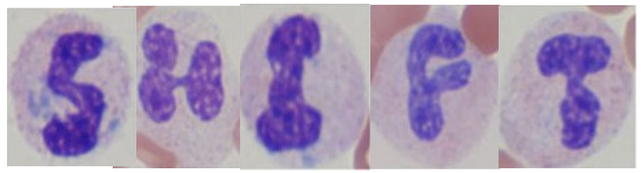
EOS	0.03 K/µL	0.17 - 1.57	LOW	
BASO	0.00 K/µL	0.01 - 0.26	LOW	

Wasabi – 9-year-old, F, Mixed breed cat

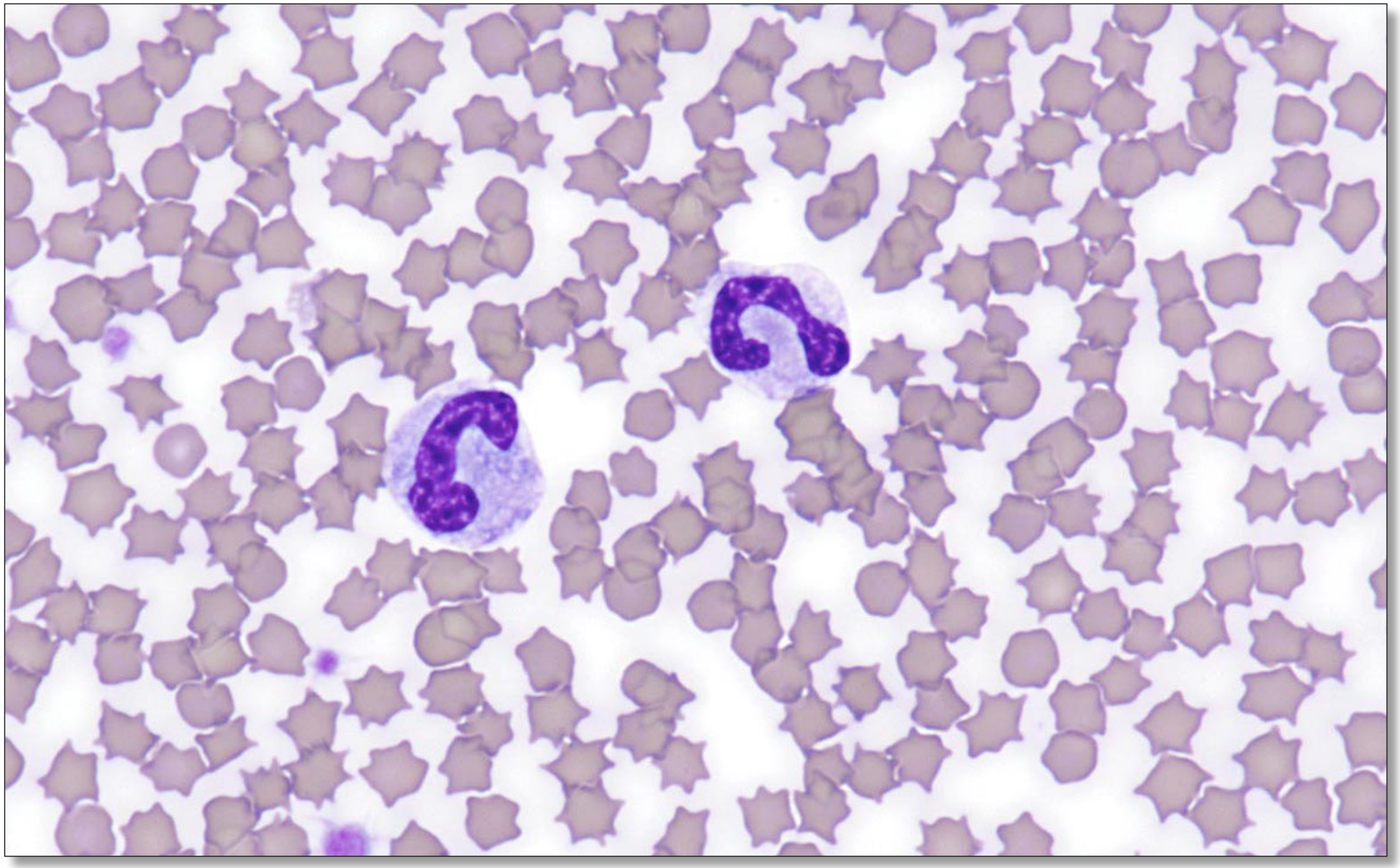








White Blood Cell Morphology
Wasabi – 9-yr, F, Mixed breed cat

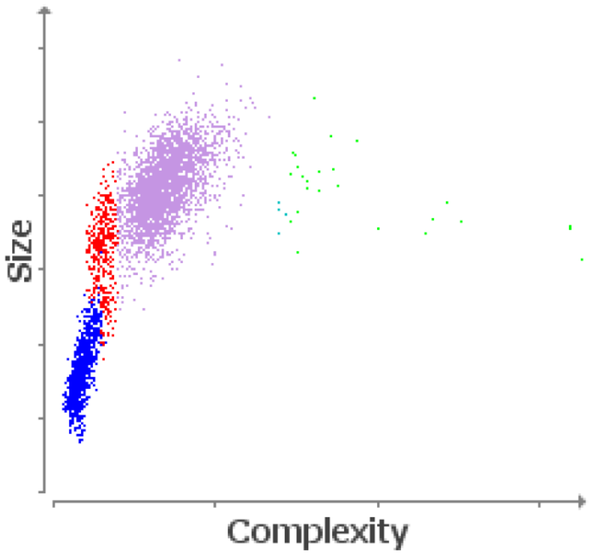


100x Oil

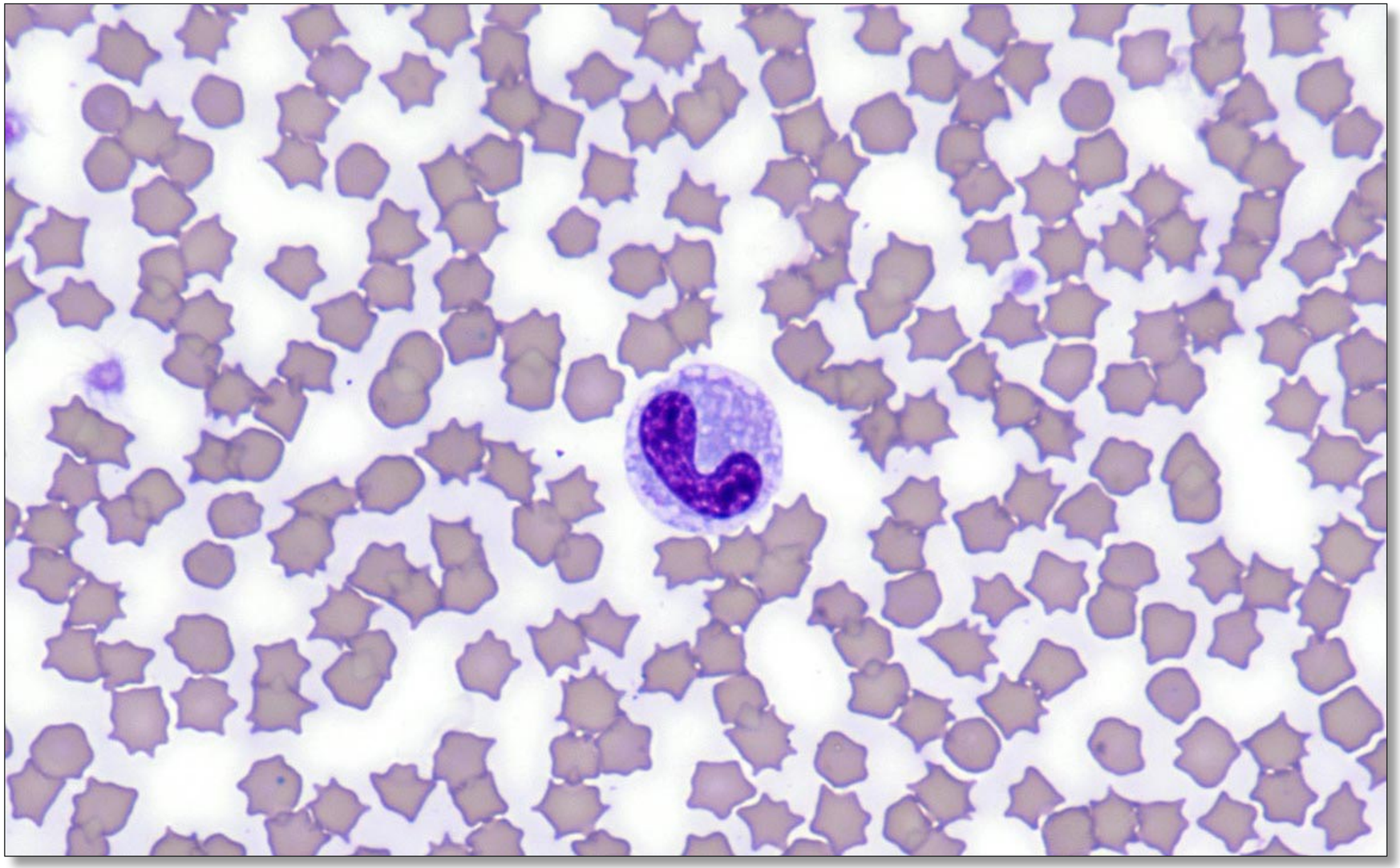
Monolayer

Marked poikilocytosis

Primarily neutrophils with bands and moderate toxicity



