Early Cancer Diagnosis: Don't Miss The Warning Signs!

Guillermo Couto, DVM, DACVIM
(SAIM, Oncology)

coutovetconsultants@gmail.com

Disclaimer

- I am an internist and oncologist, not a clinical pathologist
- I am an Idexx consultant
- I have used Idexx equipment for > 20 years
- Thanks to Dr. Dana Connell

Today's Lecture

- Importance of cancer
- Human Vs veterinary oncology
- Warning signs
- Clinical evaluation
- Clinical pathology
- Imaging
- Liquid biopsies
  - Cancer DX

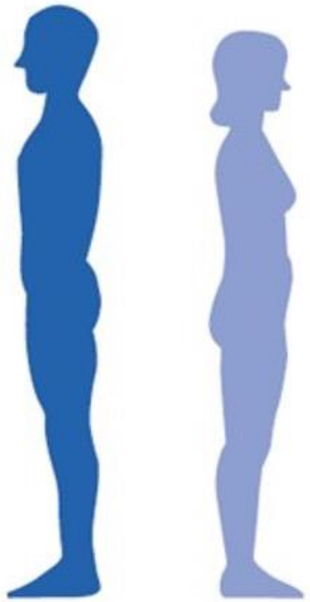
How Important Is Cancer In People (US)?

- In the US:
  - 2 million cases in 2023
  - Lifetime probability of cancer
    - women 1/3
    - men 1/2
  - 600,000 deaths in 2023
    - yes, >1,600/day!!

Cancer Statistics 2023

Estimated New Cancer Cases in the US in 2023

Male		
Prostate	288,300	29%
Lung & bronchus	117,550	12%
Colon & rectum	81,860	8%
Urinary bladder	62,420	6%
Melanoma of the skin	58,120	6%
Kidney & renal pelvis	52,360	5%
Non-Hodgkin lymphoma	44,880	4%
Oral cavity & pharynx	39,290	4%
Leukemia	35,670	4%
Pancreas	33,130	3%
All sites	**1,010,310**	



Female		
Breast	297,790	31%
Lung & bronchus	120,790	13%
Colon & rectum	71,160	8%
Uterine corpus	66,200	7%
Melanoma of the skin	39,490	4%
Non-Hodgkin lymphoma	35,670	4%
Thyroid	31,180	3%
Pancreas	30,920	3%
Kidney & renal pelvis	29,440	3%
Leukemia	23,940	3%
All sites	**948,000**	

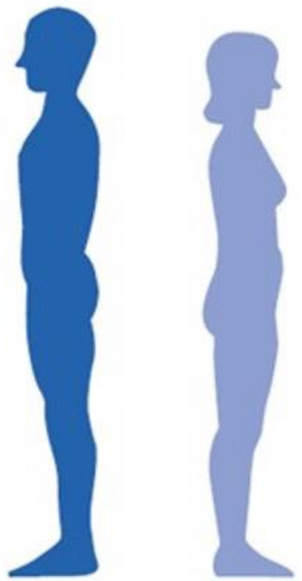
1,010,310

948,000

Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Estimated Cancer Deaths in the US in 2023

Male		
Lung & bronchus	67,160	21%
Prostate	34,700	11%
Colon & rectum	28,470	9%
Pancreas	26,620	8%
Liver & intrahepatic bile duct	19,000	6%
Leukemia	13,900	4%
Esophagus	12,920	4%
Urinary bladder	12,160	4%
Non-Hodgkin lymphoma	11,780	4%
Brain & other nervous system	11,020	3%
All sites	**322,080**	



Female		
Lung & bronchus	59,910	21%
Breast	43,170	15%
Colon & rectum	24,080	8%
Pancreas	23,930	8%
Ovary	13,270	5%
Uterine corpus	13,030	5%
Liver & intrahepatic bile duct	10,380	4%
Leukemia	9,810	3%
Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	7,970	3%
All sites	**287,740**	

322,080

287,740

How Important Is Cancer In People (UK)?

CANCER RESEARCH UK

Together we are beating cancer

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Donate

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Home › Health professional › Data and Statistics › Cancer Statistics for the UK

Cancer Statistics for the UK

Population: 69 million

Cases

385,477

New cases of cancer, 2017-2019, UK.

Deaths

167,142

Deaths from cancer, 2017-2019, UK.

Survival

Survive cancer for 10 or more years, 2010-11, England and Wales

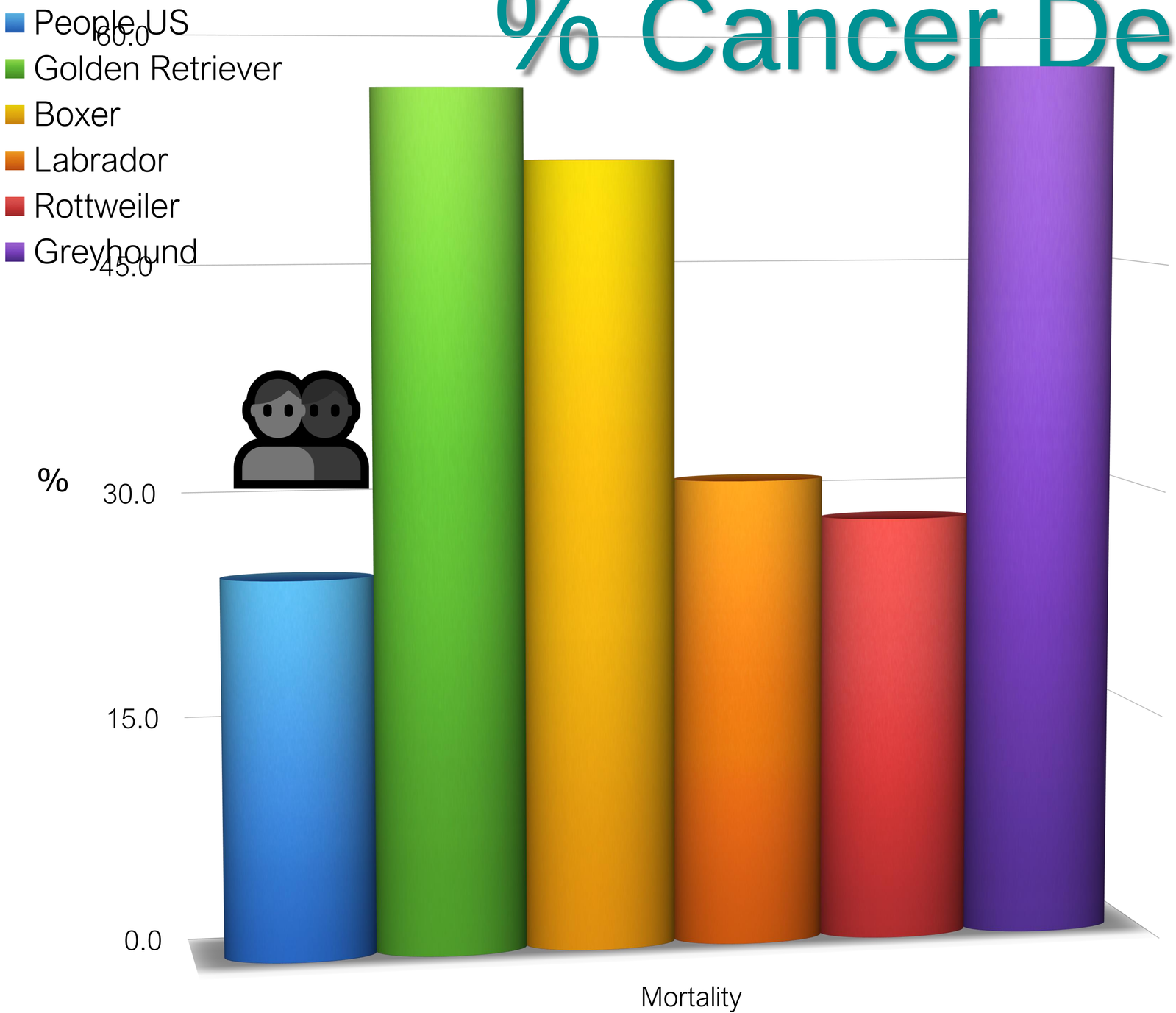
Preventable cases

Cancer cases are preventable, UK, 2015

How Important Is Cancer In Pets?

- Most common senior dog disease
- Common senior cat disease
- Most common cause of death in most dog breeds
- Common cause of death in cats

% Cancer Deaths



Craig, LE: *J Am Anim Hosp Assoc 2001; 37, 438.*

Cancer

Cancer In Pets

- Human Vs Vet Oncology
  - TOTALLY different goals!
  - Can we change the outcome without affecting QOL?
  - Cost and third-party payment

Cancer in Pets - Education

- Families and vets often don’t know the facts
- To some, cancer = euthanasia
  - Yes, for vets too…
- Lots of families interested in potential treatment

Clinical Evaluation

- History
- Physical exam
- Clinical pathology
  - CBC
  - Chemistry
  - UA
  - Cytology
- Other diagnostics
  - Liquid biopsy

Does early cancer diagnosis improve prognosis?

Warning Signs Of Cancer

10 common signs of neoplasia in small animals

1. Abnormal swellings that persist or continue to grow
2. Sores that do not heal
3. Weight loss
4. Loss of appetite
5. Bleeding or discharge from any body opening
6. Offensive odor
7. Difficulty eating or swallowing
8. Hesitation to exercise or loss of stamina
9. Persistent lameness or stiffness
10. Difficulty breathing, urinating, or defecating

History and Physical Examination

- Weight loss/emaciation
- Pallor
- Petechiae/ecchymoses
- Hyphema
- Masses
- Fluid accumulation

