Diagnostic Update for Practitioners: Case Studies.

Bill Saxon, DVM, DACVIM, DACVECC, IDEXX Field Medical Specialist

IDEXX

Objectives:

o Through case presentations and review, choose the appropriate diagnostic tests for each patient

o Properly interpret hematology, chemistry, electrolyte, urinalysis and other routine initial tests for each case

o Determine what other diagnostic testing is necessary for each case presentation

o Discuss treatment options and monitoring protocols

IDEXX

Getting the full picture in case management.

History and physical exam most important

o Body condition score

o **Muscle condition score**

o Blood pressure

o Fundic exam

o Rectal exam

IDEXX

Record BCS AND MCS on every pet on every exam

History and physical exam most important

o Body condition score

o Muscle condition score

o **Blood pressure**

o Fundic exam

o Rectal exam

IDEXX

Hypertension update – new normal SBP <140mm Hg

CONSENSUS STATEMENT | 🔓 Open Access | (cc) (i) (S)

ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats

Mark J. Acierno, Scott Brown, Amanda E. Coleman, Rosanne E. Jepson, Mark Papich, Rebecca L. Stepien, Harriet M. Syme

First published: 24 October 2018 | https://doi.org/10.1111/jvim.15331

Normotensive (minimal TOD risk)	SBP <140 mm Hg
Prehypertensive (low TOD risk)	SBP 140-159 mm Hg
Hypertensive (moderate TOD risk)	SBP 160-179 mm Hg
Severely hypertensive (high TOD risk)	SBP ≥180 mm Hg

IDEXX

Hypertension – real or 'white coat'?

o Acclimate 5-10 minutes in designated quiet room

o Ventral or lateral recumbency with minimal restraint, owner present

o Appropriate cuff width = 30-40% limb circumference

o Limb or tail – base on conformation, tolerance, user preference

o Same nurse each time

o Average 5-7 measurements if <20% variation, discard first

o Fractious pet – don't bother, look for evidence of TOD – where?

IDEXX

History and physical exam most important

o Body condition score

o Muscle condition score

o Blood pressure

o **Fundic exam**

o Rectal exam

IDEXX

The minimum data base and beyond...

- o Components
  - Minimal starting point
    - Complete blood count (CBC)
    - Complete biochemistry profile (now includes the IDEXX SDMA™ Test)
      – always includes electrolytes
    - Complete urinalysis (UA)
  - Additions to the MDB depending on signalment, geography, clinical presentation, and physical examination findings:

Total T_4	SNAP® 4Dx® Plus	SNAP® FIV/FeLV Combo
NTproBNP	Imaging	Blood pressure
PCR	Fecal Antigen Testing	UP/C

IDEXX

The minimum data base and beyond...

o Components
- Minimal starting point
  - Complete blood count (CBC)
  - Complete biochemistry profile (now includes the IDEXX SDMA™ Test)
    – always includes electrolytes
  - Complete urinalysis (UA)
- Additions to the MDB depending on signalment, geography, clinical presentation, and physical examination findings:

Total T$_4$ Test		SNAP® 4Dx® Plus Test			Bile Acid Test	
Cardiopet® proBNP Test		SNAP® fPL/cPL			CRP	
PCR	Blood Gas	PT/PTT	Resting Cortisol	LACTATE	SNAP® Lepto	

IDEXX

Worth a look...

Journal of Feline Medicine and Surgery (2016) **18**, 400–416

SPECIAL ARTICLE

2016 AAFP Guidelines for the Management of Feline Hyperthyroidism

IDEXX

Reading between the lines to get most from lab results
CBC
Biochemical profile
Complete urinalysis

RBC parameters: what's significant and what isn't

o Hemoglobin x 3 = PCV

o Absolute reticulocyte count most accurate way to determine if anemia regenerative
  - Changes in RBC indices ($\uparrow$ MCV, $\downarrow$ MCHC) in only 8-11% with regenerative anemia

o Reticulocytosis without anemia may indicate underlying disease

o Reticulocyte-hemoglobin early marker of iron deficiency – RETIC-HGB
  - RBC indices are mean values – slow to change when new cells produced

IDEXX

Is this patient truly anemic?

RBC	**5.32**	**5.65 - 8.87 M/µL**	L
Hematocrit	**35.8**	**37.3 - 61.7 %**	L
Hemoglobin	13.2	13.1 - 20.5 g/dL	
MCV	67.3	61.6 - 73.5 fL	
MCH	24.8	21.2 - 25.9 pg	
MCHC	36.9	32.0 - 37.9 g/dL	
RDW	15.0	13.6 - 21.7 %	
% Reticulocyte	0.4	%	
Reticulocyte	21.8	10.0 - 110.0 K/µL	

IDEXX

RBC parameters: what's significant and what isn't

○ Hemoglobin x 3 = PCV

○ Absolute reticulocyte count most accurate way to determine if anemia regenerative
   • Changes in RBC indices (↑ MCV, ↓ MCHC) in only 8-11% with regenerative anemia

○ Reticulocytosis without anemia may indicate underlying disease

○ Reticulocyte-hemoglobin early marker of iron deficiency – RETIC-HGB
   • RBC indices are mean values – slow to change when new cells produced

IDEXX

Is this anemia regenerative or nonregenerative?
(Do the RBC indices help classify?)

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx (May 13, 2019 2:41 AM)					
RBC	2.28 M/µL	5.65 - 8.87	LOW		
HCT	15.9 %	37.3 - 61.7	LOW		
HGB	5.1 g/dL	13.1 - 20.5	LOW		
MCV	69.7 fL	61.6 - 73.5			
MCH	22.4 pg	21.2 - 25.9			
MCHC	32.1 g/dL	32.0 - 37.9			
RDW	18.7 %	13.6 - 21.7			
%RETIC	18.2 %				
RETIC	413.8 K/µL	10.0 - 110.0	HIGH		
RETIC-HGB	17.1 pg	22.3 - 29.6	LOW		

IDEXX

RBC parameters: what's significant and what isn't

o Hemoglobin x 3 = PCV

o Absolute reticulocyte count most accurate way to determine if anemia regenerative
   - Changes in RBC indices (↑ MCV, ↓ MCHC) in only 8-11% with regenerative anemia

o Reticulocytosis without anemia can indicate underlying disease

o Reticulocyte-hemoglobin early marker of iron deficiency – RETIC-HGB
   - RBC indices are mean values – slow to change when new cells produced

IDEXX

10-year-old, spayed female mixed-breed dog

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx					
RBC	6.2 x10^12/L	5.7 - 8.9			
HCT	43.2 %	37.5 - 61.7			
HGB	14.4 g/dL	13.1 - 20.5			
MCV	69.4 fL	61.6 - 73.5			
MCH	23.1 pg	21.2 - 25.9			
MCHC	33.3 g/dL	32.0 - 37.9			
RDW	19.1 %	13.6 - 21.7			

IDEXX
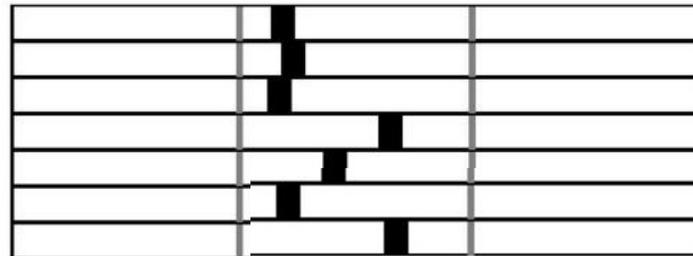
Reticulocyte count high in 5-10% dogs *without* anemia*

Reticulocytosis without anemia

Healthy pet

Older, 'ADR'