White Blood Cell Morphology
Wasabi – 9-yr, F, Mixed breed cat

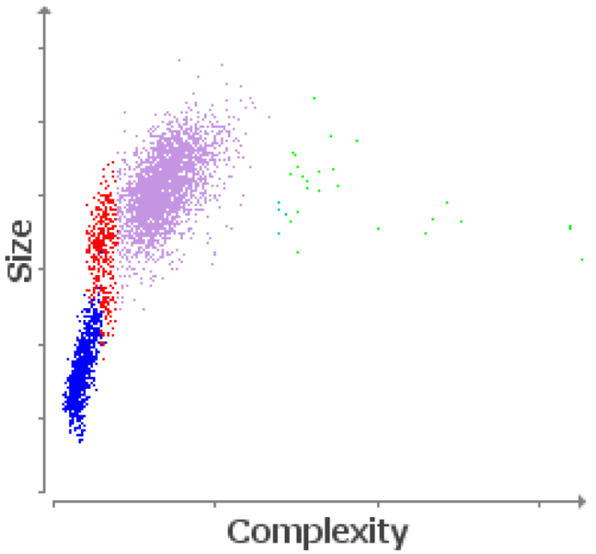


100x Oil

Monolayer

Marked poikilocytosis
Anisocytosis

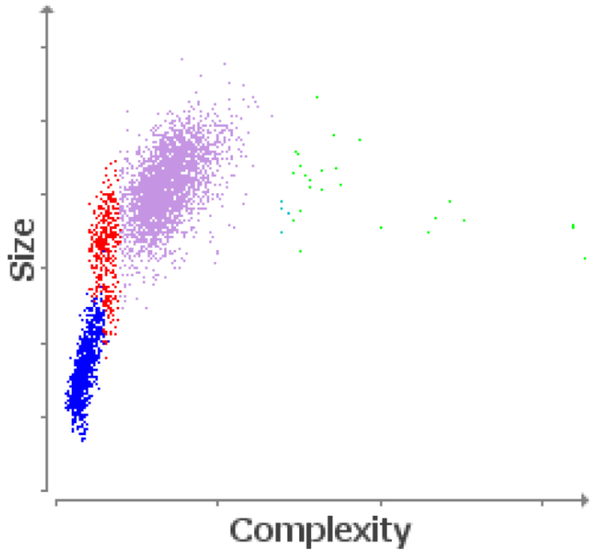
Toxic band



Wasabi – 9-yr, F, Mixed breed cat

Diagnosis/Treatment Plan

- Open pyometra
- Did ovariohysterectomy and "Wasabi" did GREAT!



Please remember!

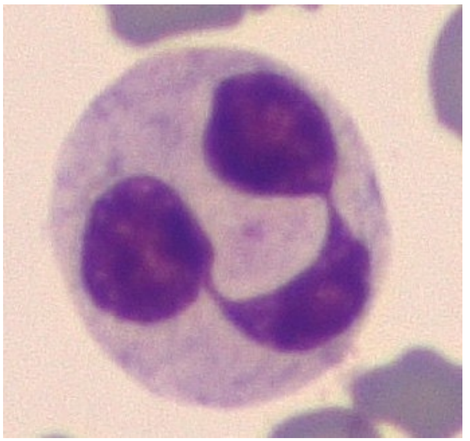
- *A normal total white blood cell count without a differential is of little to no use*
- *<u>Morphology</u>:*
  - *Smear*
  - *Graphics (not helpful with impedance)*

Please remember!

A normal total WBC or neutrophil count DOES NOT exclude inflammation/infection!

Conclusions

- Hematology is EASY, but it's a bit of an art
  - *"Practice makes perfect"*
- I know you will not look at blood smears…
  - so please look at the graphics!
- *coutovetconsultants@gmail.com*