And PLEASE, do a rectal exam…

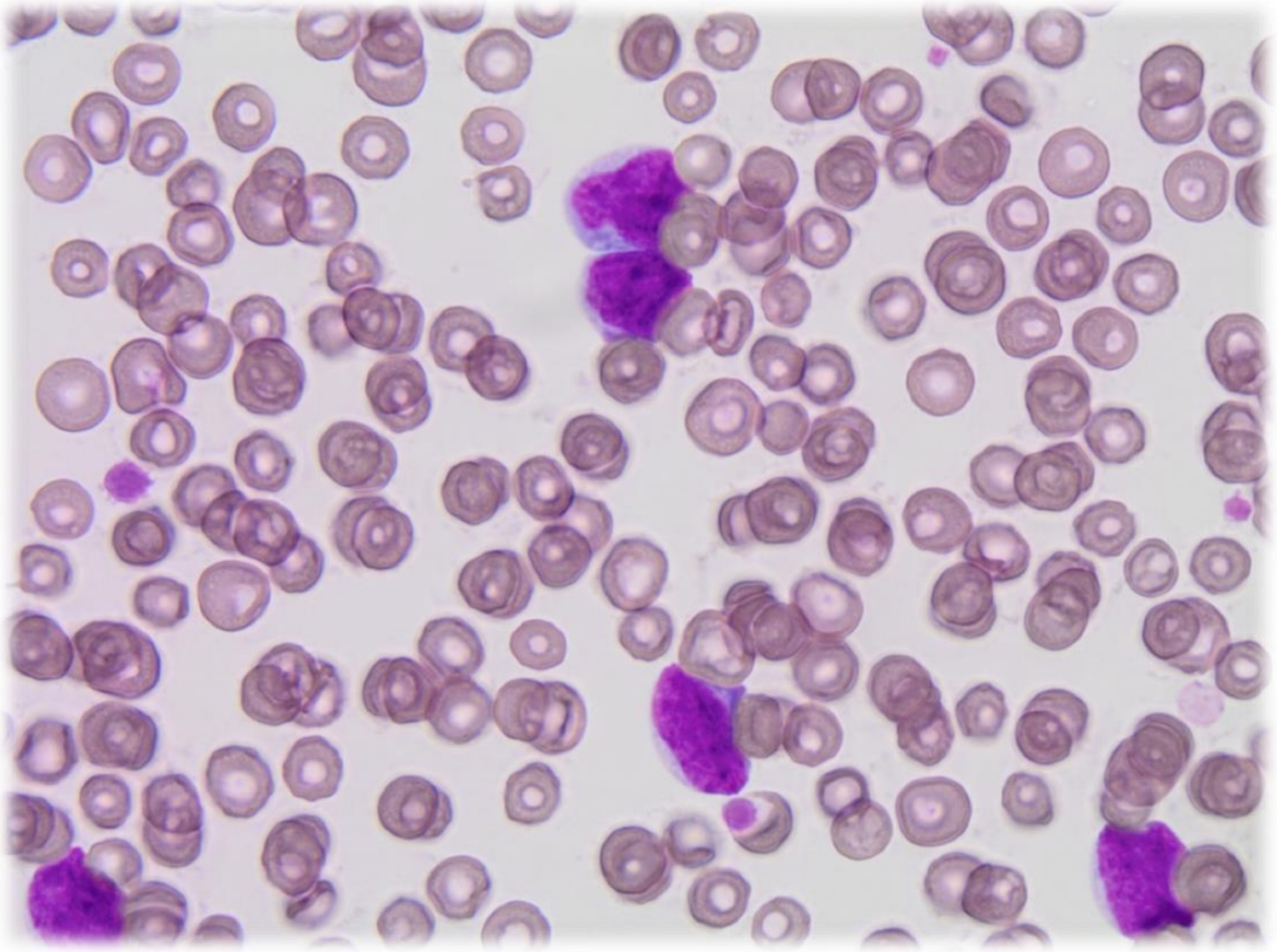

U BLADDER
1 Dist = 1.614cm
2 Dist = 0.732cm

Clin Path In Oncology

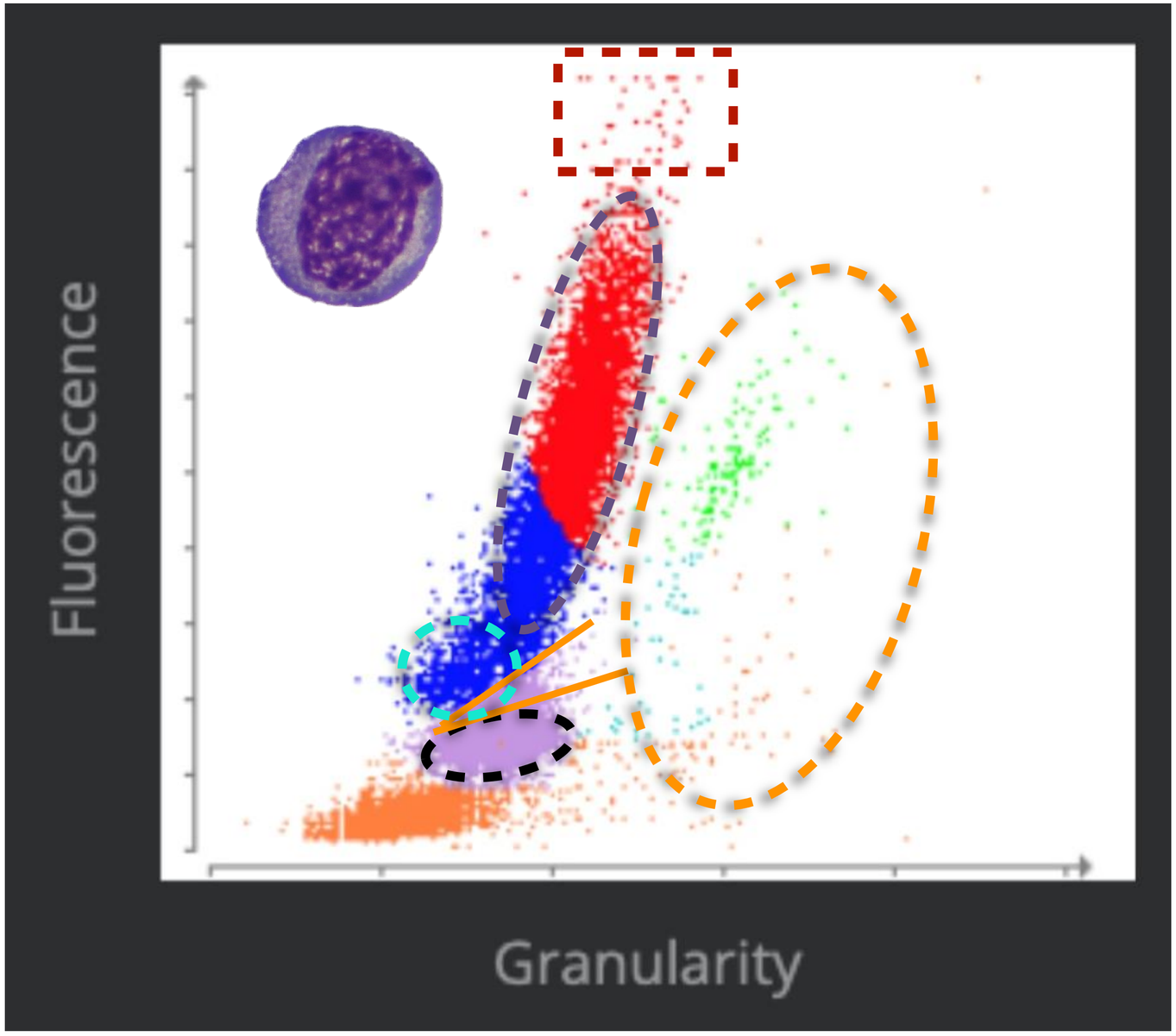
- Provides diagnosis
- Suggests subclinical neoplasia
- Staging
- Monitoring response to Rx
- Cancer screening

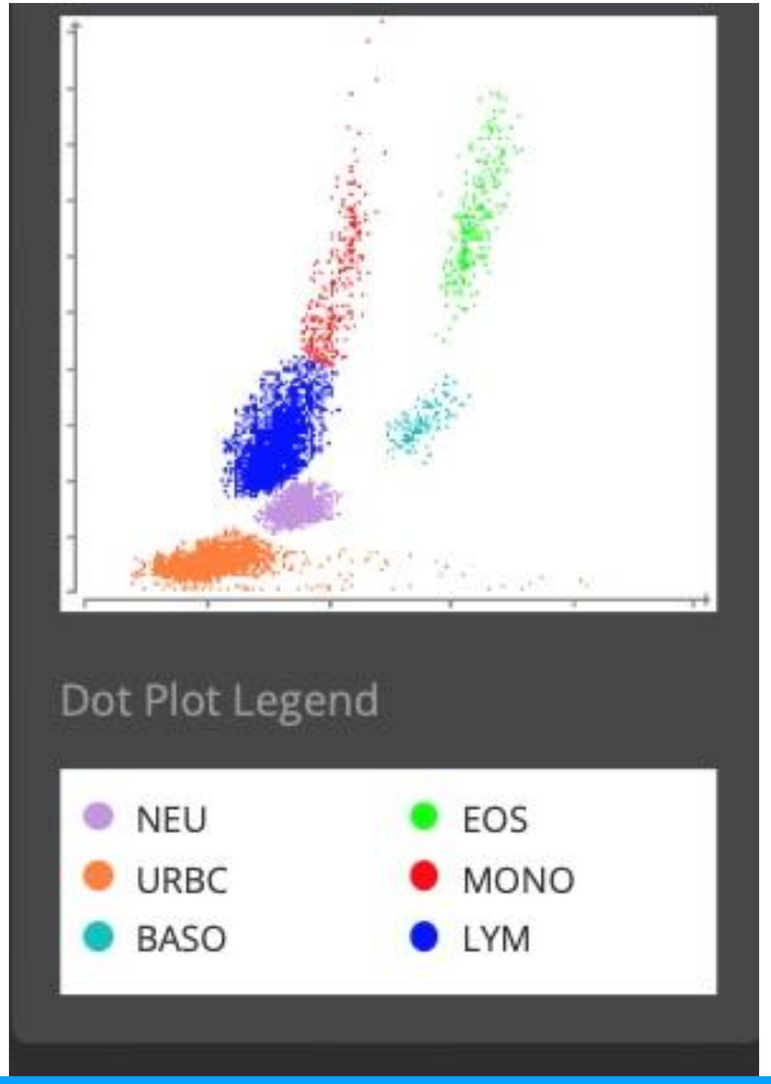
Clin Path In Oncology

- Provides diagnosis



Simon-WBC Dot Plots





Drs. Kate Sycamore and Jason Couto

Clin Path In Oncology

- Suggests subclinical neoplasia
  - Anemia
  - Leukocytosis
  - Hypercalcemia
  - Gammopathy
  - Etc, etc

Clin Path In Oncology

- Cancer Screening
  - Cancer Dx

Clin Path In Oncology

- Hematology
  - Red cells
  - White cells
  - Platelets
  - Hemostasis

Clin Path In Oncology

- Red blood cells
  - Anemia
  - Erythrocytosis

Anemia

Regenerative

"Macrocytic
Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

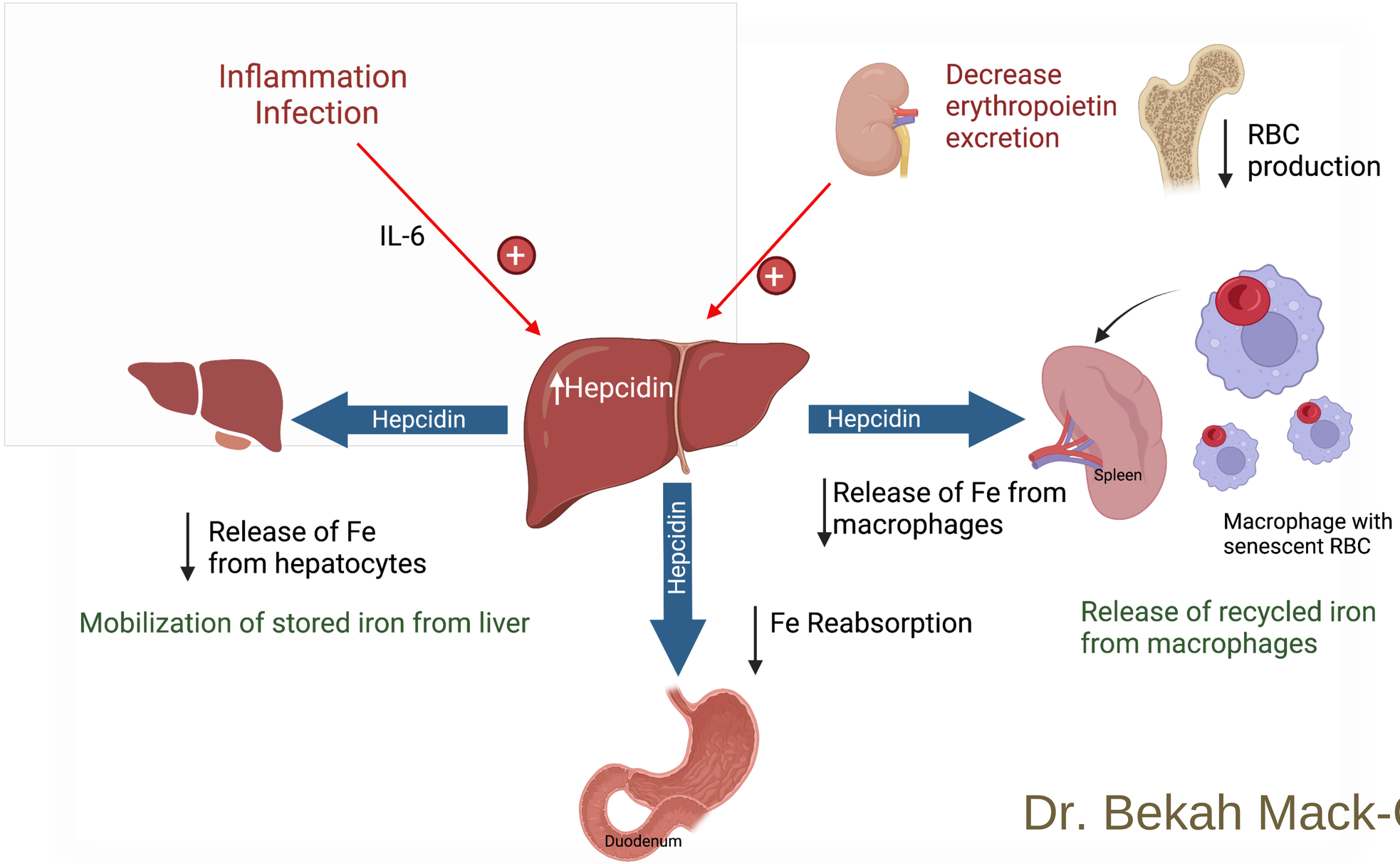
ACD
CKD
BM
(Endocrine)

With impedance analyzers,
90% of regenerative anemias
are NOT macrocytic, hypochromic

Anemia Of Chronic Disease (ACD)

- Most common anemia in cancer patients
- Mild, normocytic, normochromic
- Chronic cytokine->hepcidin release
- Fe “hoarding” by macrophages in BM/decreased Fe absorption
- Clinically relevant?