- Splenic contraction
- *Mild* bleeding/hemolysis
- Hookworm

- Splenic tumor
- Other cancer
- *Occult* bleeding/hemolysis
- Other
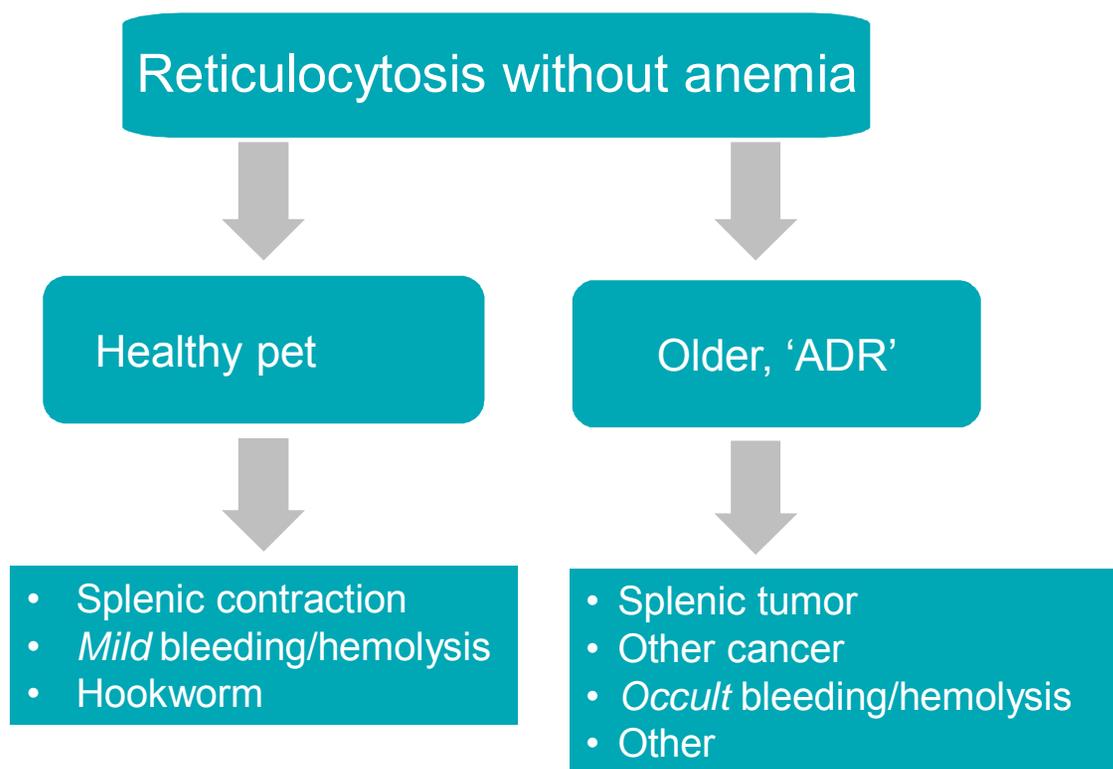
*I million CBCs, Dr. DeNicola

IDEXX

Find this before it ruptures
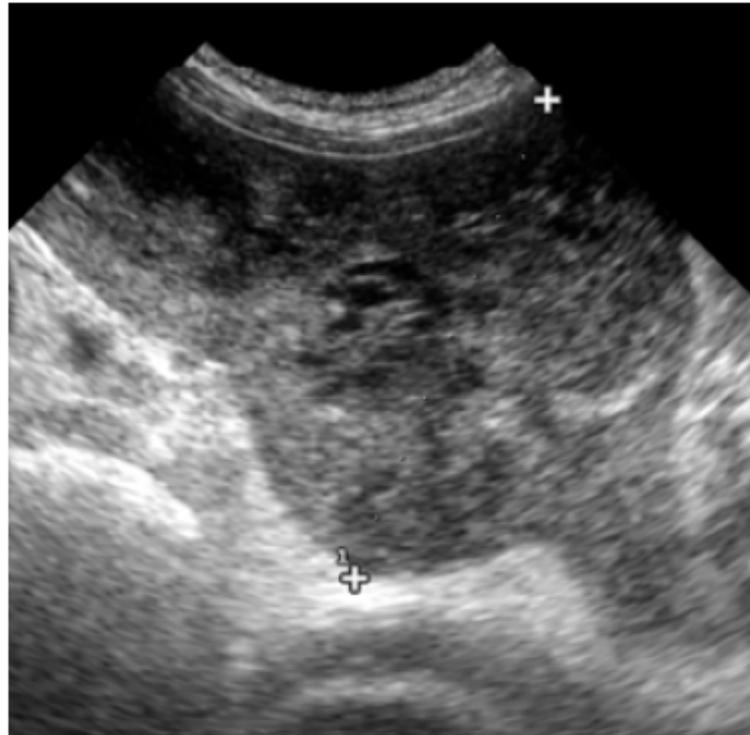
IDEXX

RBC parameters: what's significant and what isn't

o Hemoglobin x 3 = PCV

o Absolute reticulocyte count most accurate way to determine if anemia regenerative
  - Changes in RBC indices (↑ MCV, ↓ MCHC) in only 8-11% with regenerative anemia

o Reticulocytosis without anemia may indicate underlying disease

o Reticulocyte-hemoglobin (RETIC-HGB) *early* marker of iron deficiency
  - Measure of iron availability for hemoglobin production in bone marrow
  - RBC indices are mean values – slow to change when new cells produced

IDEXX

Reticulocyte hemoglobin. RETIC-HGB.
Measure of iron availability

Iron required for hemoglobin production

Must be available in the bone marrow.
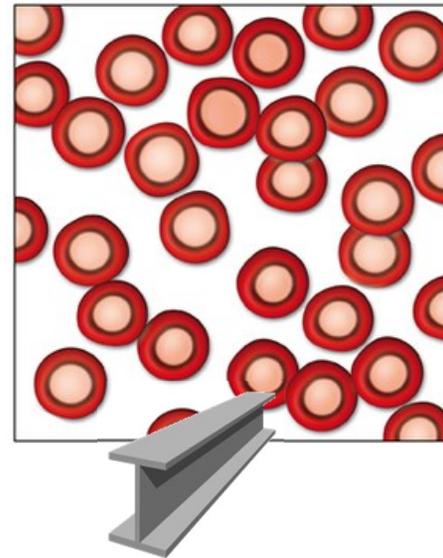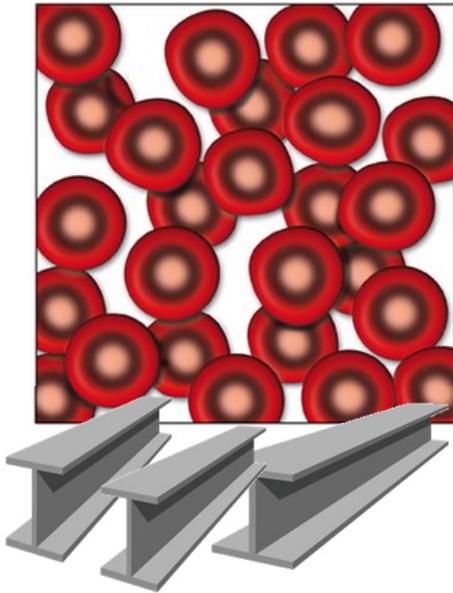
Courtesy of Dr. Graham Bilbrough

IDEXX

Macrophages in bone marrow 'feed' iron to developing RBCs

Erythroblastic island

Erythroblast-macrophage adhesion

Central macrophage

Phagocytosis of nuclei, cell organelles

Iron release from macrophage

IDEXX
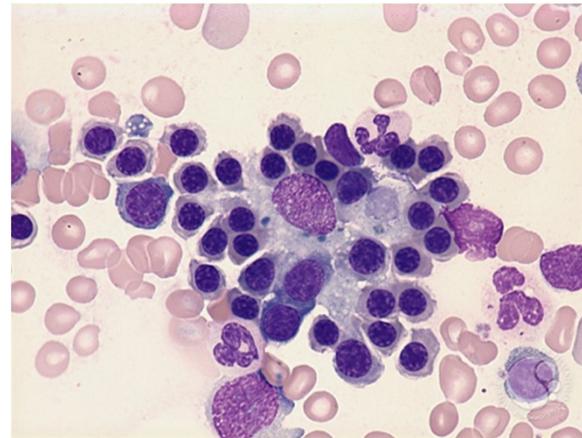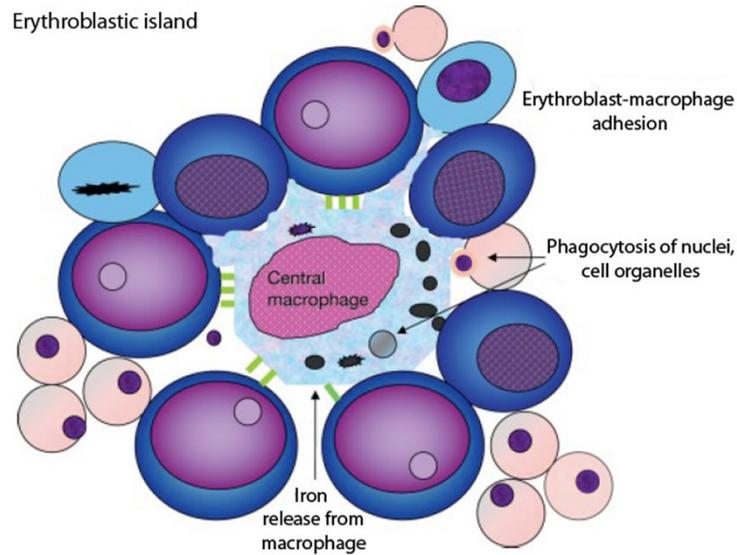
RETIC-HGB indicates iron availability in bone marrow. It *decreases* with...