Bonus Case

Dr. DeNicola

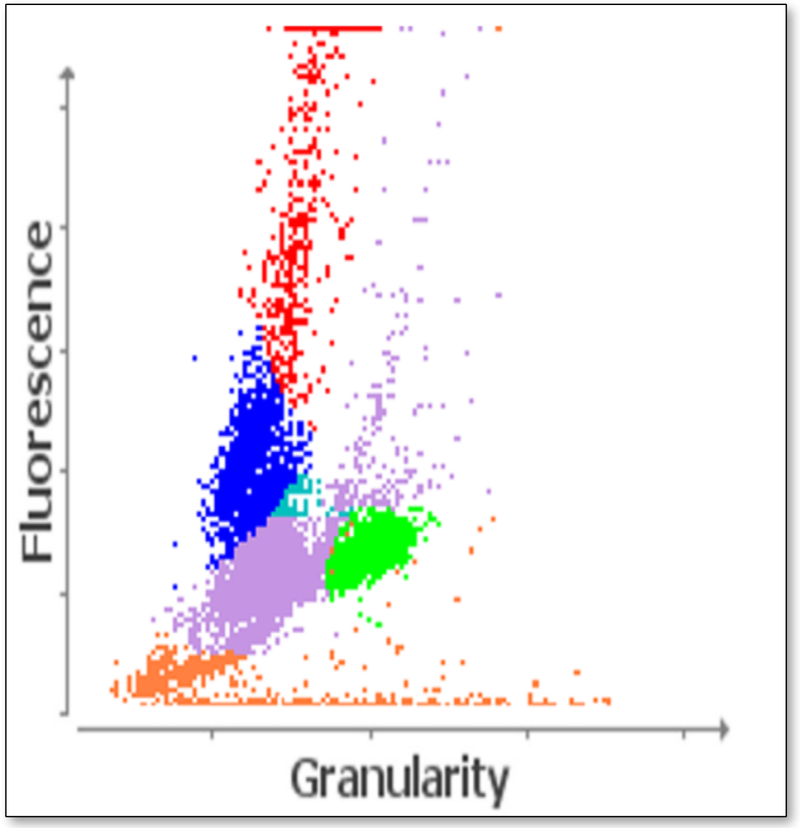
Rosie

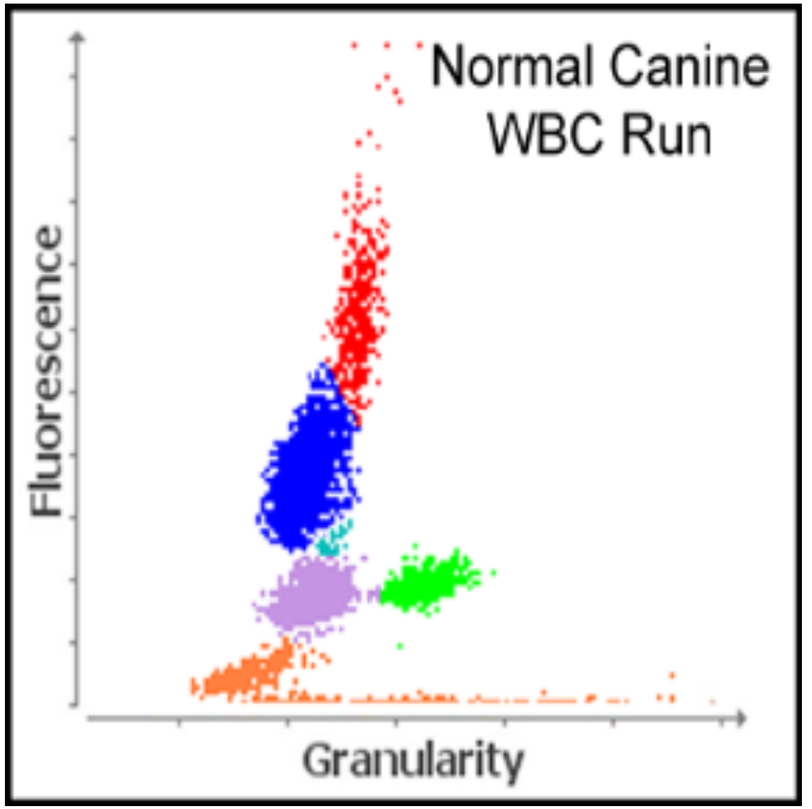
Patient

13 year old, spayed female, mixed breed

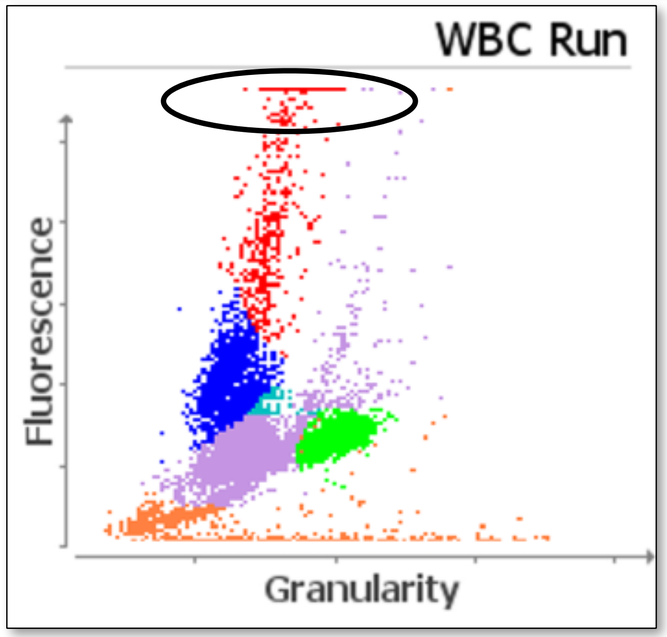
Presenting Complaints

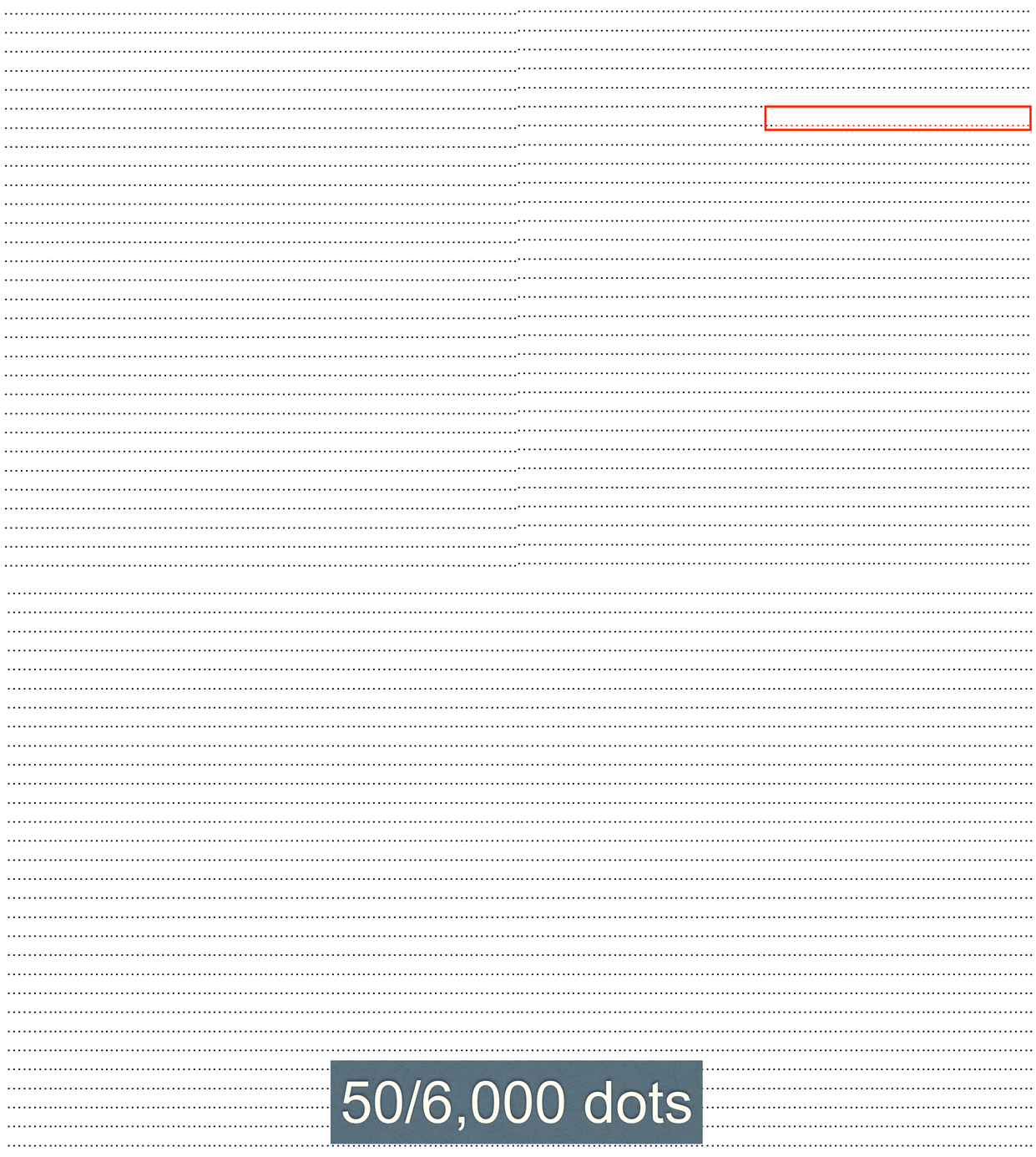
- Slowly developing anorexia
- Slight weight loss
- Slight decreased activity level


Fluorescence
Granularity


Normal Canine
WBC Run
Fluorescence
Granularity

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx					
WBC	11.34 K/µL	5.05 - 16.76			
%NEU	64.1 %				
%LYM	11.1 %				
%MONO	5.8 %				
%EOS	2.1 %				
%BASO	0.7 %				
NEU	7.26 K/µL	2.95 - 11.64			
LYM	1.26 K/µL	1.05 - 5.10			
MONO	0.66 K/µL	0.16 - 1.12			
EOS	**2.08 K/µL**	**0.06 - 1.23**	**HIGH**		
BASO	0.08 K/µL	0.00 - 0.10			