ACD



Dr. Bekah Mack-Gertig

Anemia

Regenerative

"Macrocytic
Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

ACD
CKD
BM
(Endocrine)

Which ones are common in cancer patients?

Anemia

Regenerative

"Macrocytic Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

ACD
CKD
BM
(Endocrine)

A dog with HSA has…

Anemia

Regenerative

"Macrocytic Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

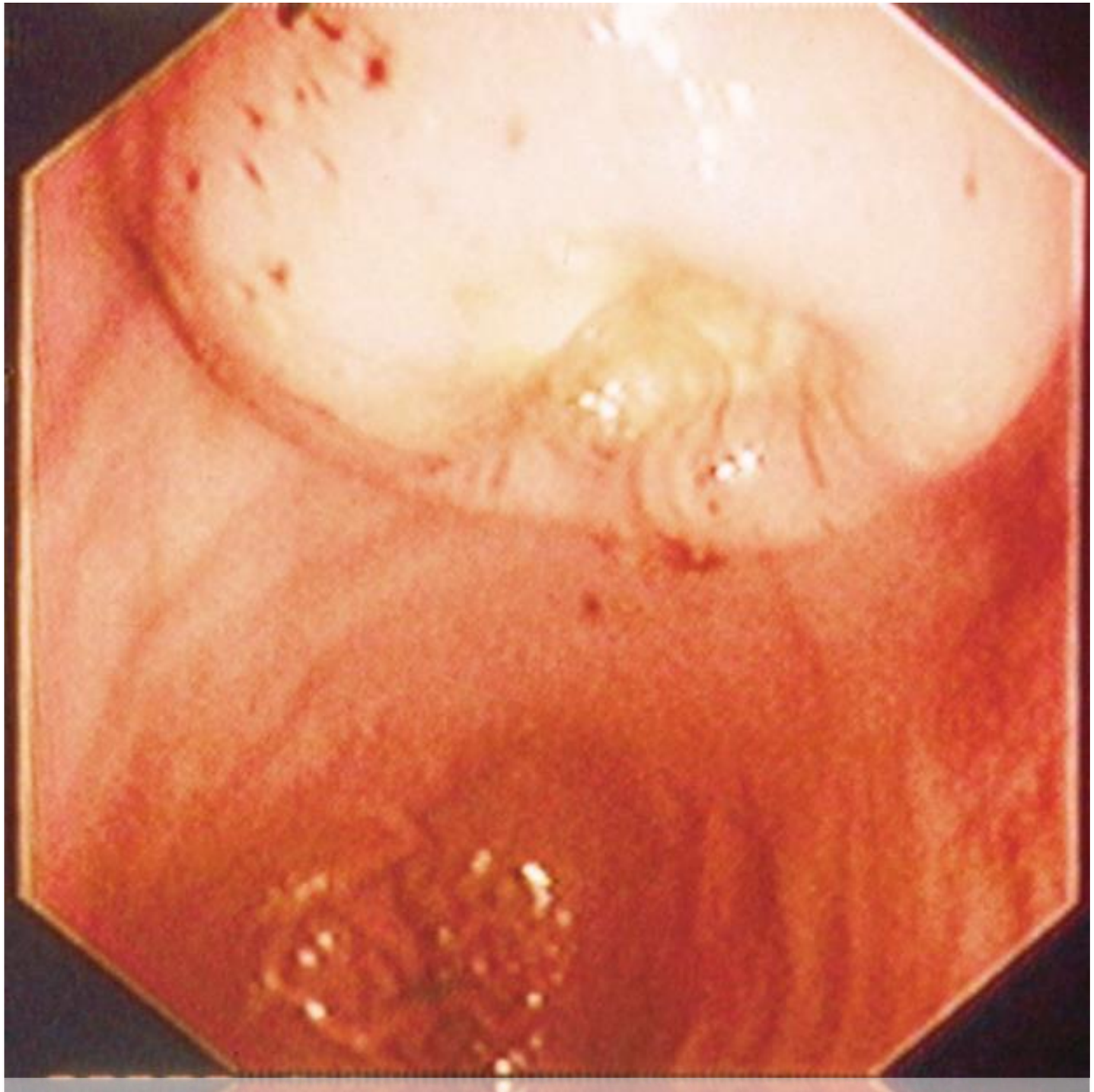
Iron deficiency

Non regenerative

Normocytic
Normochromic

ACD
CKD
BM
(Endocrine)