External bleeding (true iron deficiency)	Inflammation (Iron trapped in macrophages)
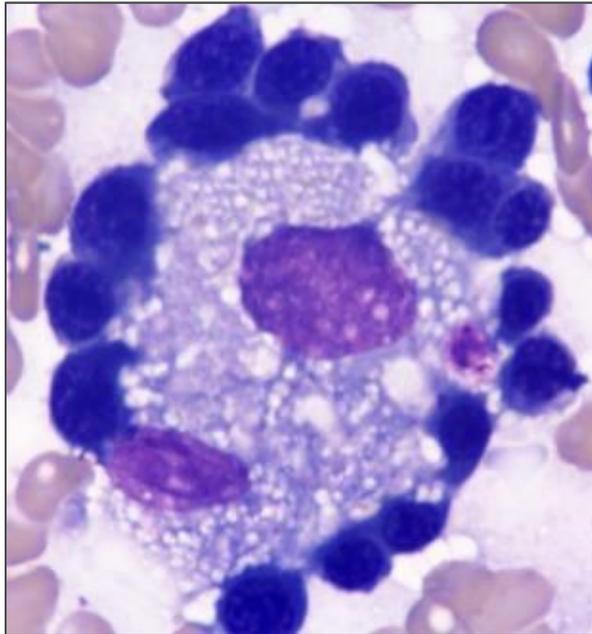
IDEXX
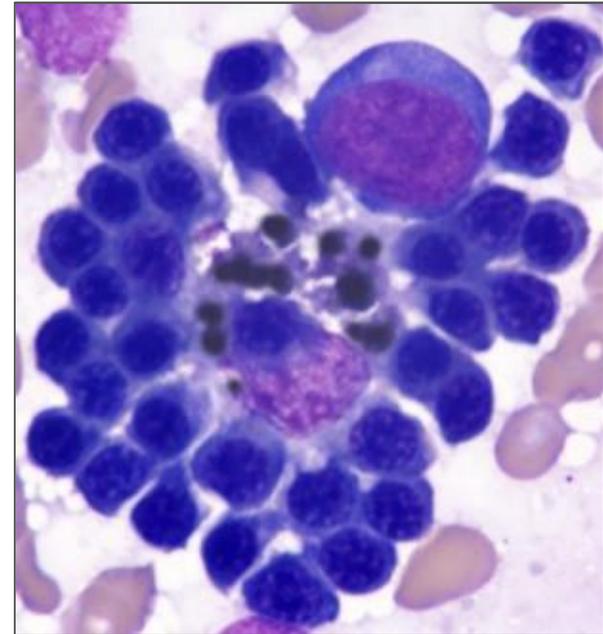
Detect decreased iron availability in **days** (not months).

Decreased RETIC-HGB
(In 10% of dog CBCs)

EXTERNAL bleeding

- *Absolute* deficiency
- GI tumor or ulcer
- Bladder tumor
- Hookworms
- Severe fleas
- **Iron +/- OK**

Inflammation

- *Relative* deficiency
- All types
- Non-specific
- **Iron No**

IDEXX
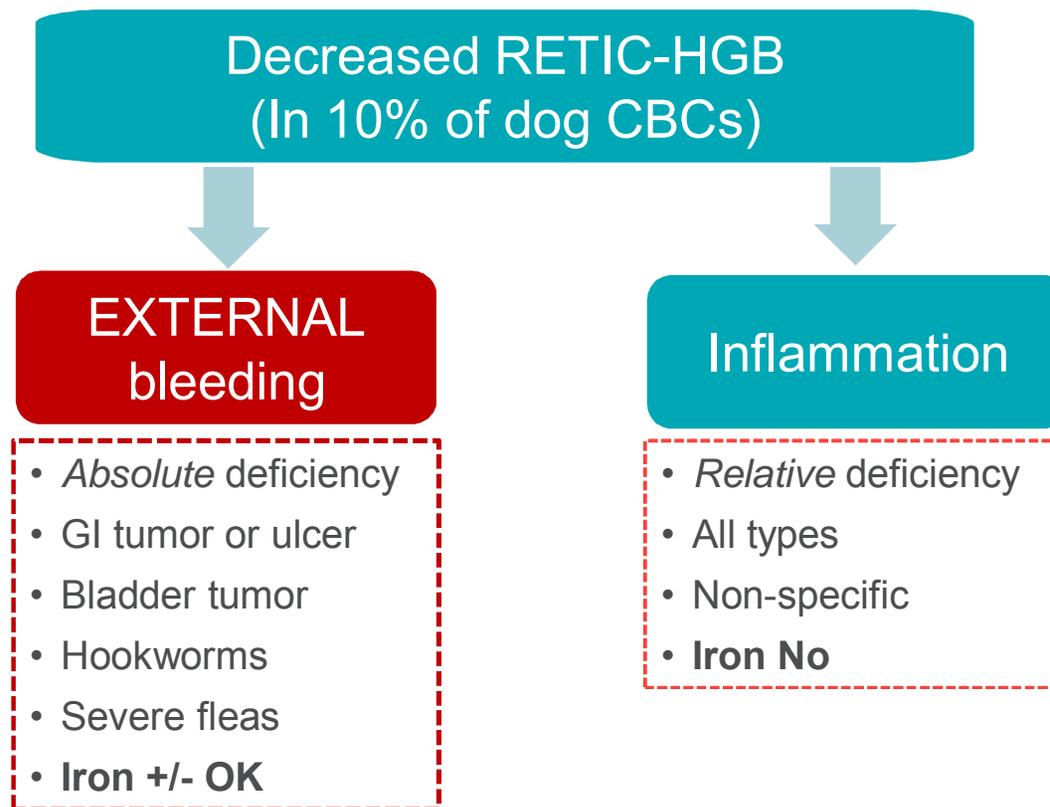
WBC facts – hidden gems of 5 (make that 6) part differential

o Total WBC and neutrophil count normal in 50% of dogs and cats with severe infection/inflammation

o Left shift and/or toxic changes double mortality

o Normal lymphocyte count in a sick patient? *Suspect which diseases…?*

o 3 'patterns' to leukogram – inflammatory, stress, and ????

o How high can neutrophil count be due to stress?

IDEXX

Apollo
14-year-old, neutered male Labrador retriever

Presenting complaints: vomiting, respiratory distress, severe sudden-onset depression

o History:
  - Referred from boarding kennel
  - Recently boarded and become ill while boarding
  - Gradual muscle mass loss over several years

o Physical examination findings:
  - Labored breathing – harsh lung sounds
  - Severe muscle wasting
  - Weakness

IDEXX

Apollo's WBC picture

Test	Results	Reference Interval		LOW	NORMAL	HIGH
ProCyte Dx (August 10, 2017 10:27 AM)						
WBC	7.16 K/µL	5.05 - 16.76				
NEU	* 0.16 K/µL	2.95 - 11.64	LOW			
BAND	* Suspected					
LYM	* 2.87 K/µL	1.05 - 5.10				
MONO	* 4.07 K/µL	0.16 - 1.12	HIGH			
EOS	0.06 K/µL	0.06 - 1.23				
BASO	0.00 K/µL	0.00 - 0.10				
Band neutrophils suspected						
WBC Abnormal Distribution						

* Qualified results—confirm with dot plot and/or blood film review

IDEXX

Apollo's daily CBCs...
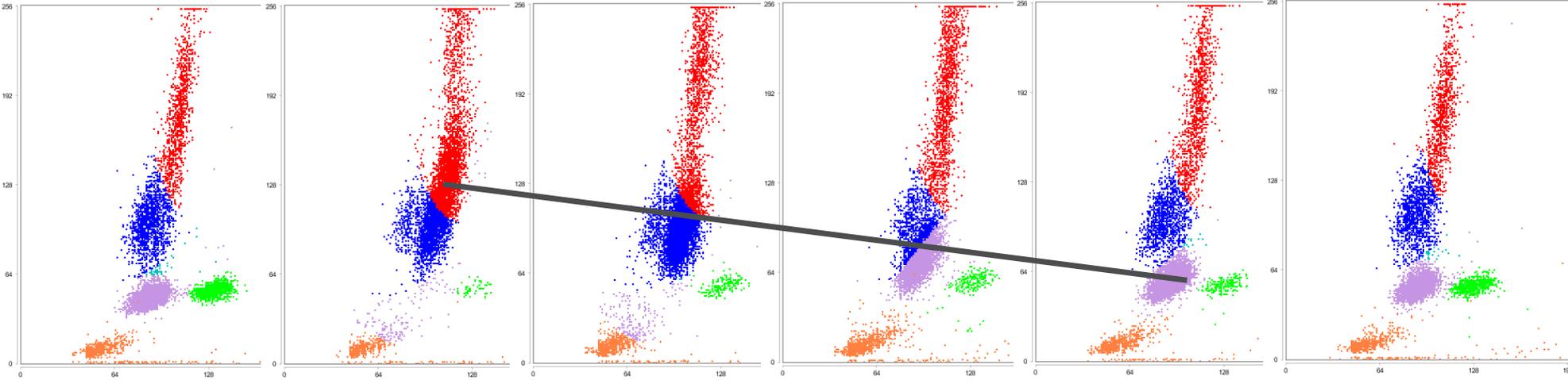
Date	4/28/17	8/10/17	8/11/17	8/12/17	8/15/17	8/31/17
Band	-	+	+	+	+	-
WBC (K/µL) (5.05–16.76)	10.58	7.16	8.72	8.84	11.08	10.23