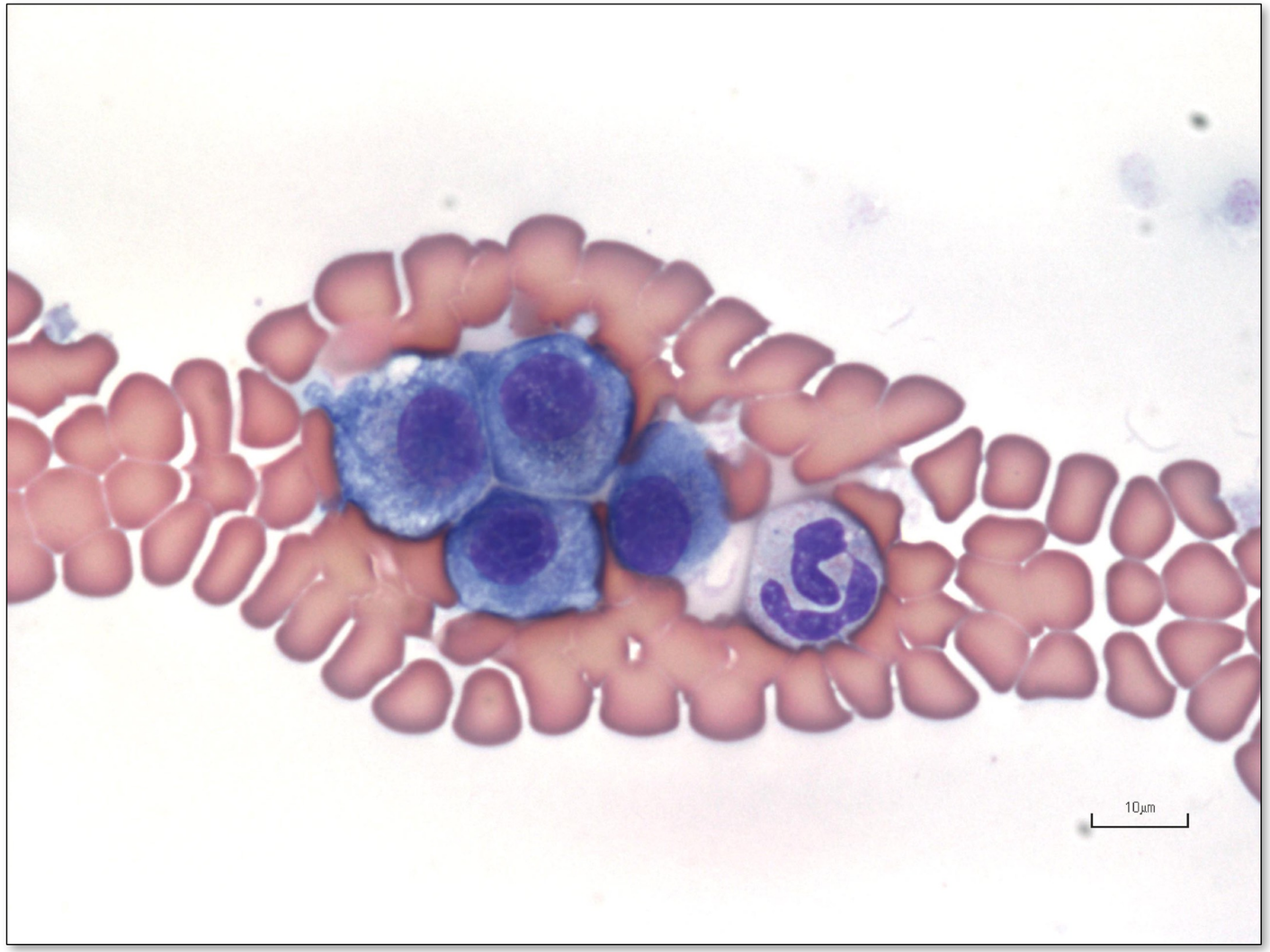

50/6,000 dots


WHERE'S
WALDO?