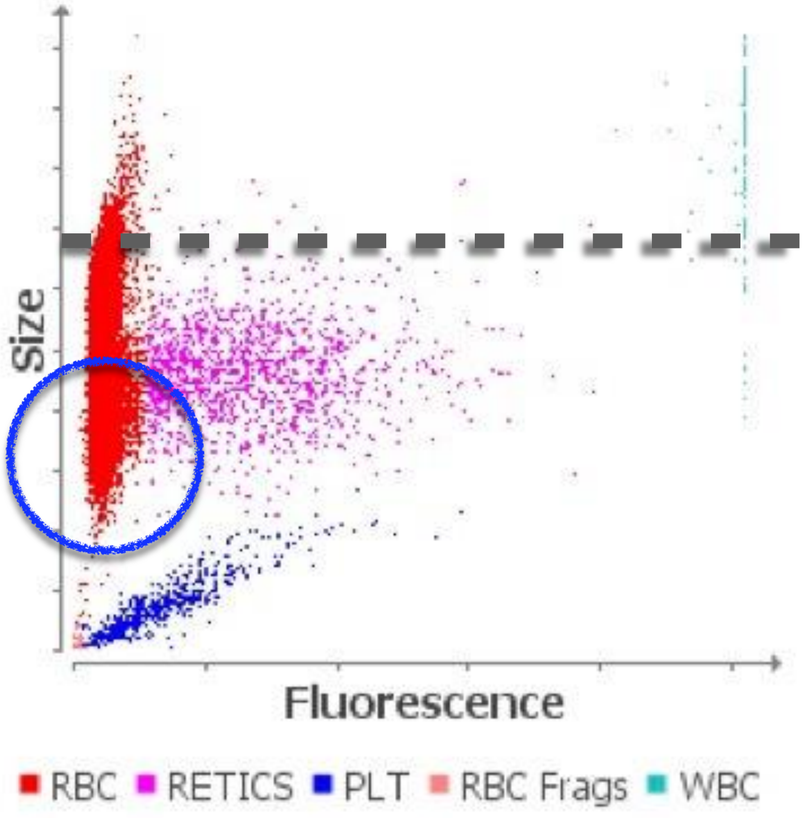
A dog with an intestinal tumor has…



Jejunal GIST

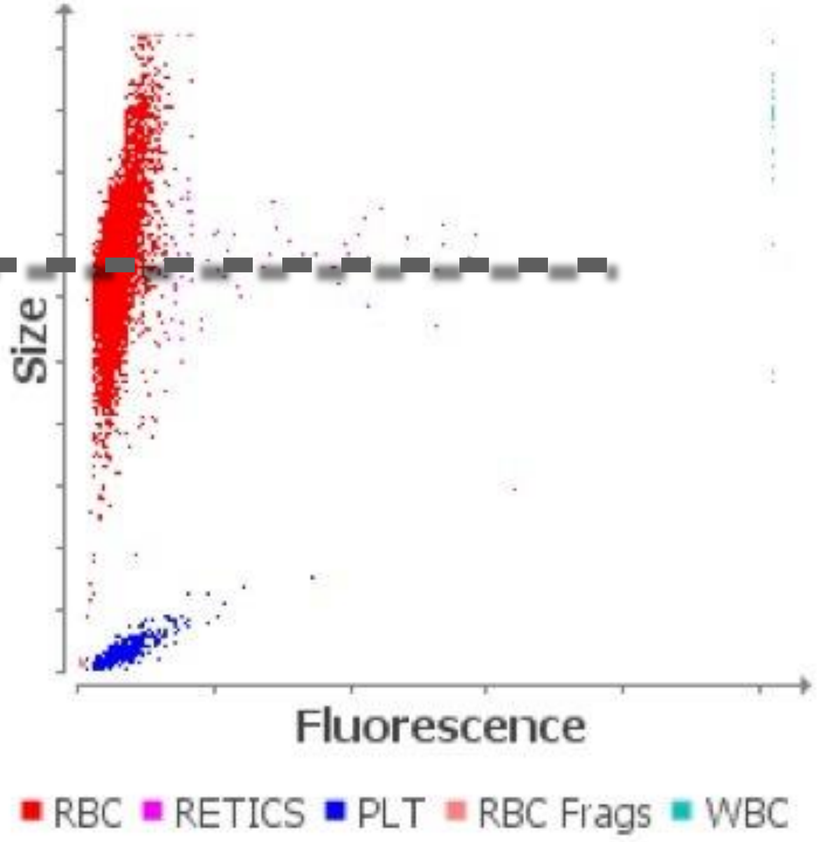
Patient

RBC Run



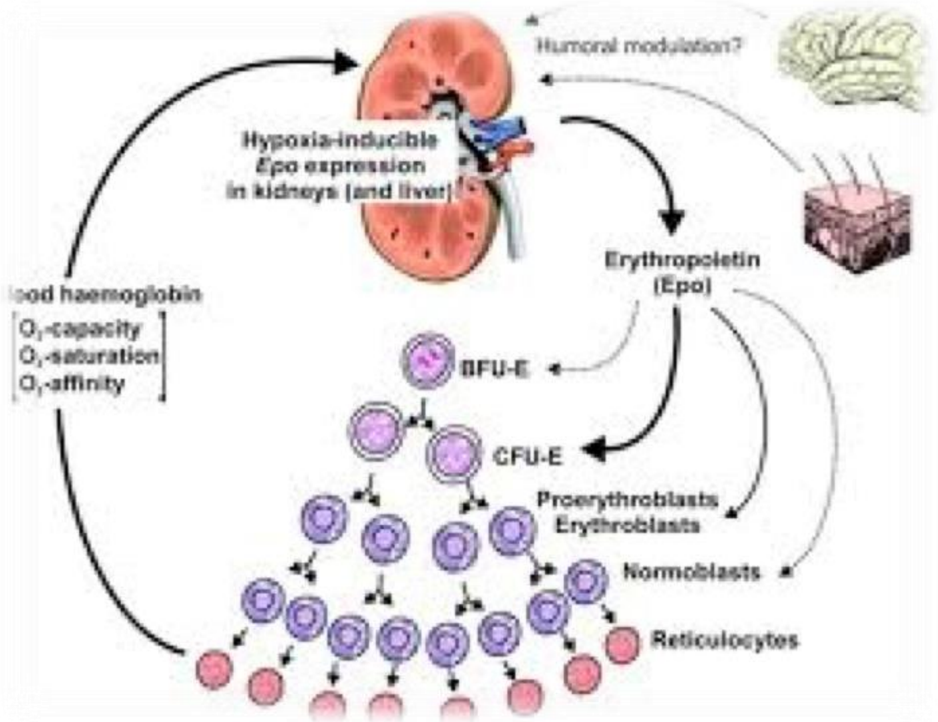
Normal

RBC Run

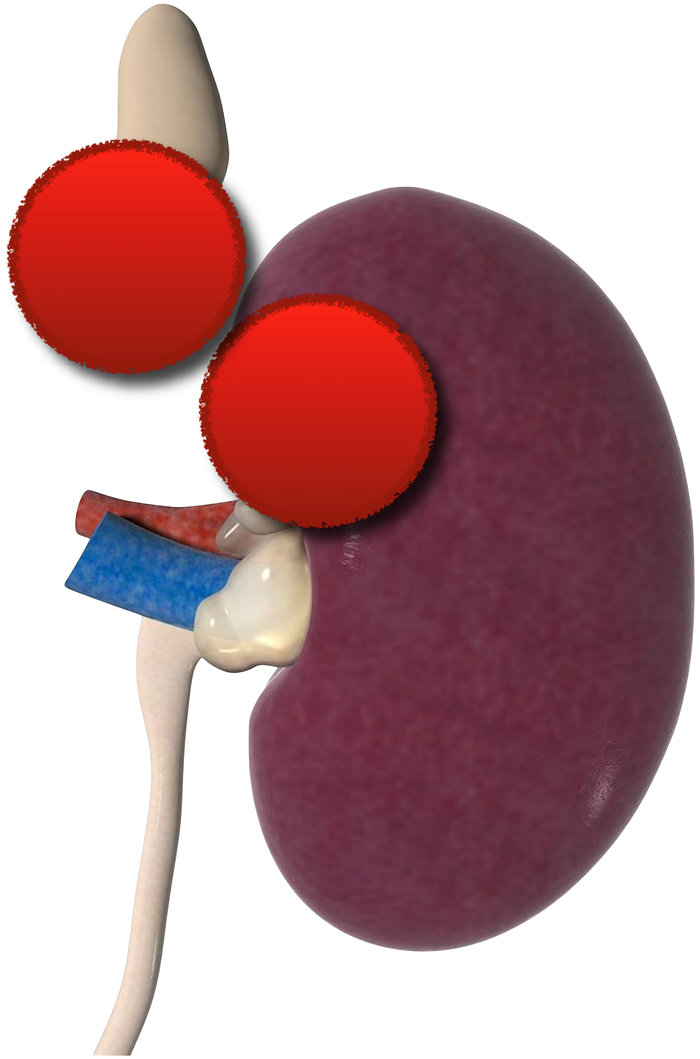


Erythrocytosis

- Appropriate or inappropriate release of EPO
- Autonomous RBC proliferation (Polycythemia vera)



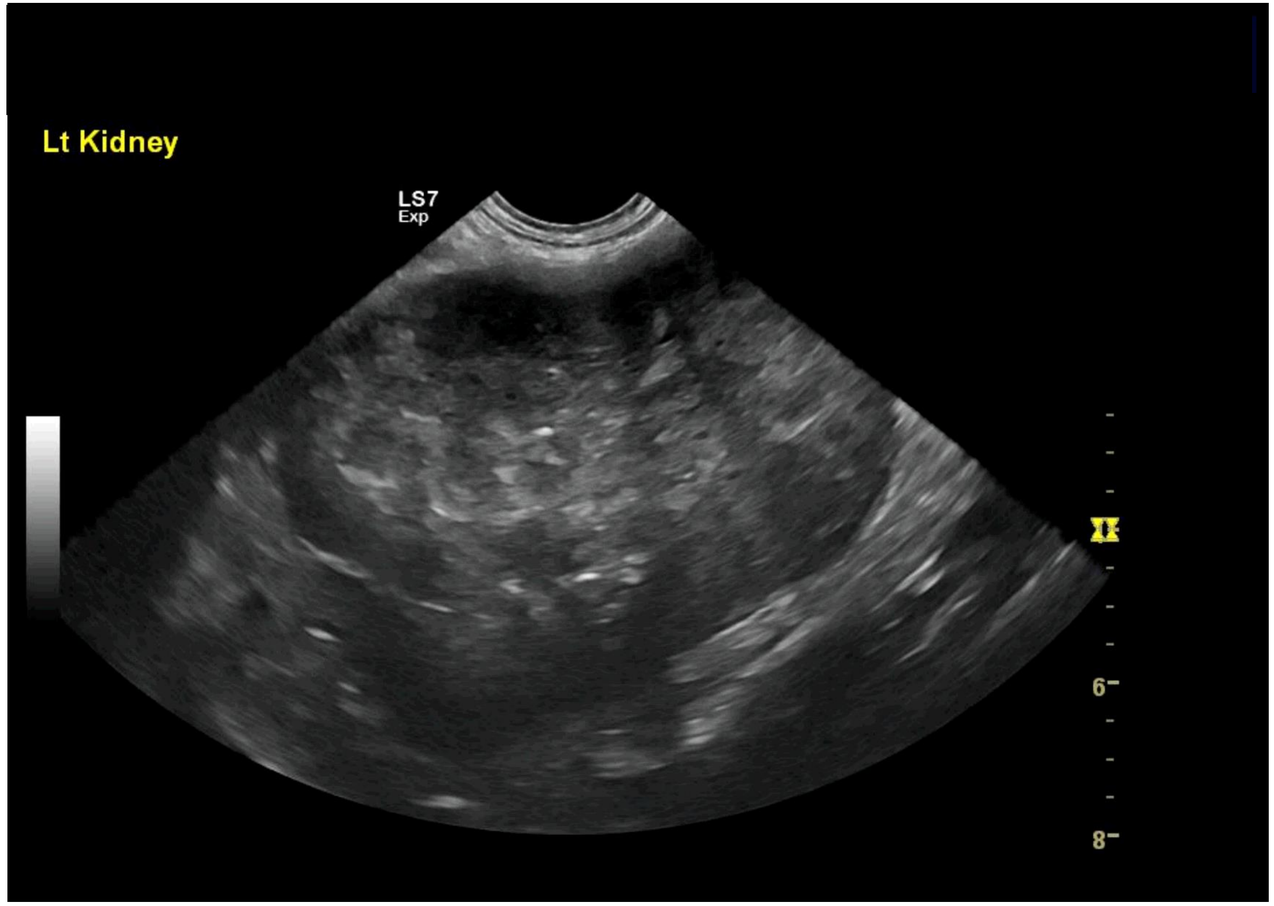
Erythrocytosis



- Renal masses
- Extrarenal compression (pheo)

Erythrocytosis

- Tumor EPO production:
  - renal carcinomas
  - nasal fibrosarcoma
  - any other tumor



Clin Path In Oncology

- White blood cells
  - **Neutrophils**
    - neutrophilia/neutropenia
  - **Lymphocytes**
    - lymphocytosis
  - **Eosinophils**
    - eosinophilia
  - **Monocytes**
    - monocytosis

Neutrophils

Neutrophilia

- Necrosis
- Systemic inflammation
- Tumor G-CSF/ GM-CSF production

Neutropenia

- BM involvement
- Immune- mediated
- Chemo

White Blood Cells

Lymphocytosis	Eosinophilia	Monocytosis
Leukemia (CLL vs ALL)	Lymphoma	Lymphoma
Lymphoma	SCCs	Necrotic tumors
Thymoma	Other CAs	“Not monocytes”