IDEXX

The truth about platelets

o Clumping is unavoidable – 70% of feline samples

o All automated analyzers are affected by platelet clumps – *count increased or decreased?*

o Verify all low platelet counts - dot plot/graphics, blood film review

o Blood film → platelets/HPF x 15,000 = platelet estimate

o Thrombocytosis on biochemical panel – what parameter changes?

o **Platelet count can be 10,000 in perfectly normal patient (no petechiae)**

IDEXX

What diseases cause thrombocytopenia? Which cause bleeding?

○ Infectious disease
- Vector-borne (may be only evidence of disease)
- FeLV/FIV
- *Many* others
- Inflammation
- Cancer

Bleeding threshold 30-50K

○ Immune-mediated thrombocytopenia
- Lowest platelet counts = highest bleeding risk
- Dogs can look perfectly normal
- Fortunately the least common

IDEXX

Biochemistry clues

TEST	RESULT	REFERENCE VALUE	
Glucose	3.83	3.5 - 6.33 mmol/L	
IDEXX SDMA [a]	13	0 - 14 µg/dL	
Creatinine	97.24	44.2 - 132.6 µmol/L	
BUN	9.28	3.21 - 11.07 mmol/L	
BUN: Creatinine Ratio	23.6		
Phosphorus	1.91	0.81 - 1.97 mmol/L	
Calcium	2.3	2.1 - 2.94 mmol/L	
Sodium	149	142 - 152 mmol/L	
Potassium	4.8	4.0 - 5.4 mmol/L	
Na: K Ratio	31	28 - 37	
Chloride	107	108 - 119 mmol/L	L
TCO2 (Bicarbonate)	24	13 - 27 mmol/L	
Anion Gap	23	11 - 26 mmol/L	
Total Protein	72	55 - 75 g/L	
Albumin	31	27 - 39 g/L	
Globulin	41	24 - 40 g/L	H
Albumin: Globulin Ratio	0.8	0.7 - 1.5	
ALT	19	18 - 121 U/L	
AST	30	16 - 55 U/L	
ALP	23	5 - 160 U/L	
GGT	1	0 - 13 U/L	
Bilirubin - Total	1.71	0 - 5.13 µmol/L	
Bilirubin - Unconjugated	0	0 - 3.42 µmol/L	
Bilirubin - Conjugated	1.71	0 - 1.71 µmol/L	
Cholesterol	6.05	3.39 - 8.92 mmol/L	
Creatine Kinase	165	10 - 200 U/L	

IDEXX

Lots to see here… electrolytes mandatory.
Look at trends to determine significance.

o Increased BUN with normal creatinine/SDMA (or increased BUN:creatinine ratio)

o ALP vs ALT increase – *which is more worrisome?*

o **ALP and GGT**

o Hyper- and hypocalcemia

o Hyperkalemia when everything else is normal *???*

o High TCO2 with low electrolytes *???*

o SDMA

IDEXX

Interpretation of ALKP and GGT together

ALKP - Hepatocellular membranes along bile canaliculi

CV

3

2

1

BD

GGT – Bile ductular epithelial cell membranes

IDEXX
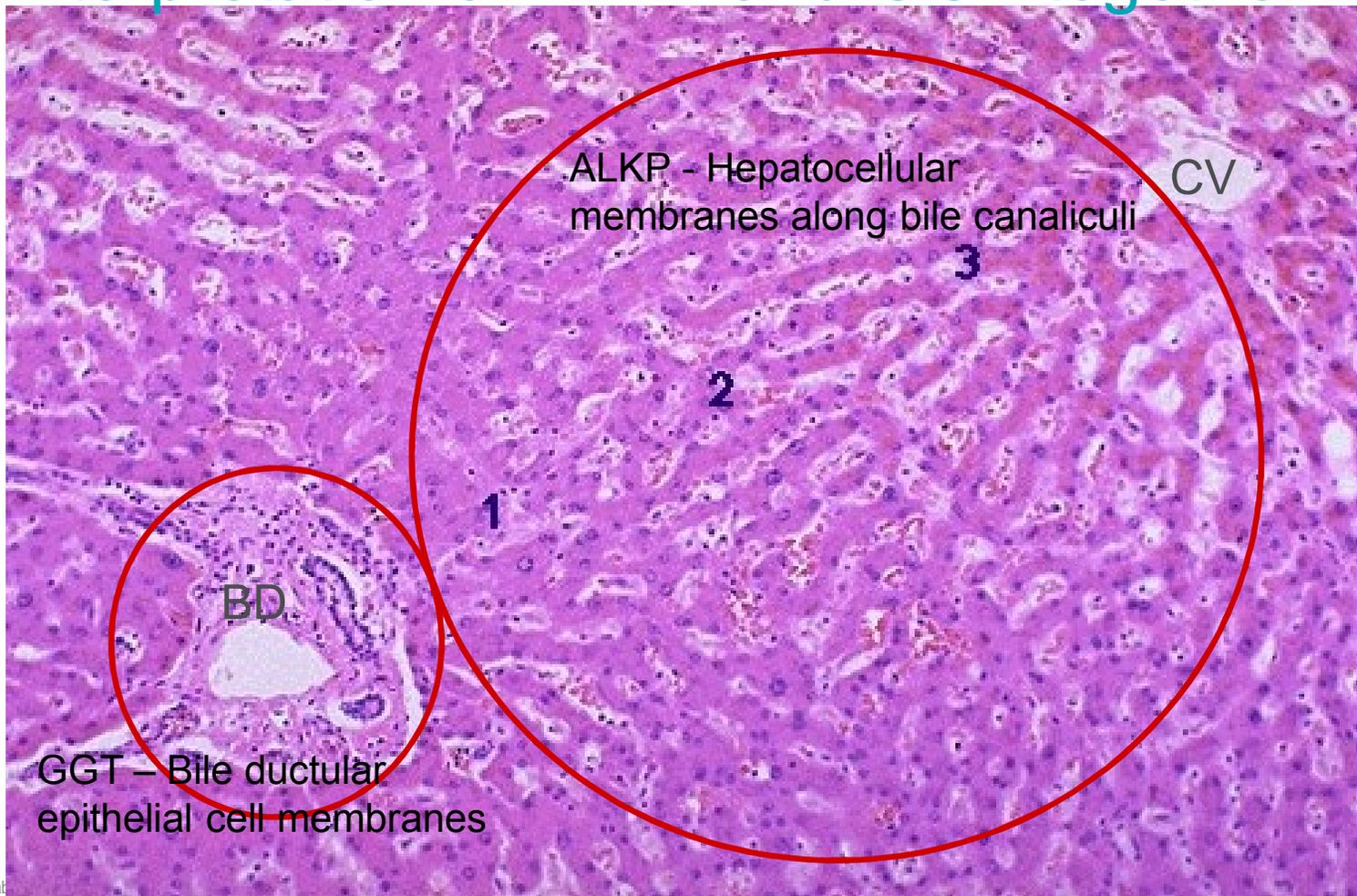
Paulie

Clinical Chemistry Profile

GLU	125	mg/dL		(	77	-	125	)
BUN	22	mg/dL		(	7	-	27	)
CREA	1.3	mg/dL		(	0.5	-	1.8	)
Caz	8.0	mg/dL		(	7.9	-	12.0	)
TP	5.5	g/dL		(	5.2	-	8.2	)
ALB	2.8	g/dL		(	2.2	-	3.9	)
GLOB	2.7	g/dL		(	2.5	-	4.5	)
ALT	275	U/L	HIGH	(	10	-	100	)
ALKP	600	U/L	HIGH	(	23	-	212	)
GGT	88	U/L	HIGH	(	0	-	7	)
TBIL	1.9	mg/dL	HIGH	(	0.0	-	0.9	)
AMY	707	U/L		(	500	-	1500	)
LIPA	2100	U/L	HIGH	(	200	-	1800	)