© Imgur

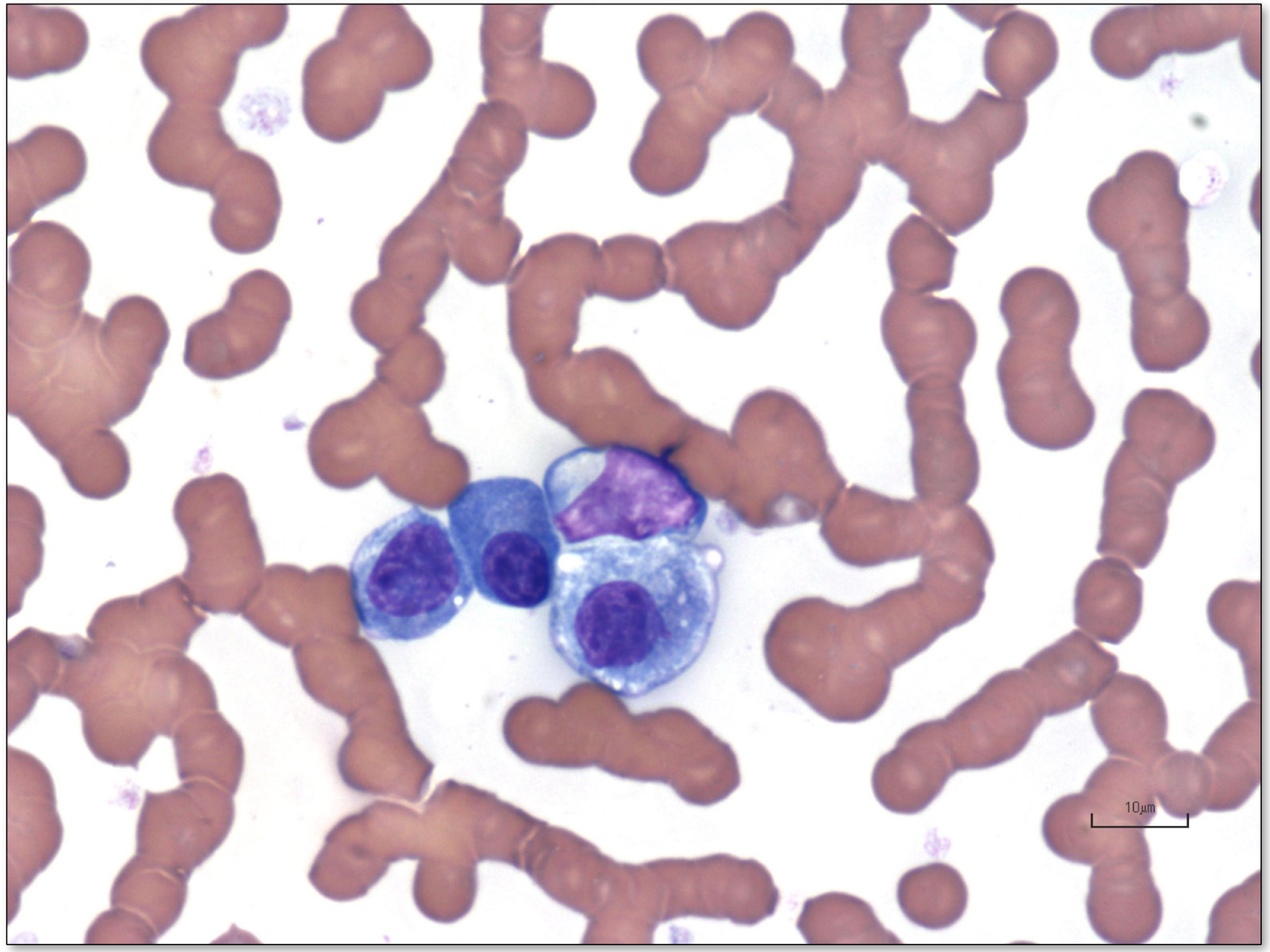
Rosie – peripheral blood film

Dr. DeNicola

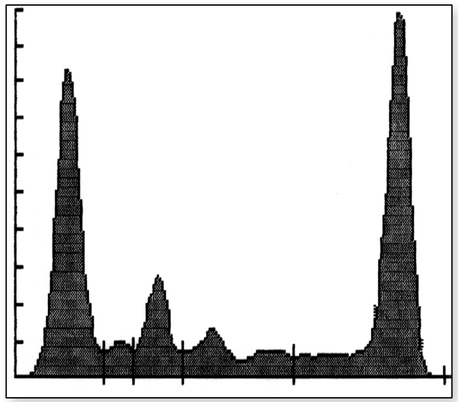


Rosie – peripheral blood film

Dr. DeNicola



Serum Protein Electrophoresis

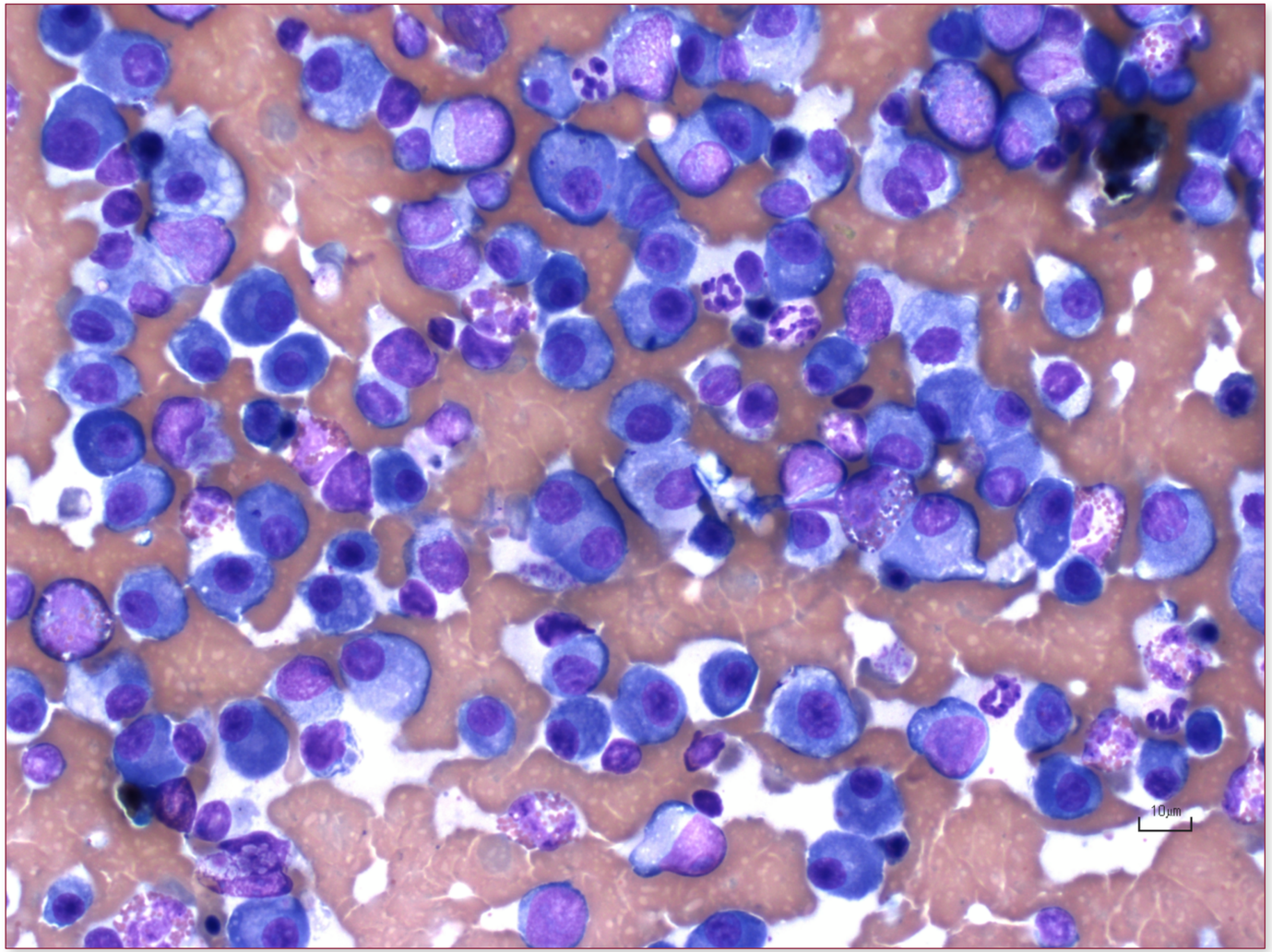


Albumin	1.8	2.5 - 4.0 g/dL	L
Total Protein	8.7	5.1 - 7.8 g/dL	H
Globulin	6.7	g/dL	
Alb / Glob Ratio	0.30		