LEUKEMIAS

ACUTE

ALL
AML

CHRONIC

CLL
CML

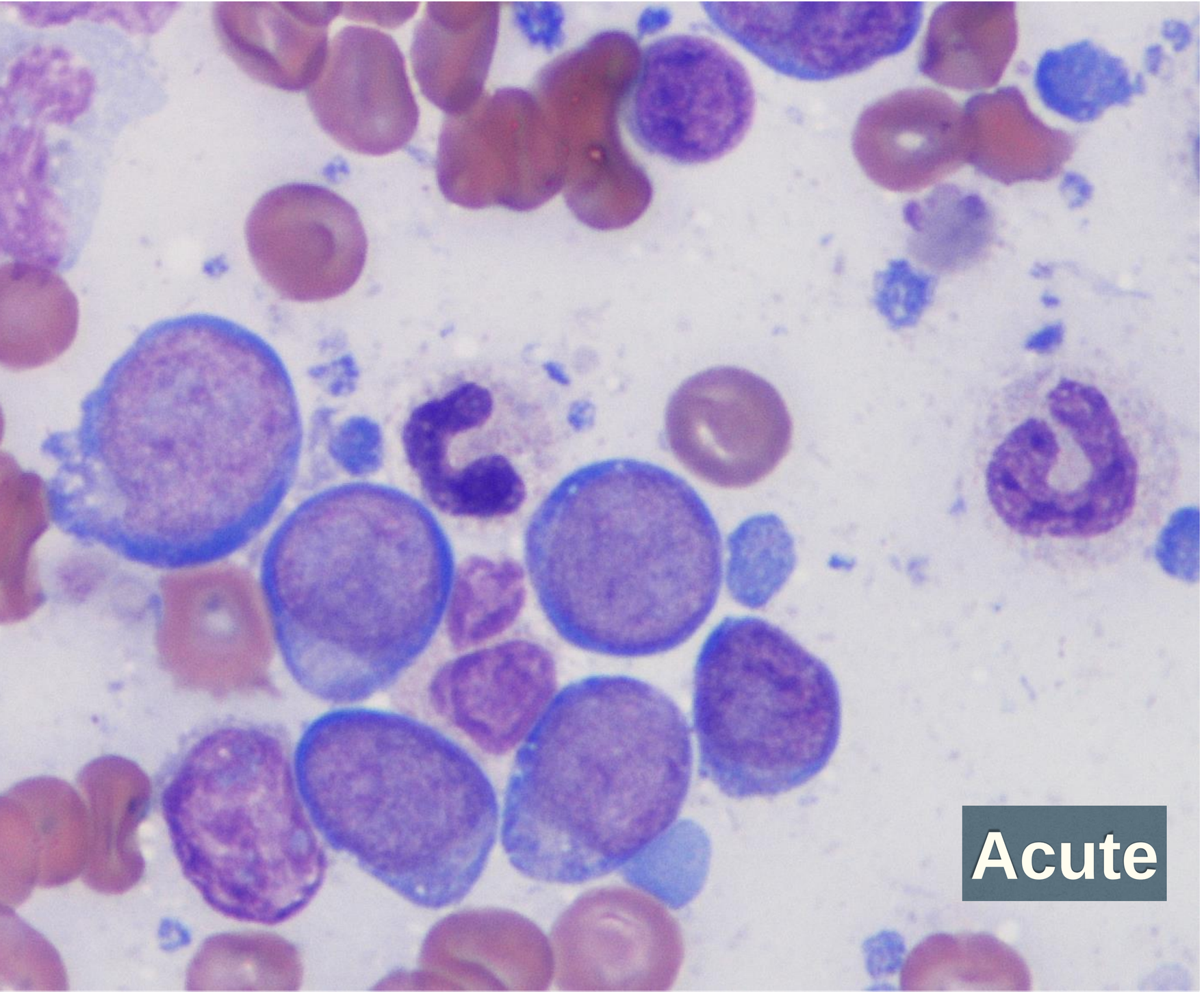
LEUKEMIAS

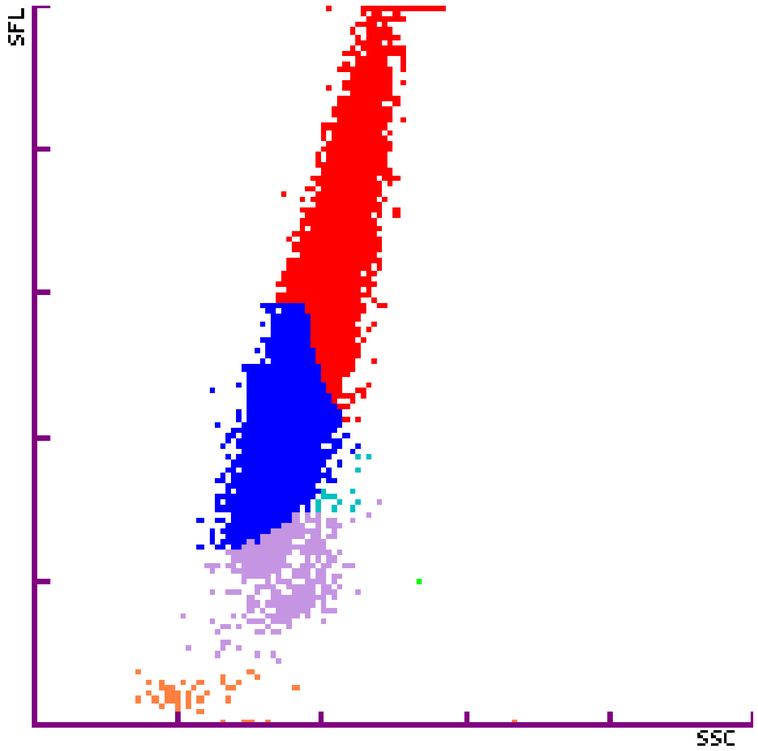
ACUTE

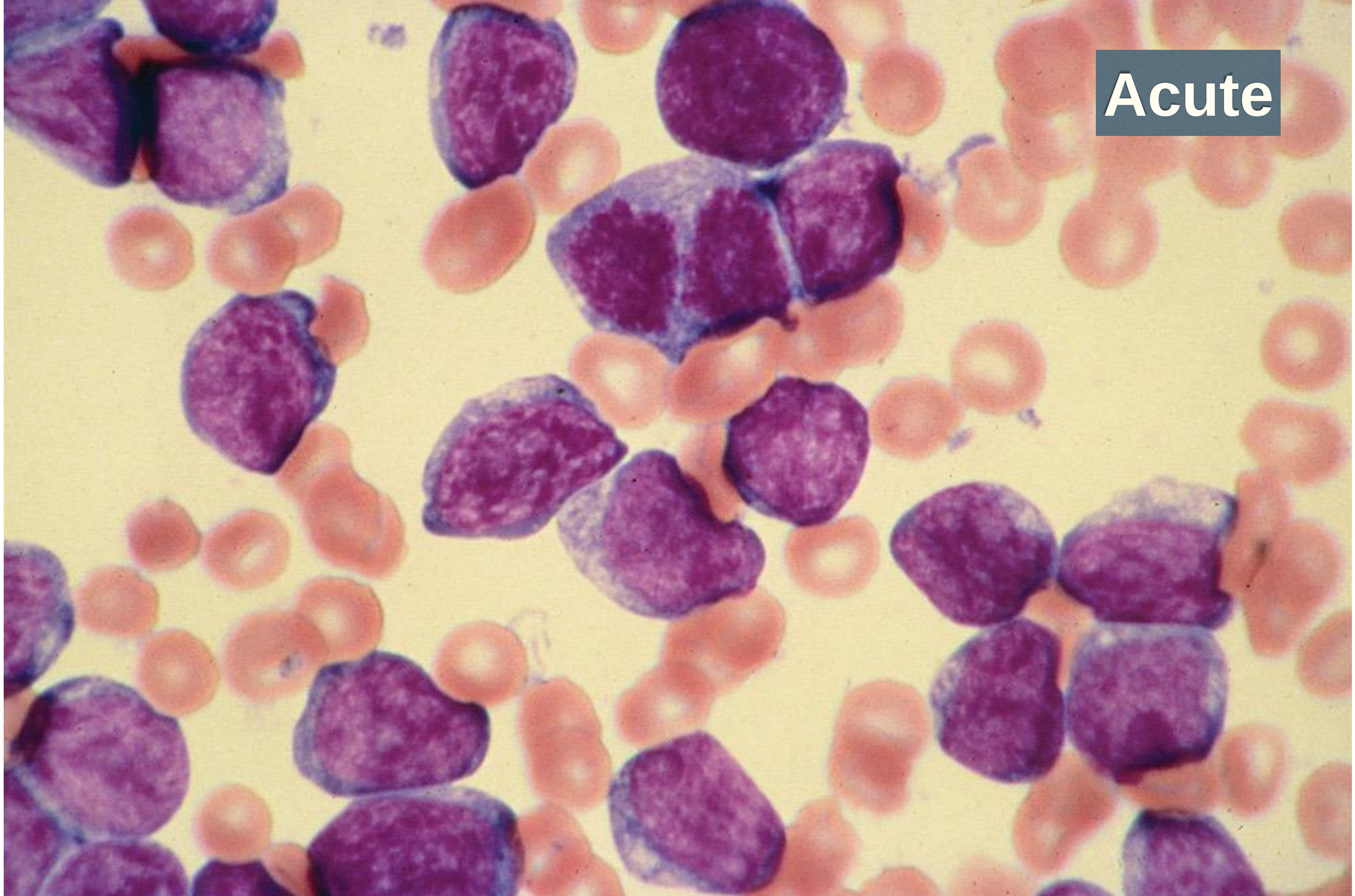
- ALL
- AML

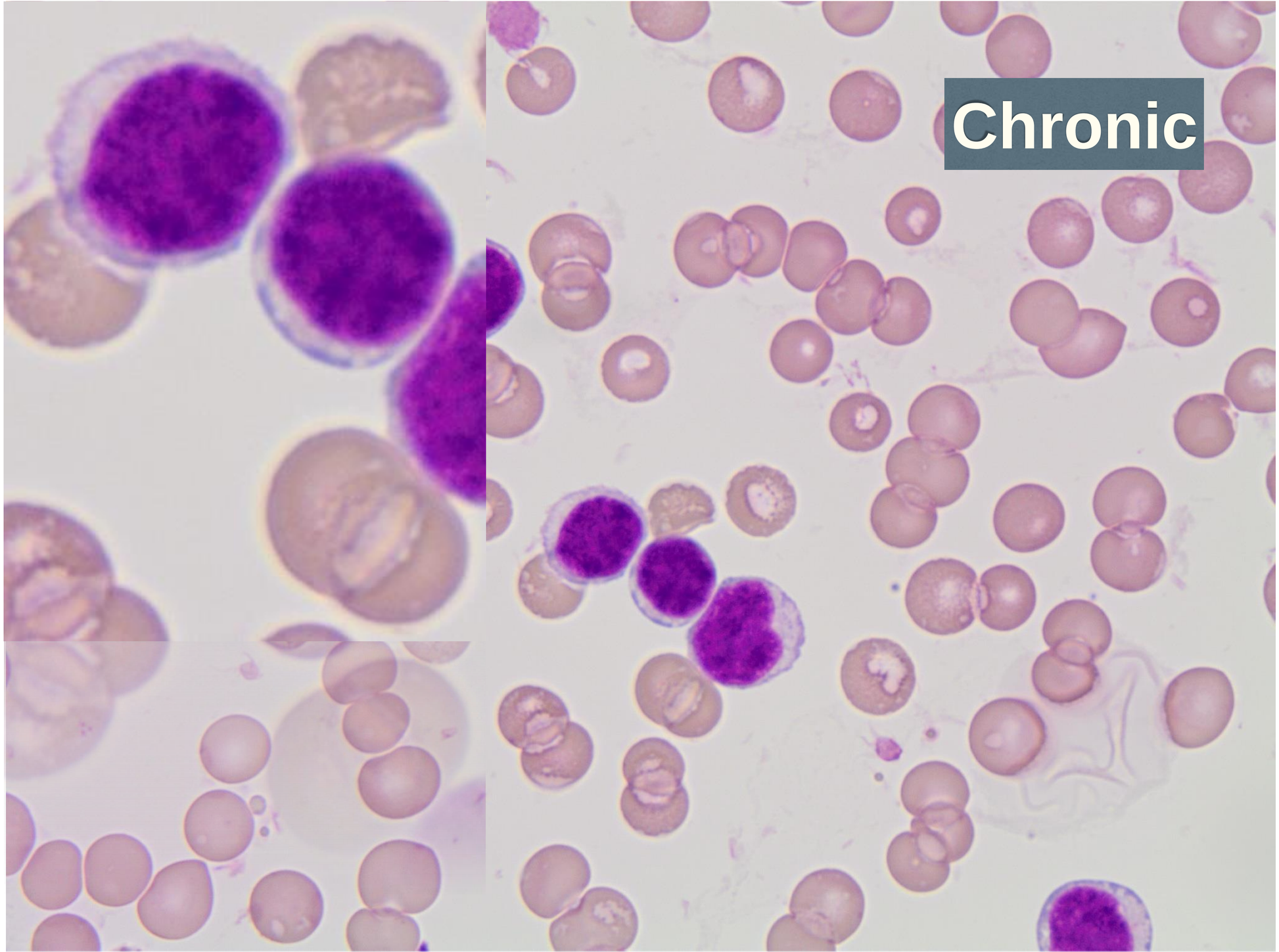
CHRONIC

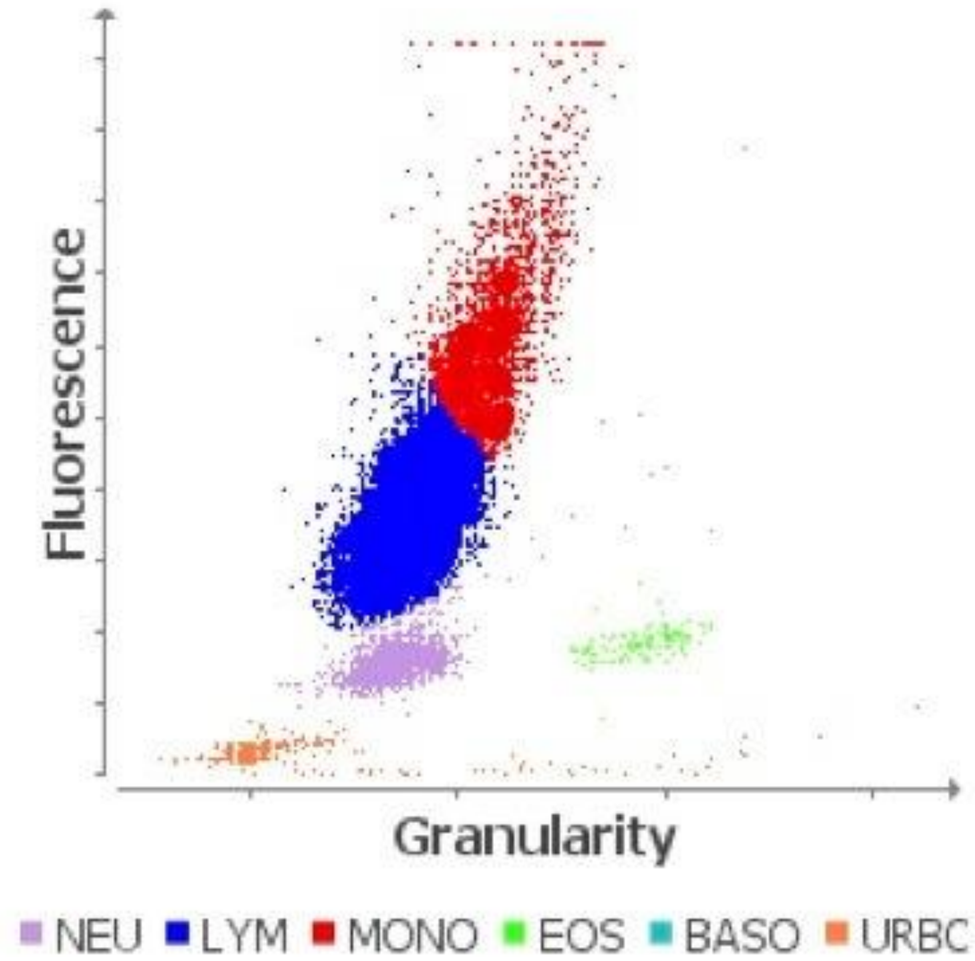
- CLL
- CML

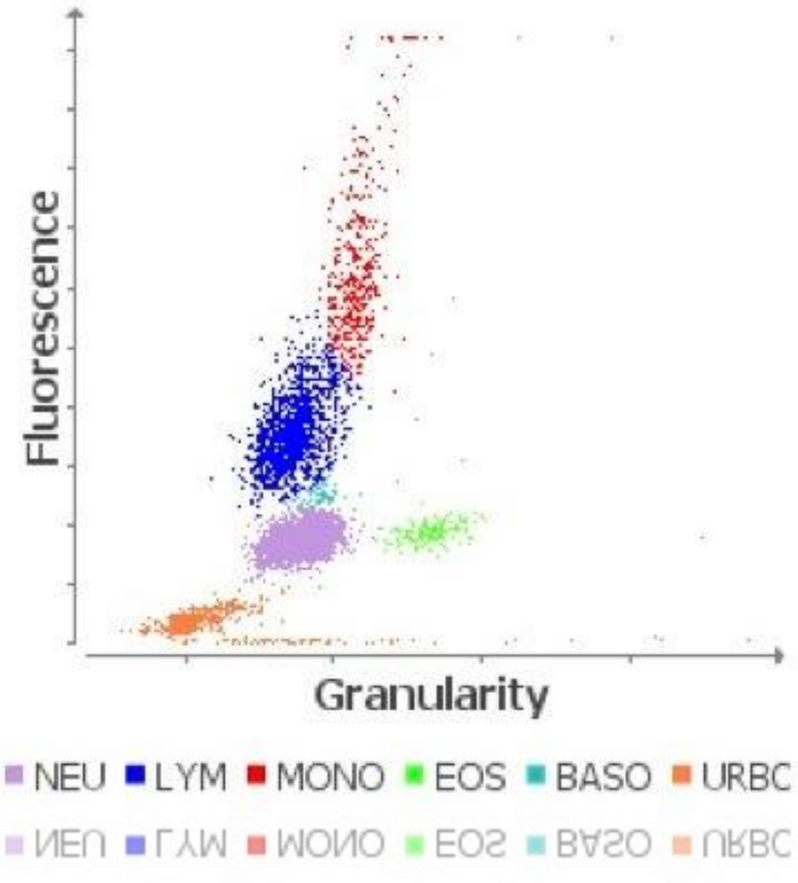

Acute


SFL
SSC


Acute


Chronic

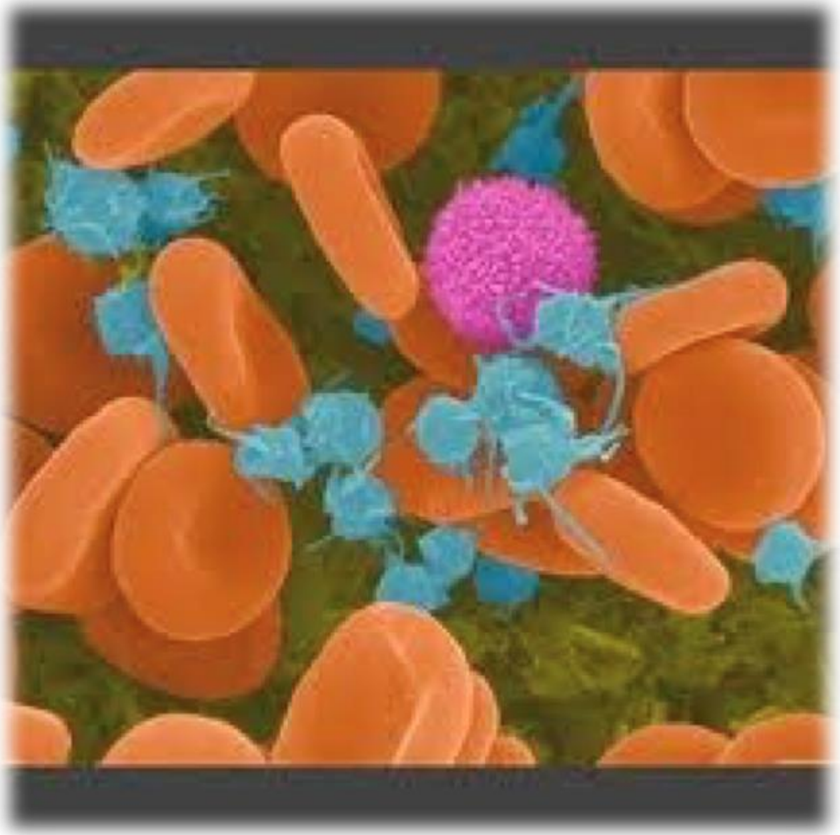




CLL/Indolent lymphoma

Clin Path In Oncology

- Platelets/hemostasis
  - thrombocytopenia
  - thrombocytosis
  - bleeding
  - thrombosis



Clin Path In Oncology

- Platelets
  - thrombocytopenia
    - 1/3 cancer patients
- leukemias
- lymphoma
- myeloma
- HSA
- MH

Clin Path In Oncology

- Platelets
  - thrombocytosis
    - 1/3 dogs with thrombocytosis have cancer
    - 50% of dogs w/carcinoma
    - Essential thrombocythemia
    - Clinically relevant?

Clin Path In Oncology

- **Platelets/hemostasis**