IDEXX

Paulie
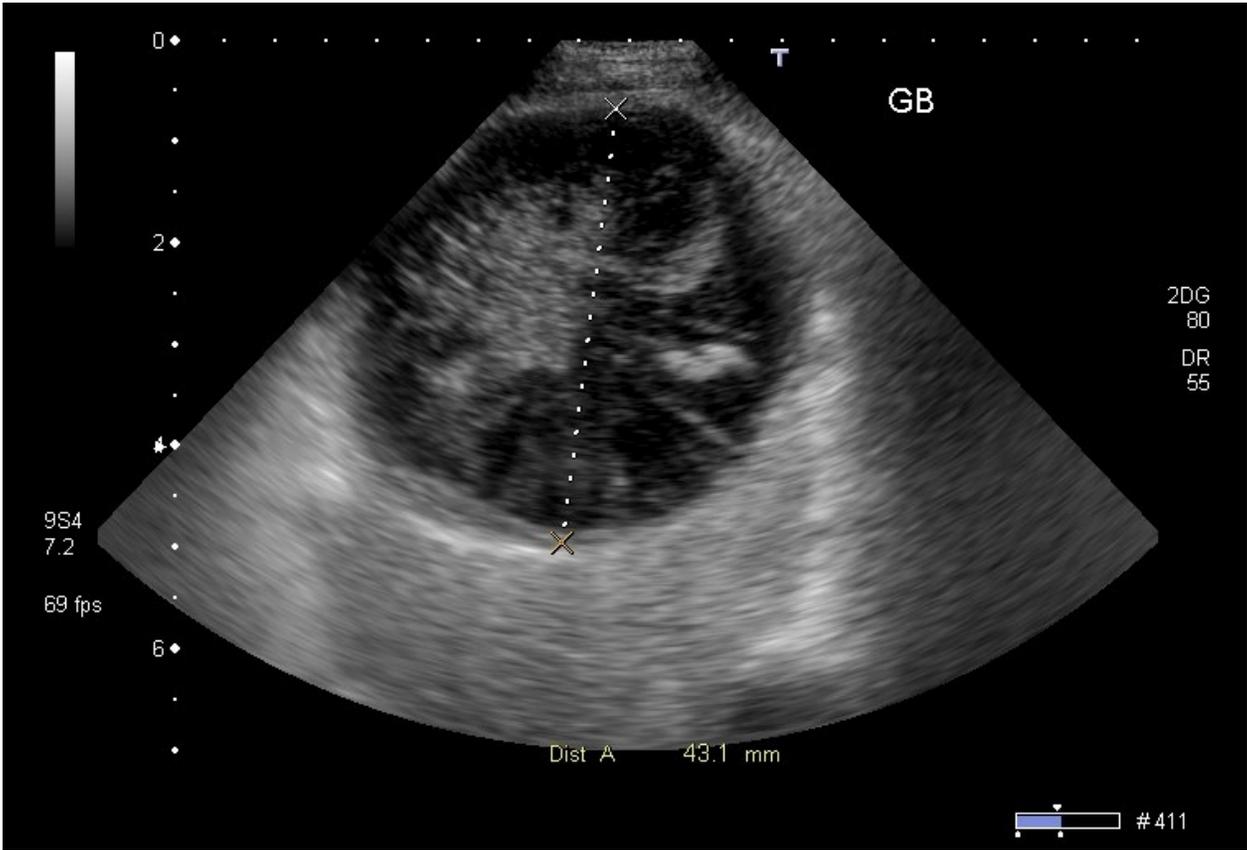
Abigail - Chemistry

Test	Results	Reference Interval	LOW	NORMAL	HIGH	1 year Earlier
Chemistry						
GLU	95 mg/dL	74 - 143				98 mg/dL
BUN	11 mg/dL	7 - 27				19 mg/dL
CREA	1.1 mg/dL	0.5 - 1.8				1.6 mg/dL
BUN/CREA	10					12
PHOS	3.9 mg/dL	2.5 - 6.8				4.0 mg/dL
CA	9.3 mg/dL	7.9 - 12.0				10.9 mg/dL
Na	160 mmol/L	144 - 160				157 mmol/L
K	3.4 mmol/L	3.5 - 5.8	LOW			4.7 mmol/L
Cl	121 mmol/L	109 - 122				116 mmol/L
TP	6.8 g/dL	5.2 - 8.2				6.8 g/dL
ALB	3.6 g/dL	2.3 - 4.0				4.0 g/dL
GLOB	3.2 g/dL	2.5 - 4.5				2.8 g/dL
ALB/GLOB	1.1					1.4
ALT	> 2000 U/L	10 - 100	HIGH			103 U/L
ALKP	945 U/L	23 - 212	HIGH			53 U/L
GGT	21 U/L	0 - 7	HIGH			< 0 U/L
TBIL	18.4 mg/dL	0.0 - 0.9	HIGH			0.4 mg/dL
CHOL	229 mg/dL	110 - 320				192 mg/dL
AMYL	267 U/L	500 - 1500	LOW			720 U/L
LIPA	407 U/L	200 - 1800				1806 U/L

ALT:Test results for the latest analyzer run have been multiplied by the dilution factor for a dilution of 1 in 2 total.

Joe – 11-yr-old MN Mixed Breed.
No clinical signs.

		12/20/2013 (Order Received) 12/21/2013 @ 7:13 am (Last Updated)	IDEXX Reference Laboratories Show Details		5/12/08 10:22 am
▷ ALT		96	5 - 107 U/L		204
▷ AST		21	5 - 55 U/L		
▷ ALP		244	10 - 150 U/L		20
▷ GGT		b 320	0 - 14 U/L		
▷ Bilirubin - Total		0.2	0.0 - 0.4 mg/dL		

IDEXX

Patty, 10-yr-old SF German shepherd:
Presenting complaint - hematuria.

Chemistry

Test	Value		Reference Range	
GLU	141 mg/dL	(	74 -	143)
BUN	11 mg/dL	(	7 -	27)
CREA	1.3 mg/dL	(	0.5 -	1.8)
BUN/CREA	8			
PHOS	3.6 mg/dL	(	2.5 -	6.8)
Ca	9.7 mg/dL	(	7.9 -	12.0)
Na	155 mmol/L	(	144 -	160)
K	3.5 mmol/L	(	3.5 -	5.8)
Cl	116 mmol/L	(	109 -	122)
TP	6.5 g/dL	(	5.2 -	8.2)
ALB	3.0 g/dL	(	2.3 -	4.0)
GLOB	3.5 g/dL	(	2.5 -	4.5)
ALB/GLOB	0.9			
ALT	10 µ/L	(	10 -	100)
ALKP	85 µ/L	(	23 -	212)
GGT	40 µ/L	HIGH (	0 -	7)
TBIL	0.1 mg/dL	(	0.0 -	0.9)
CHOL	154 mg/dL	(	110 -	320)
AMYL	1329 µ/L	(	500 -	1500)
LIPA	430 µ/L	(	200 -	1800)
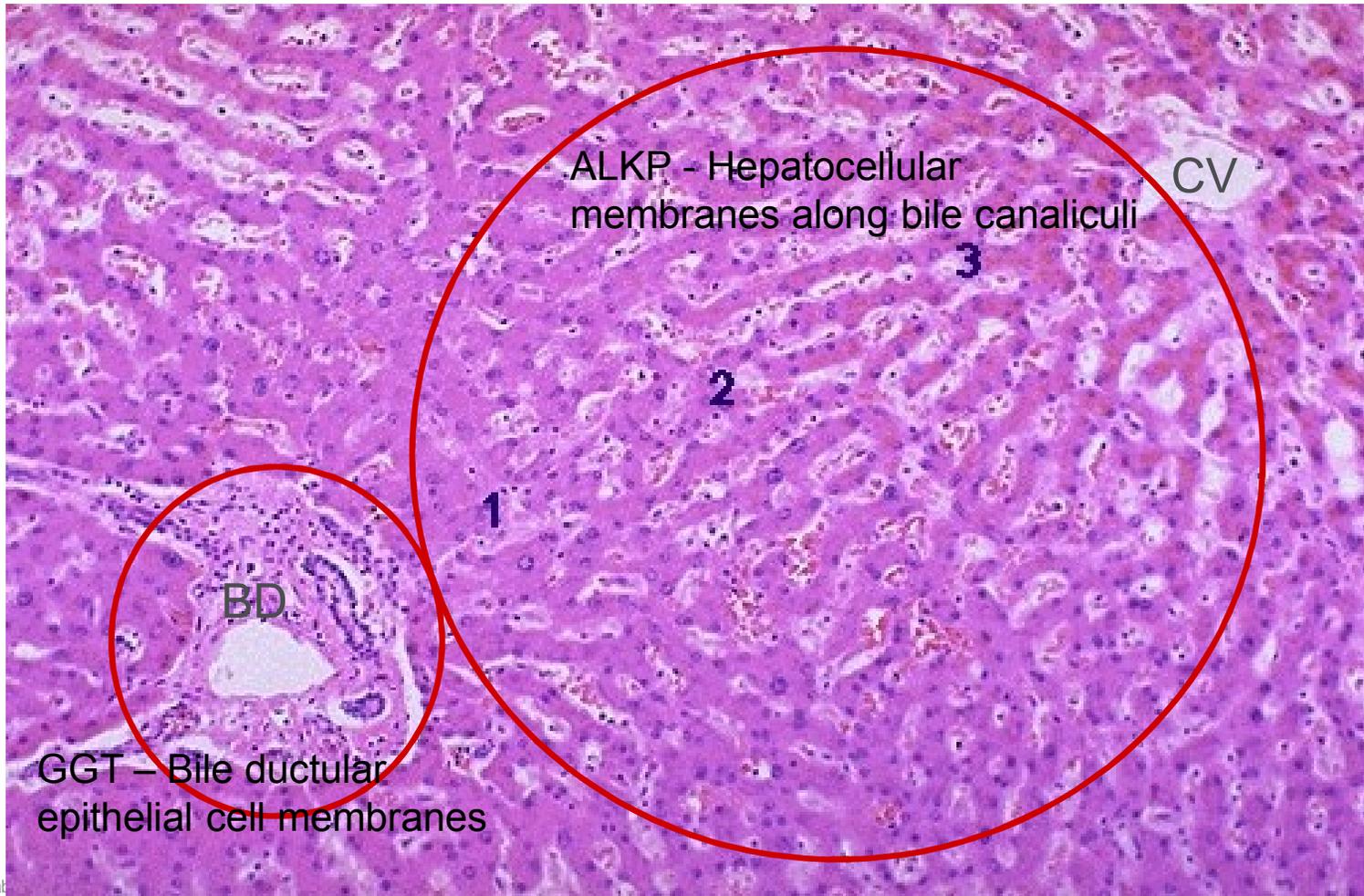
IDEXX