Alpha 1	0.42	0.2 - 0.5 g/dL	
Alpha 2	0.64	0.3 - 1.1 g/dL	
Beta 1	0.53	0.6 - 1.2 g/dL	L
Beta 2	1.31	0.6 - 1.40 g/dL	
Gamma 1	3.80	0.5 - 1.3 g/dL	H

THERE IS A MARKED, MONOCLONAL SPIKE (MONOCLONAL GAMMOPATHY)

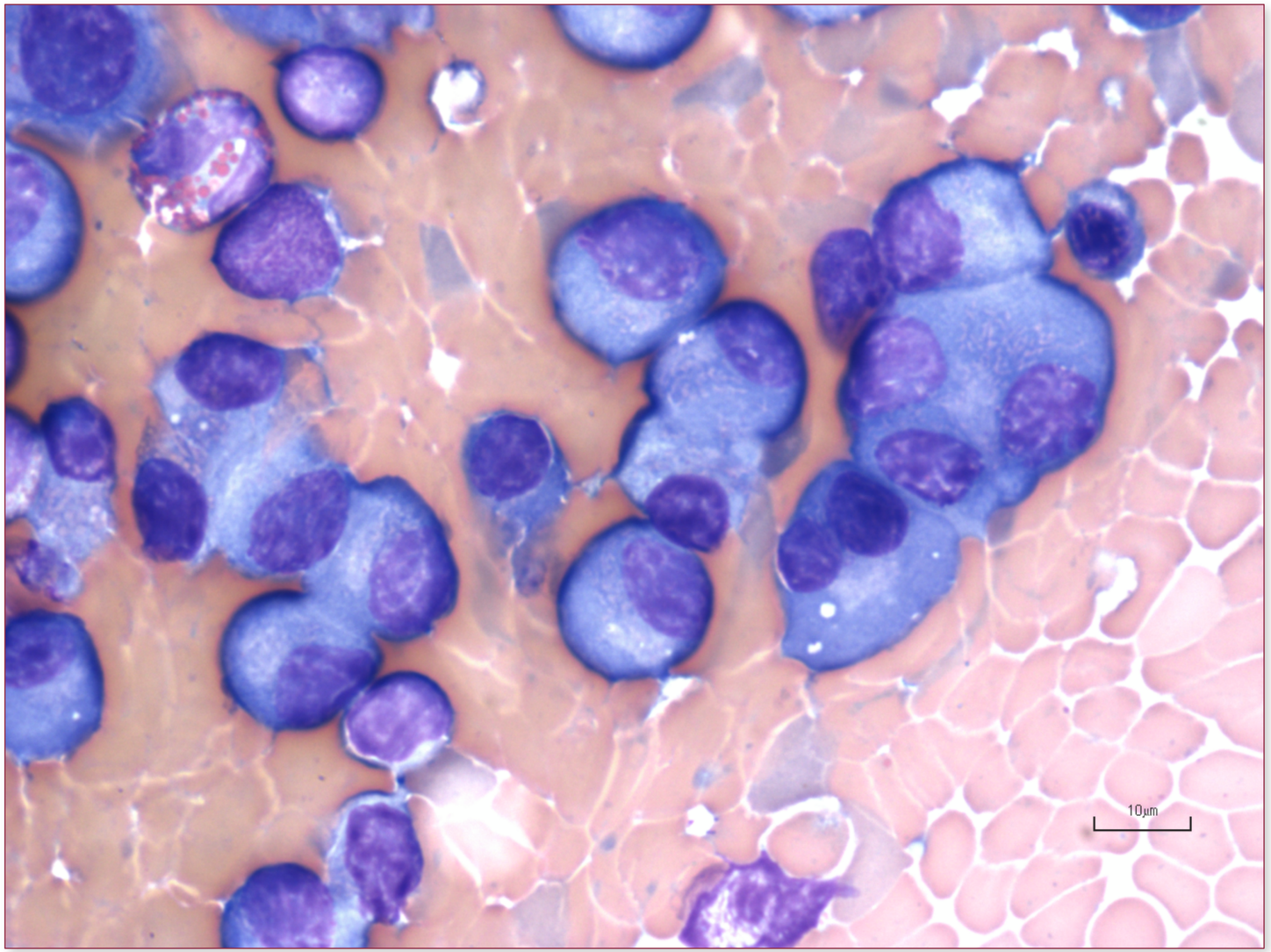
Rosie – Spleen FNA

Dr. DeNicola



Rosie – Spleen FNA

Dr. DeNicola



Final Dx: Multiple myeloma