  - bleeding
    - thrombocytopenia
    - DIC
    - “tumor anticoagulants”
  - thrombosis
    - “tumor procoagulant”

Clin Path In Oncology

The Veterinary Journal 190 (2011) e78–e83

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Hemostatic abnormalities in dogs with carcinoma: A thromboelastographic characterization of hypercoagulability ☆

Paulo Vilar Saavedra [a,b,*], Ana Lara García [a,c], Sara Zaldívar López [a], Guillermo Couto [a,d]

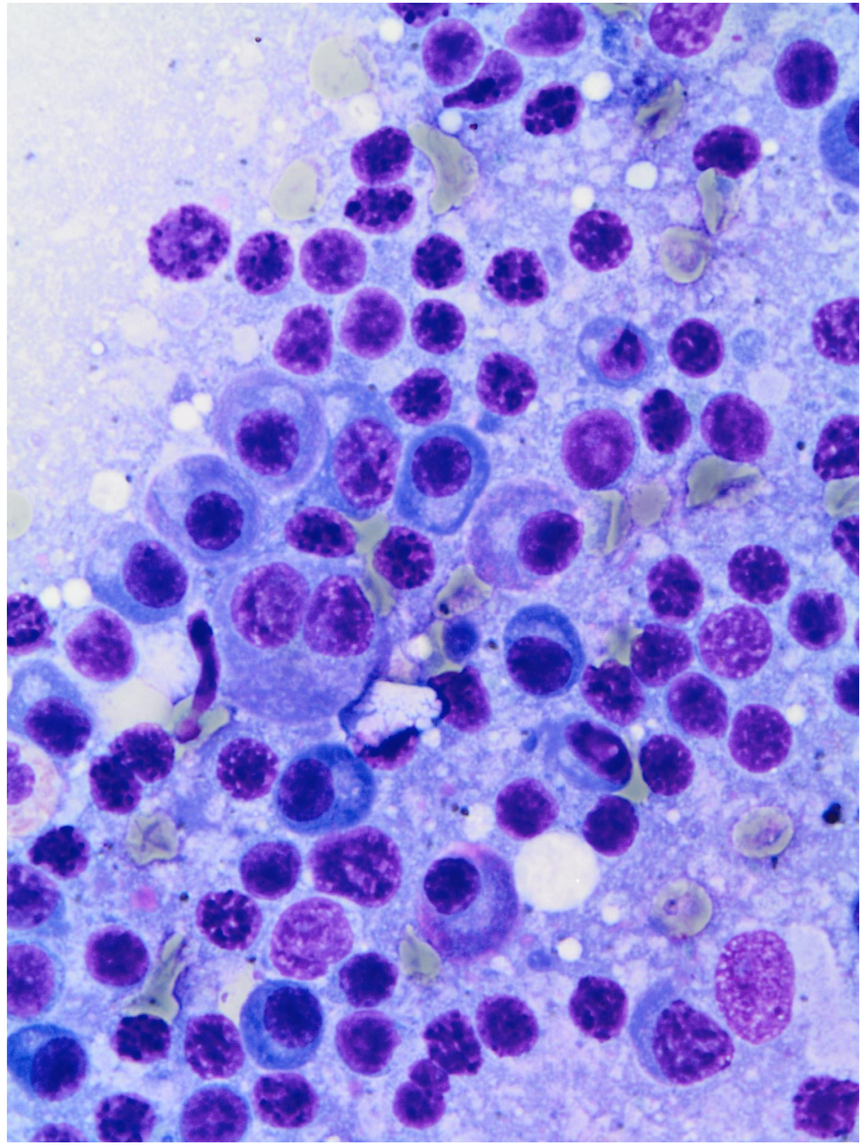
50% dogs w/carcinomas hypercoagulable

DIC

- Death Is Coming
- Dead In Cage
- Dog In Cooler
- Systemic activation of coagulation/anticoagulation
- Bleeding and thrombosis

Clin Path In Oncology

- Bi- or Pancytopenia
  - ✓leukemia
  - ✓lymphoma
  - ✓myeloma
  - ✓MH (hemophagocytic)



Clin Path In Oncology

- Clinical Chemistry
  - hypercalcemia
  - monoclonal gammopathies
  - high SDMA
  - high GGT
  - other…