What about cats?

ALKP - Hepatocellular membranes along bile canaliculi

CV

3

2

1

BD

GGT – Bile ductular epithelial cell membranes

IDEXX

Lots to see here… electrolytes mandatory

o When only the BUN is high (or increased BUN:creatinine ratio)

o ALP vs ALT increased – *which is more worrisome?*

o ALP and GGT

o **Hyper- and hypocalcemia**

o Hyperkalemia when everything else is normal ???

o High TCO2 with low electrolytes ???

o SDMA

IDEXX

Calcium detour:
Should we be talking about ionized calcium?

Total or ionized calcium?

o Total = ionized (free) + protein bound + complexed

o Normal total calcium does not rule out ionized hypercalcemia

o Canine study[1]: 40% with ionized hypercalcemia had normal total calcium
  • Hypoalbuminemia in only 7 of 31 with normal total calcium

o Dogs with kidney disease: total hypercalcemia 20%, ionized hypercalcemia 10%

o Feline study: 64% of cats with ionized hypercalcemia had normal total calcium

o Cats with kidney disease: total hypercalcemia 20%, ionized hypercalcemia 30%

1. Johnsen CT et al. ECVIM-CA Congress. 2019.

IDEXX

Investigation of the Relationship Between Ionised and Total Calcium in Dogs with Ionised Hypercalcaemia

29th ECVIM-CA Congress, 2019

C.T. Johnsen; T. Schnabel; A. Gow; J. del-Pozo; E. Milne; V. Macklin; C. Fisher; I. Handel; R. Mellanby

University of Edinburgh, Midlothian, UK

o Teaching hospital 2012-2017
- 75 dogs had ionized hypercalcemia of which 31 had normal total calcium
- 7 of those 31 had hypoalbuminemia
- Most common diagnoses in dogs with ionized hypercalcemia – neoplasia (n=38), primary hyperparathyroidism (n=6)

o 40% dogs with ionized hypercalcemia had normal total calcium concentration

o Cannot be assumed that dogs with normal calcium do not have ionized hypercalcemia.

IDEXX

Hypercalcemia revisited

o Cats
- Idiopathic
- Renal failure (tCa 20%, iCa 30%)
- Neoplasia (lymphoma=carcinoma)

o Dogs
- Neoplasia (lymphoma>>>>>carcinoma)
- Hypoadrenocorticism
- Primary hyperparathyroidism
- Renal failure (tCa 20%, iCa 10%)

IDEXX

Idiopathic hypercalcemia

o Most common cause of hypercalcemia in cats; uncommon in dogs

o Young to middle-age

o No breed or sex predilection, longhaired cats overrepresented

o No clinical signs in 50%; wt loss, anorexia, GI signs in 50%

o Most non azotemic initially, may develop over time

o Calcium oxalate uroliths in 10-15%

o Diagnosis of exclusion, r/o neoplasia, kidney disease, primary hyperparathyroidism

Diagnostic criteria for idiopathic hypercalcemia

o *Ionized* hypercalcemia

o Decreased (or low normal) parathormone

o Exclusion of other causes of hypercalcemia

IDEXX

Idiopathic hypercalcemia treatment

o Diet - questionable benefit, not harmful, worth a 6-8 wk trial?
- Canned – increased moisture content minimizes CaOx
- Hi fiber - Purina OM Overweight Management, Royal Canin Gastrointestinal Fiber Response HF, Iams Intestinal Plus Low-Residue, Hill's w/d
- Renal Diets – protein restriction may cause muscle wasting
- "Stone' Diets - Royal Canin Urinary SO, Purina UR Urinary St/Ox, Iams Urinary-O Plus Moderate pH/O, Hill's c/d
- Home prepared Ca-restricted – nutritionist
- Natural composition – hi protein/fat, low carbohydrate

IDEXX

Idiopathic hypercalcemia medical management

o Prednisone (catabolic, diabetogenic)
  - 5 mg/cat/day, recheck at 1 mo
  - Dose increase to 10, 15, 20 mg/cat/day
  - 1/3 cats develop diabetes
o Bisphosphonates
  - Alendronate (Fosomax®) 10 mg PO/cat/week (up to 30 mg)
  - 12 hr fast imperative; maintain fast >2 h post pill
  - Esophagitis – 6 cc H20, butter on lips (licking/salivation)
  - Not diabetogenic
  - Pamidronate, 1-2 mg/kg IV in 0.9% NaCl over 1-2 h, q3-4 wk
    - Q 1-2 mo for IHC

IDEXX

6-yr-old male neutered Boxer

Test	Results	Reference Interval	LOW	NORMAL	HIGH

Catalyst Dx (September 28, 2009   10:15 AM)

Test	Results	Reference Interval		
GLU	106 mg/dL	74 - 143		
BUN	14 mg/dL	7 - 27		
CREA	1.6 mg/dL	0.5 - 1.8		
BUN/CREA	9			
PHOS	3.1 mg/dL	2.5 - 6.8		
CA	14.3 mg/dL	7.9 - 12.0	HIGH	
TP	7.2 g/dL	5.2 - 8.2		
ALB	3.4 g/dL	2.3 - 4.0		
GLOB	2.7 g/dL	2.5 - 4.5		
ALB/GLOB	1.3			
ALT	17 U/L	10 - 100		
ALKP	78 U/L	23 - 212		
GGT	1 U/L	0 - 7		
TBIL	0.5 mg/dL	0.0 - 0.9		
CHOL	290 mg/dL	110 - 320		
AMYL	1101 U/L	500 - 1500		
LIPA	2397 U/L	200 - 1800	HIGH	

VetLyte (September 28, 2009   10:15 AM)

Test	Results	Reference Interval		
Na	160 mmol/L	144 - 160		
K	4.7 mmol/L	3.5 - 5.8		
Cl	109 mmol/L	109 - 122		

SNAPshot Dx (September 28, 2009   10:15 AM)

T4	1.7 µg/dL	
Canine:		
	< 0.8 µg/dl	Low
	0.8 - 1.5 µg/dl	Borderline Low
	1.6 - 5.0 µg/dl	Normal
	> 5.0 µg/dl	High
	3.0 - 6.0 µg/dl	Therapeutic Range

Dogs with no clinical signs of hypothyroidism and results within the normal reference range are likely euthyroid. Dogs with low T4 concentrations may be hypothyroid or "euthyroid sick". Occasionally, hypothyroid dogs can have T4 concentrations that are low normal. Dogs with clinical signs of hypothyroidism and low or low normal T4 concentrations may be evaluated further by submission of freeT4 (fT4) and canine TSH. A high T4 concentration in a clinically normal dog is likely a variation of normal; however elevations may occur secondary to thyroid autoantibodies or rarely thyroid neoplasia. For dogs on thyroid supplement, acceptable 4-6 hour post pill total T4 concentrations generally fall within the higher end or slightly above the reference range.

UA Analyzer (September 28, 2009   10:15 AM)

GLU	neg
pH	7.5
PRO	neg
KET	neg
UBG	neg
BIL	neg
BLD	3+
S.G.	_____

6-yr-old male neutered Boxer

PTH	10.50	pmol/L		(3.0 -17.0)
iCa	1.95	mmol/L	H	(1.25 - 1.45)
*PRP	0.0	pmol/L		(0.0)

* Parathyroid-related protein

IDEXX

What is the diagnosis?

	1/13/2014 (Order Received) 1/21/2014 @ 1:45 am (Last Updated)	IDEXX Reference Laboratories Show Details	
Calcium	a 2.6	8.8 - 11.2 mg/dL	
Ionized Calcium	b 0.32	1.07 - 1.40 mmol/L	

a RESULT VERIFIED BY REPEAT ANALYSIS

b Referral test performed at Michigan State University.

	1/13/2014 (Order Received) 1/21/2014 @ 1:45 am (Last Updated)	IDEXX Reference Laboratories Show Details	
Parathyroid Hormone	0.1	0.5 - 5.8 pmol/L	

Same approach with glucose insulin panel for insulinoma.

First look at glucose. If low what SHOULD insulin level be…?

IDEXX

Lots to see here… electrolytes mandatory

o When only the BUN is high (or increased BUN:creatinine ratio)

o ALP vs ALT increased – *which is more worrisome?*

o ALP and GGT

o Hyper- and hypocalcemia

o Hyperkalemia when everything else is normal ???

o High TCO2 with low electrolytes ???

o **SDMA**

IDEXX

SDMA greater sensitivity - may be the first *and only* sign of decreased kidney function; not affected by ↓ muscle mass.

SDMA is more sensitive: Increases earlier than creatinine and decreased specific gravity.

Creatinine
75% loss

USG
66% loss

SDMA
25-40% loss
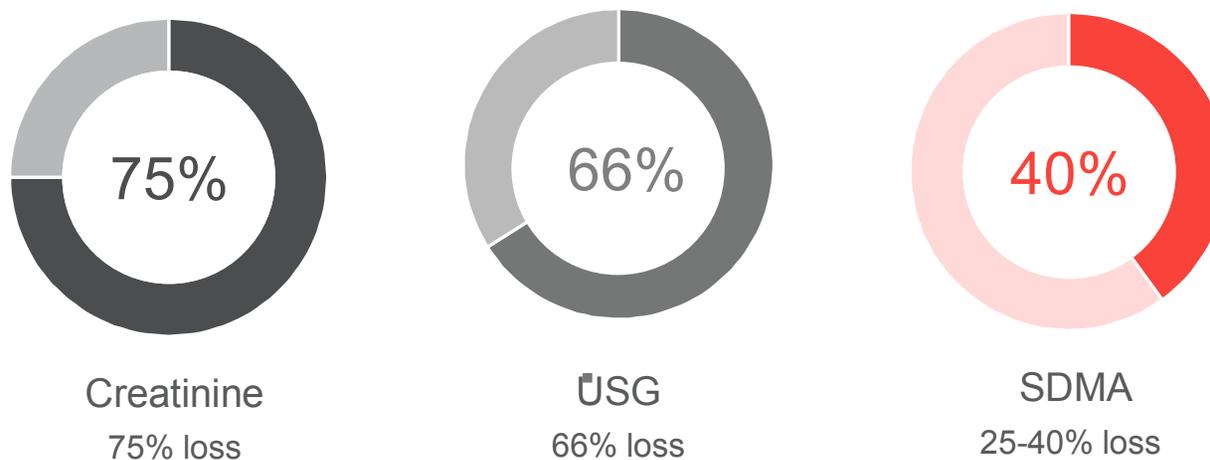
Sources
1. Nabity ,MB, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for the early detection of chronic kidney disease in dogs. *J Vet Intern Med.* 2015;29(4):1036–1044.
2. Hall JA et al. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. *J Vet Intern Med.* 2016;30(3):794–802.
3. Hall JA, et al. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med.* 2014;28(6):1676–1683.

IDEXX

What increased SDMA means…

SDMA↑   GFR↓

Courtesy of Dr. Jeff Niziolek

IDEXX

Any cause of decrease GFR may increase SDMA. Correct underlying cause and SDMA may normalize.

- Prerenal
  - **Dehydration**
  - **Trauma/shock—hypotension**
  - **Anesthesia**
  - **Cardiac disease**
  - Sepsis
  - Thrombosis, infarct
  - Burn injury, heat stroke
  - Transfusion reaction
  - Hyperviscosity, polycythemia

- Renal:
  - Kidney disease: CKD, acute kidney injury, kidney stones
  - Infection/infectious: **pyelonephritis**, FIP, sepsis, heartworm
  - Immune mediated: **Lyme nephritis**, vasculitis
  - Metabolic: **pancreatitis**, hypercalcemia
  - Neoplasia: **lymphoma**
  - Toxin: **lily**, **NSAID**, ethylene glycol (antifreeze), aminoglycoside antibiotics

- Postrenal:
  - **Urethral obstruction**
  - **Ureteral obstruction**
  - Urinary tract trauma/disruption: tear, rupture, blood clot

IDEXX

Within 12 months of first *mild* increase in SDMA:

SDMA
persistently
increased
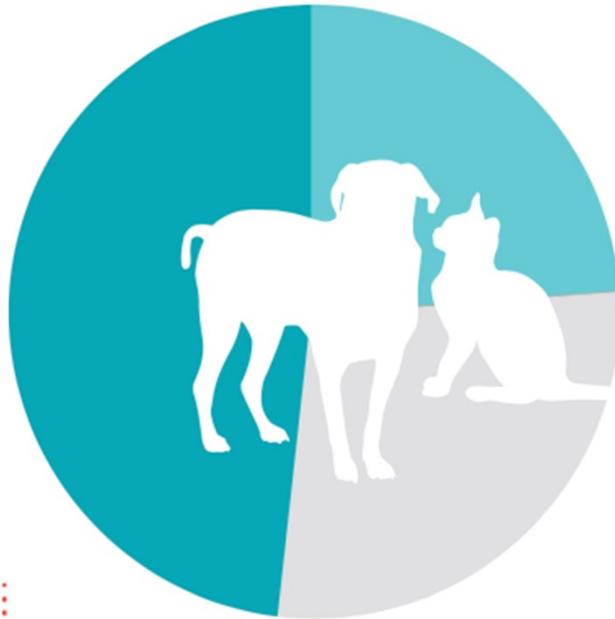
SDMA reverts to
normal…climbs again
later
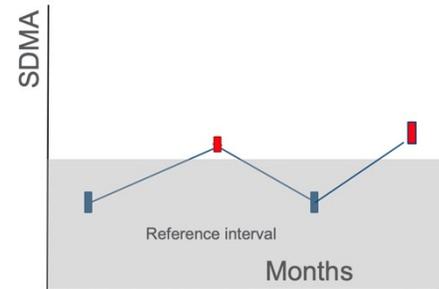
72% of patients **risk impaired kidney function**

IDEXX

The IDEXX SDMA® Algorithm

IDEXX SDMA | 14 | **ELEVATED**

15–19 μg/dL

≥20 μg/dL

Evaluate complete urinalysis

Other evidence of kidney disease?