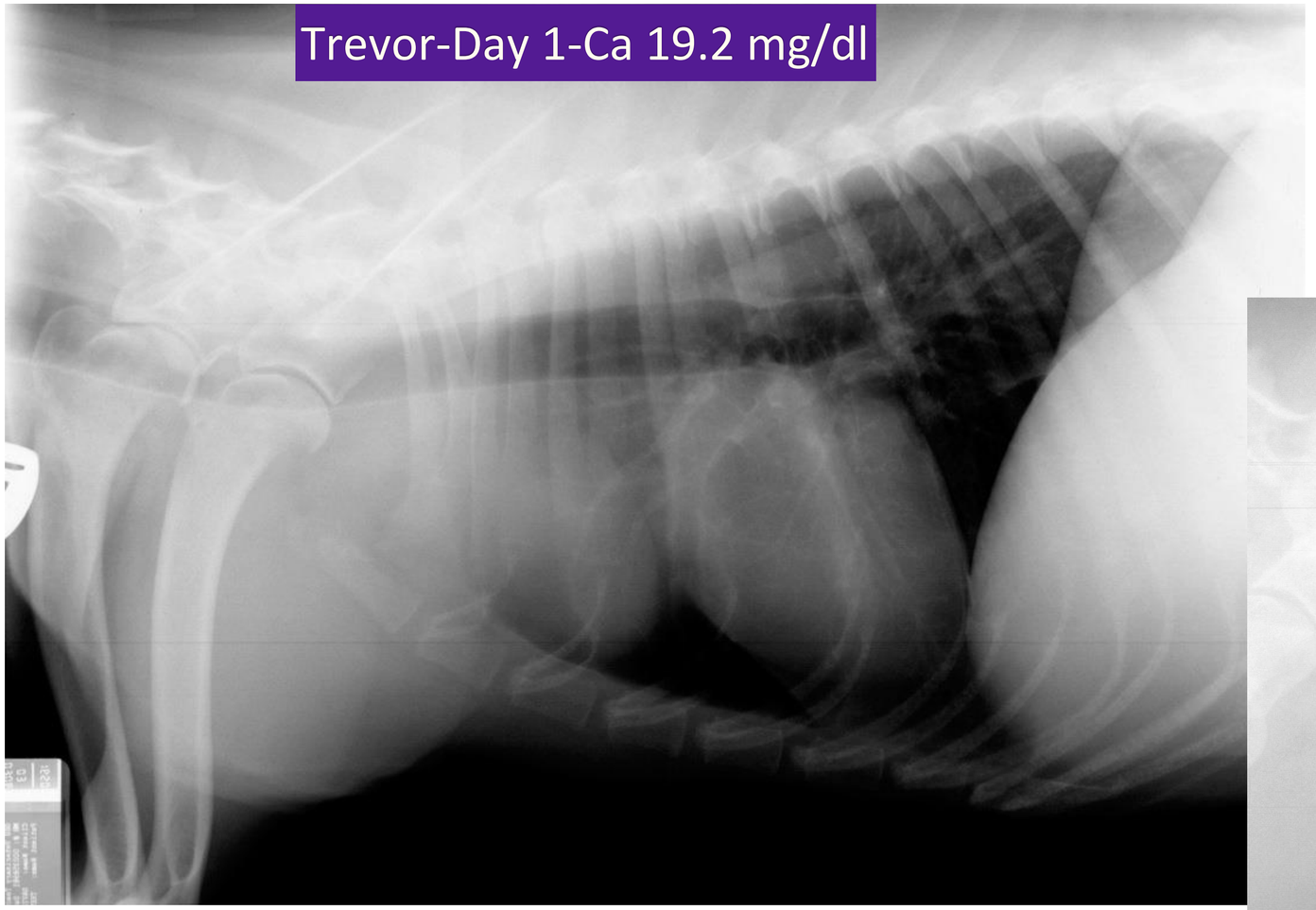
Clin Path In Oncology

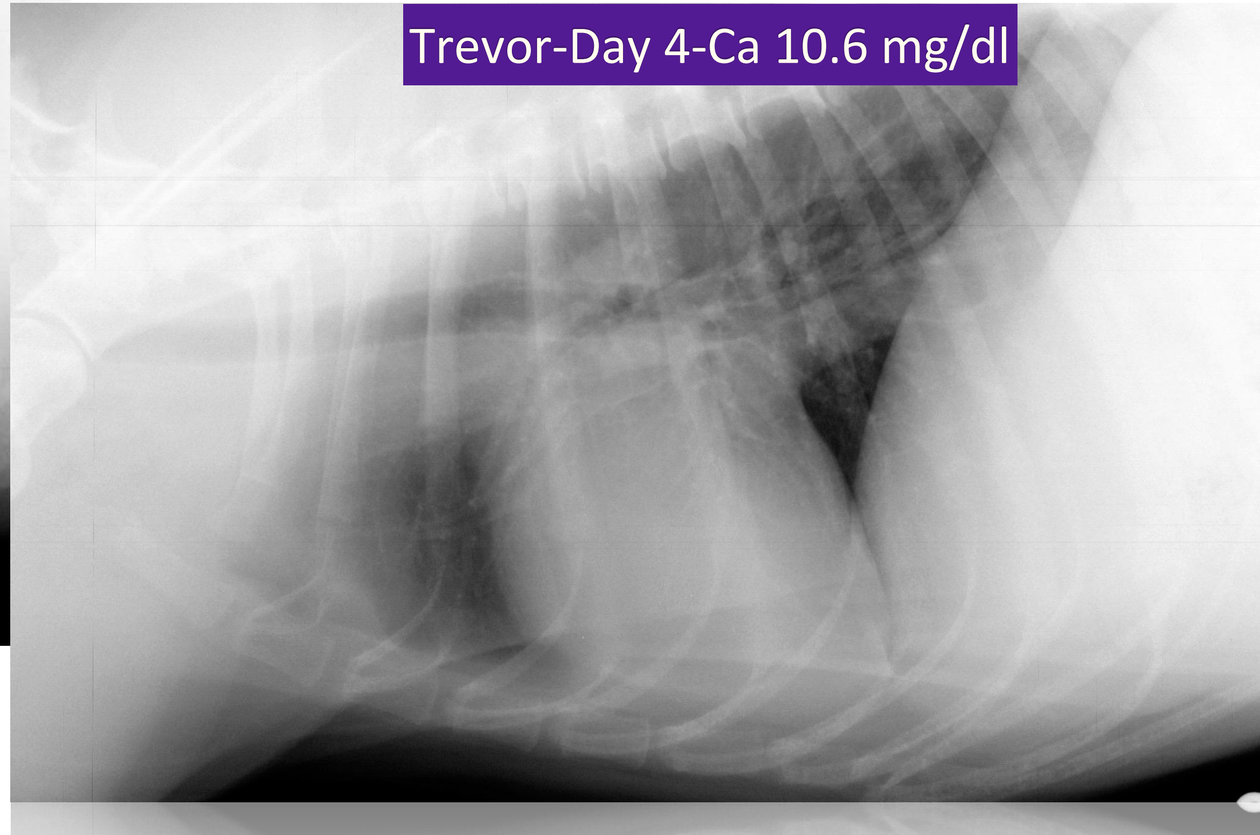
- Clinical Chemistry
  - **hypercalcemia**
    - lymphoma
    - anal sac (apocrine) CA
    - myeloma
- always do:
  - rectal exam
  - thoracic rads

Hypercal

Trevor

Hypercal

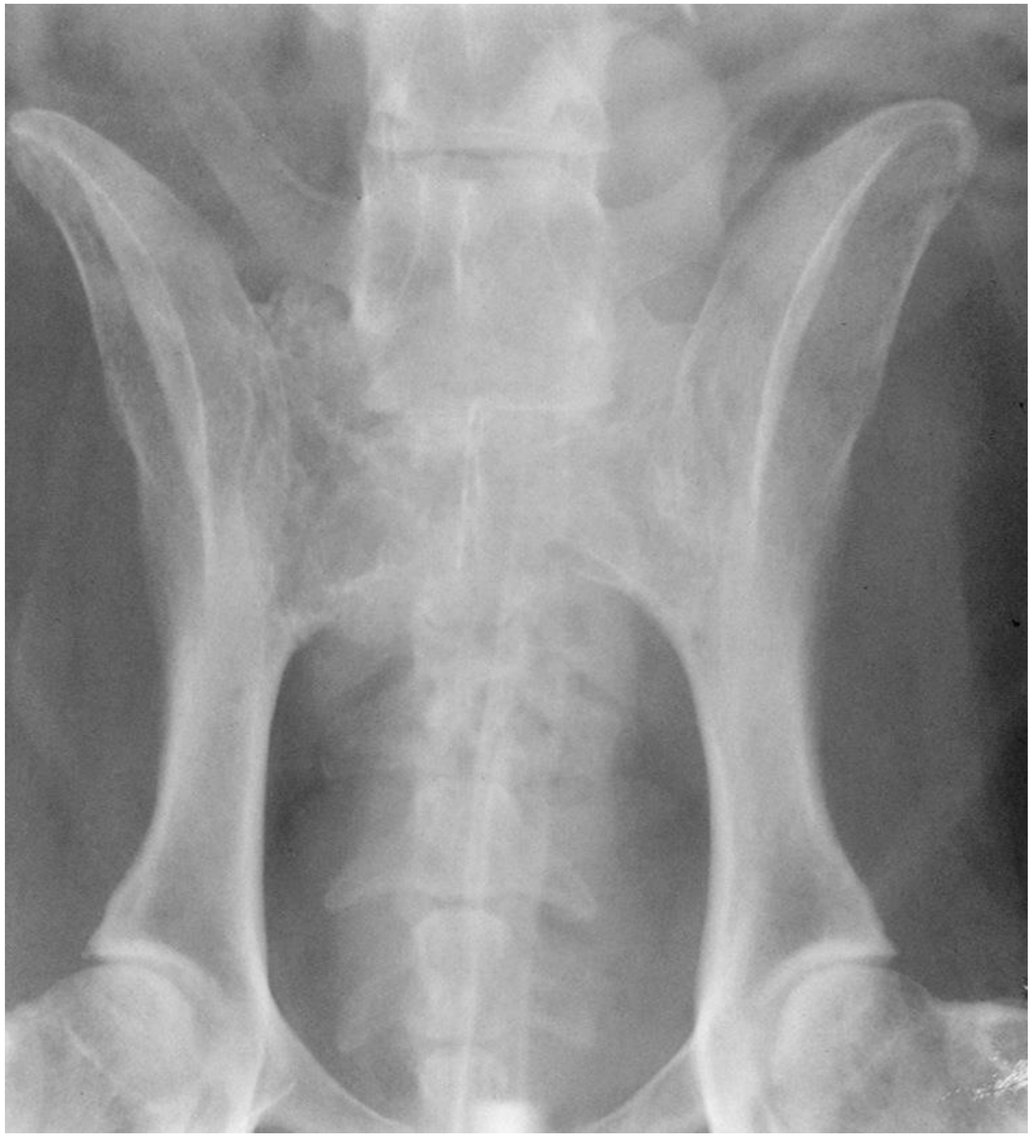


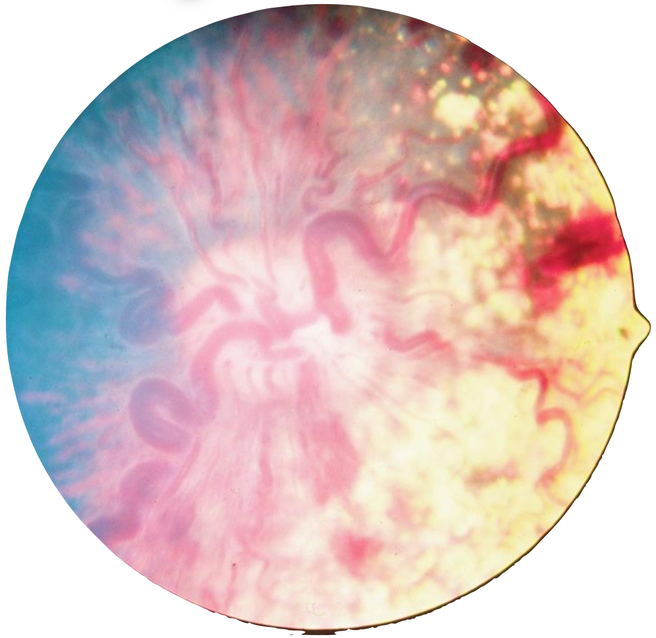


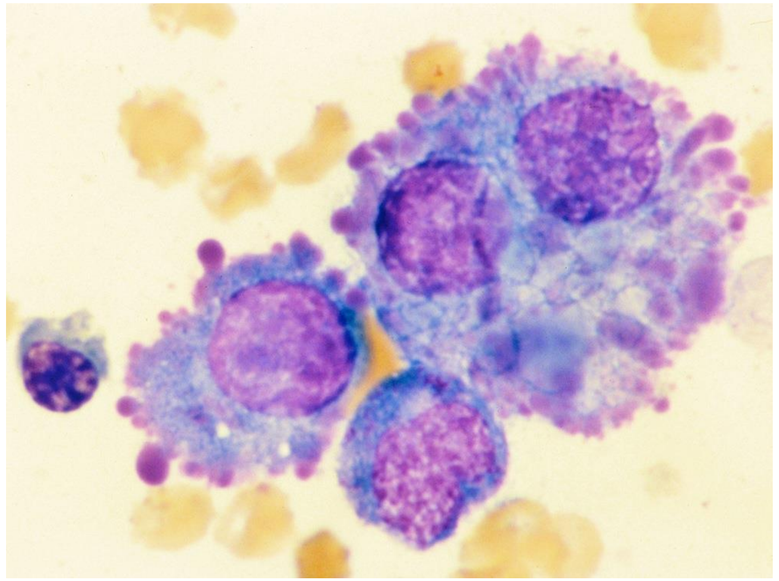
Clin Path In Oncology

- Clinical Chemistry
  - monoclonal gammopathies
    - myeloma
    - CLL
    - lymphoma
  - but also ehrlichiosis, leishmaniasis, or FIP

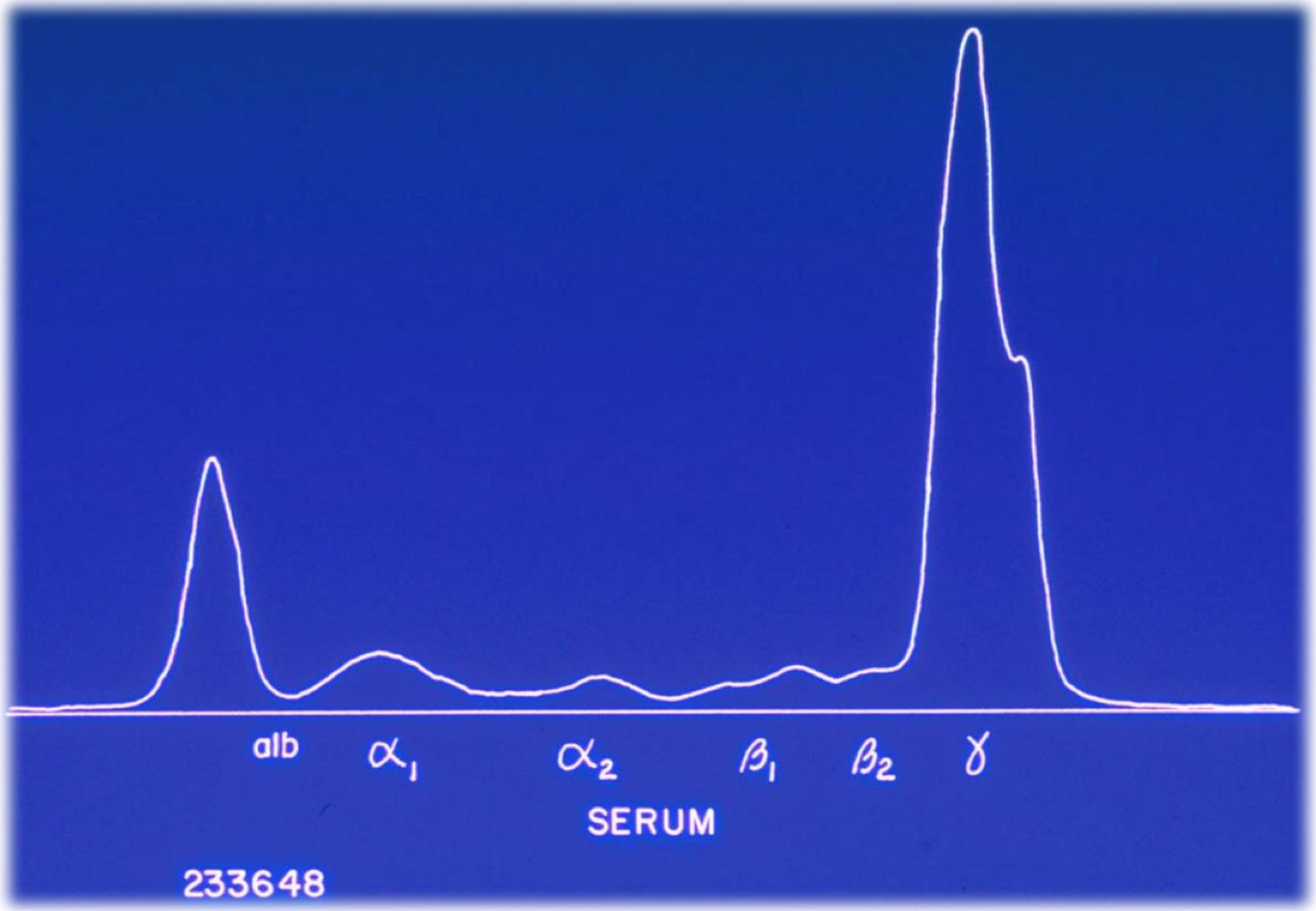
Monoclonal Gammopathy







Monoclonal Gammopathy



Clin Path In Oncology

- Clinical Chemistry
  - High SDMA (w/normal BUN/CREAT/UA)
    - Lymphoma
    - Lymphoid leukemias

Received: 13 January 2022 | Revised: 15 June 2022 | Accepted: 15 June 2022

DOI: 10.1111/vco.12845

Veterinary and Comparative Oncology

WILEY

ORIGINAL ARTICLE

The association between symmetric dimethylarginine concentrations and various neoplasms in dogs and cats

Michael J. Coyne | Corie Drake | Donald J. McCrann | David Kincaid

1803 dogs and cats with neoplasia

TABLE 1 Median SDMA and Cr concentrations by tumour type

Tumour type	SDMA µmol/L (range)			Cr µmol/L (range)		
	Case animals	Control animals	*p* value	Case animals	Control animals	*p* value
Canine hemangiosarcoma	0.54 (0.1–1.53)	0.49 (0.2–2.97)	.136	79.6 (17.7–265.2)	79.6 (26.5–875.2)	.105
Canine lipoma	0.44 (0.1–1.24)	0.49 (0.15–2.03)	.004	79.6 (26.5–229.8)	79.6 (26.5–415.5)	.099
Canine lymphoma	3-98.8 µg/dL	0.49 (0.15–2.47)	<.0001	79.6 (17.7–406.6)	79.6 (35.4–919.4)	.897
Canine mammary adenocarcinoma	0.44 (0.1–1.33)	0.49 (0.1–2.82)	.006	61.9 (26.5–327.1)	70.7 (26.5–724.9)	<.0001
Canine mammary carcinoma	0.44 (0.1–2.22)	0.49 (0.05–4.94)	.008	61.9 (26.5–229.8)	79.6 (17.7–574.6)	<.0001
Feline lymphoma	2-98.8 µg/dL	0.54 (0.15–3.46)	<.0001	114.9 (44.2–1007.8)	123.8 (53.0–795.6)	<.0001
Feline visceral mast cell tumour	0.64 (0.25–1.93)	0.54 (0.25–4.35)	.566	132.6 (53.0–716.1)	132.6 (44.2–539.3)	.826

Cancer type	*N*	OR (95% CI)	*p*
Canine lymphoma	307	10.00 (5.98–16.72)	$p < .001$
Feline lymphoma	224	3.04 (1.95–4.73)	$p < .001$
Feline visceral mast cell tumour	55	1.63 (0.67–3.92)	$p = .275$
Canine hemangiosarcoma	230	1.11 (0.66–1.87)	$p = .691$
Canine mammary carcinoma	387	0.49 (0.28–0.84)	$p = .009$
Canine mammary adenocarcinoma	388	0.41 (0.231–0.71)	$p = .001$
Canine lipoma	212	0.39 (0.18–0.85)	$p = .013$

RESEARCH ARTICLE

PLOS ONE | https://doi.org/10.1371/journal.pone.0250839 May 14, 2021

Validation of protein arginine methyltransferase 5 (PRMT5) as a candidate therapeutic target in the spontaneous canine model of non-Hodgkin lymphoma

Shelby L. Sloan[1,2☯], Kyle A. Renaldo[3☯], Mackenzie Long[1,2], Ji-Hyun Chung[2], Lindsay E. Courtney[3], Konstantin Shilo[4], Youssef Youssef[2], Sarah Schlotter[2], Fiona Brown[2], Brett G. Klamer[5], Xiaoli Zhang[5], Ayse S. Yilmaz[5], Hatice G. Ozer[5], Victor E. Valli[6†], Kris Vaddi[7], Peggy Scherle[7], Lapo Alinari[2], William C. Kisseberth[2,3‡*], Robert A. Baiocchi[2‡*]

- 42.4% of lymphomas positive for PRMT5
- PRMT5 inhibition → Cell death

Clin Path In Oncology

- Clinical Chemistry
  - High GGT
    - Renal carcinoma

Clin Path In Oncology - Screening/Liquid Biopsies

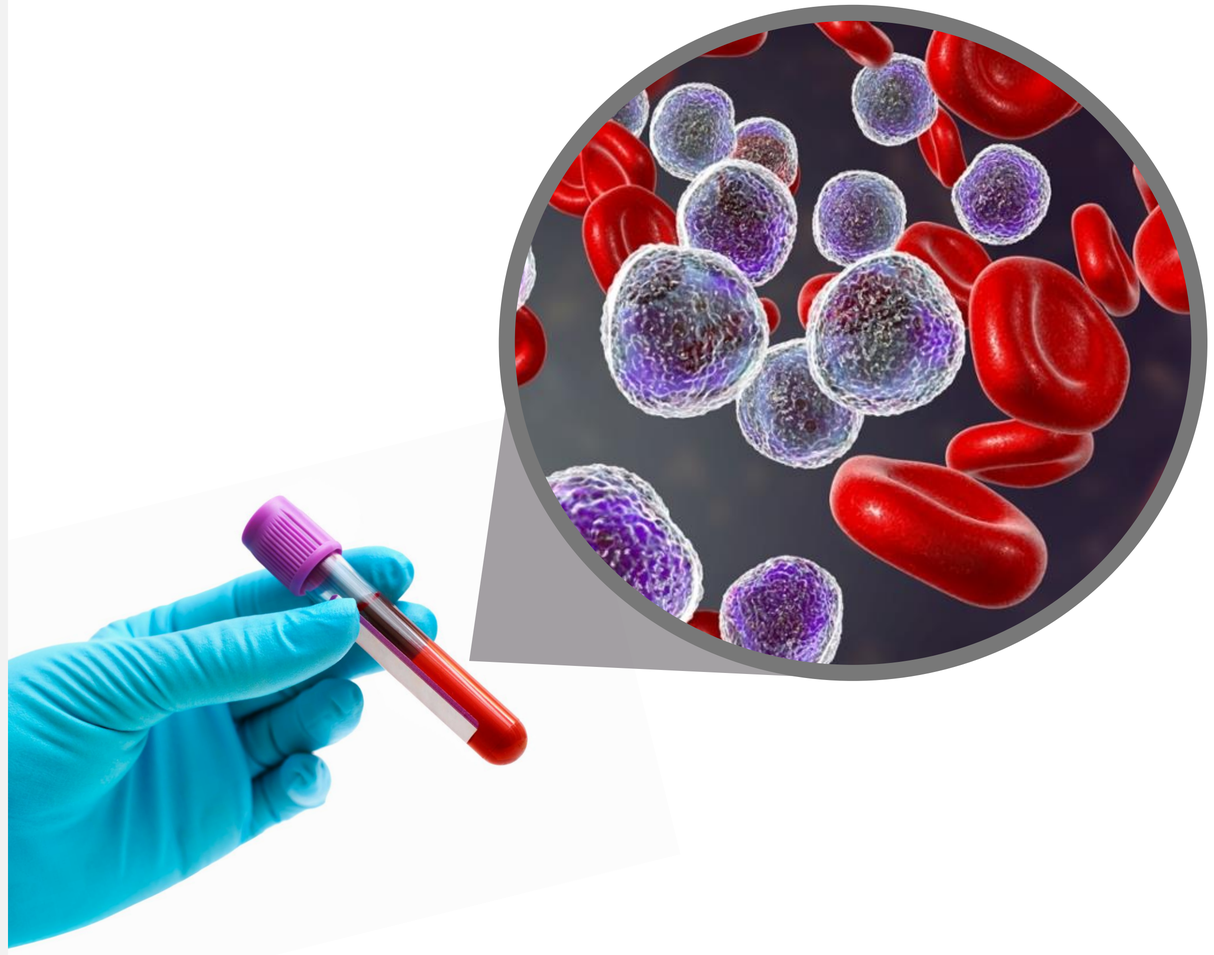
- To be used during routine wellness visits or in sick patients without a definitive diagnosis
- Narrow window of opportunity in healthy patients

IDEXX Cancer Dx Transforms Care Through Wellness Screening

IDEXX Cancer Dx™ will launch with canine lymphoma in 2025

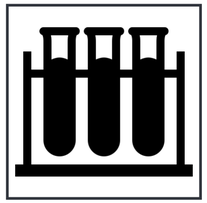
- Early detection
- B-cell vs. T-cell cancer classification

+ Panel will expand over ~36 months to cover majority (>50%) of canine cancer cases, providing detection by cancer type.
+ Technology enables affordable inclusion in preventive care profiles.
+ Software and data enable commercial targeting based on breed and age.



Cancer Dx Is A New Diagnostic Test That Can Improve Patient Care

What is Cancer Dx?



Molecular test performed at Idexx Reference Lab specific for lymphoma

Who is it for?

Suspected lymphoma (or well-patients with increased risk of lymphoma)

Who is at risk?

Dogs suspected of having lymphoma
All dogs 7 and above
At risk breeds 4 and above*

Conclusions

- Don’t miss the opportunity to diagnose cancer early!
- Listen to what the patient and the lab are telling you!
- It’s the only senior disease we can potentially cure!
- Thanks!
  - *coutovetconsultants@gmail.com*