No → Yes →

Impaired GFR: ACT NOW

Detects diseases of the kidney sooner[1–3] — and/or — **Reflects** other disease processes affecting the kidneys[4]

Recheck kidney panel in 2–4 weeks → **Persistent elevation in SDMA concentration** →

No ↓

Evaluate patient in 6 months
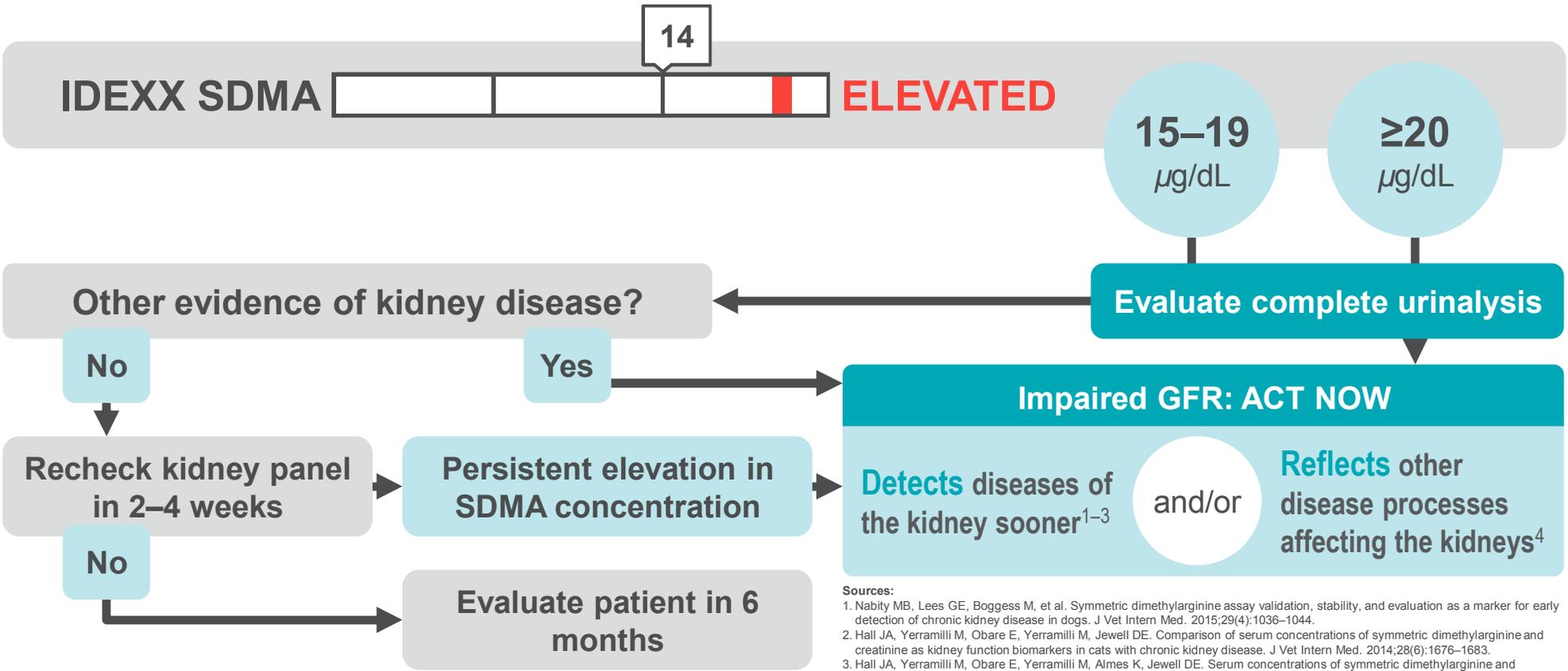
Sources:
1. Nabity MB, Lees GE, Boggess M, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. J Vet Intern Med. 2015;29(4):1036–1044.
2. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. J Vet Intern Med. 2014;28(6):1676–1683.
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. J Vet Intern Med. 2016;30(3):794–802.
4. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.

IDEXX

IRIS guidelines for diagnosing, staging, and treating chronic kidney disease in dogs and cats. Wait there's more…
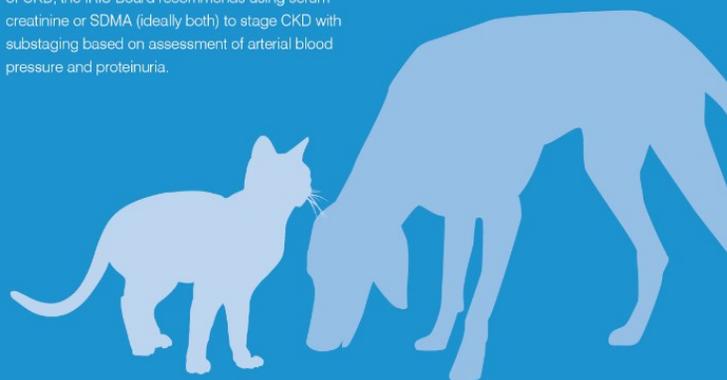
Updated September 2019

Welcome to the website of the
International Renal Interest Society*

This website is designed to bring you news and information regarding the work of IRIS. The mission of IRIS is to help veterinary practitioners better diagnose, understand and treat kidney disease in cats and dogs. We hope you find this site useful and informative.

IRIS Guidelines

For assistance in your day to day management of patients with CKD:

- IRIS Staging of Chronic Kidney Disease (CKD) - including algorithms
- IRIS Treatment Recommendations for CKD
- IRIS Grading of Acute Kidney Injury (AKI)

Read more

Education

- Provides additional information on specific aspects of kidney diseases.
- Contains regularly updated articles written by IRIS Board members.

Read more

Emerging Themes NEW

- Current topics being discussed and investigated in veterinary nephrology
- Includes occasional articles from IRIS Board members and invited authors

Read more

About IRIS

For information on:

- Members of IRIS
- IRIS and Osborne Awards
- Projects supported by IRIS
- IRIS Newsletters
- Bylaws

Read more

IDEXX

IRIS 2019 update…Creatine *and* SDMA for primary staging
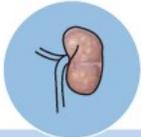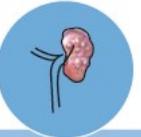
		Stage 1 No azotemia (Normal creatinine)	Stage 2 Mild azotemia (Normal or mildly elevated creatinine)	Stage 3 Moderate azotemia	Stage 4 Severe azotemia
Creatinine in μmol/L Stage based on stable creatinine	Canine	Less than 125 (1.4 mg/dL)	125–250 (1.4–2.8 mg/dL)	251–440 (2.9–5.0 mg/dL)	Greater than 440 (5.0 mg/dL)
	Feline	Less than 140 (1.6 mg/dL)	140–250 (1.6–2.8 mg/dL)	251–440 (2.9–5.0 mg/dL)	Greater than 440 (5.0 mg/dL)
SDMA* in μg/dL Stage based on stable SDMA	Canine	Less than 18	18–35	36–54	Greater than 54
	Feline	Less than 18	18–25	26–38	Greater than 38
UPC ratio Substage based on proteinuria	Canine	Nonproteinuric <0.2 Borderline proteinuric 0.2–0.5 Proteinuric >0.5			
	Feline	Nonproteinuric <0.2 Borderline proteinuric 0.2–0.4 Proteinuric >0.4			
Systolic blood pressure in mm Hg Substage based on blood pressure		Normotensive <140 Prehypertensive 140–159 Hypertensive 160–179 Severely hypertensive ≥180			

IDEXX

Complete urinalysis – you'll be glad you did.

Urinalysis (continued)

TEST	RESULT	REFERENCE VALUE
Clarity	CLEAR	
Specific Gravity	1.011	
pH	7.0	
Urine Protein [a]	2+ (200-300 mg/dL)	
Glucose	NEGATIVE	
Ketones	NEGATIVE	
Blood / Hemoglobin	NEGATIVE	
Bilirubin	NEGATIVE	
Urobilinogen	NORMAL	
White Blood Cells	0-2	0 - 5 HPF
Red Blood Cells	0-2	HPF
Bacteria	NONE SEEN	
Epithelial Cells	RARE (0-1)	
Mucus	NONE SEEN	
Casts	NONE SEEN	
Crystals	NONE SEEN	

[a] Protein test is performed and confirmed by the sulfosalicylic acid test.

IDEXX

Complete u/a with sediment – fresh is best. Within 30 min.

○ Crystals form – *which?*

○ Bacteria – increase or decrease (lyse) or become nonviable

○ RBCs, WBCs – decrease

○ Casts – decrease

○ Epithelial cell morphology – changes

○ *Rule out postrenal proteinuria before submitting UP/C*

○ *Gross AND microscopic hematuria can affect UP/C*

IDEXX

2015 Big year for proteinuria and urine protein:creatinine.
IRIS updated proteinuria recommendations.

o *New* normal UP/C → <0.2

o *New* treatment trigger UP/C → >0.4 (cat), >0.5 (dog)

o *New* treatment stage → Stage I CKD

o Clinical relevance → more UP/Cs

o **Urine protein/creatinine ratio (UP/C) a MUST** - dipstick not quantitative regardless of USG

IDEXX

When to run a UP/C

○ Dipstick positive for protein → any amount regardless of specific gravity
  • Sediment exam to rule out pre and post renal proteinuria before running UP/C

○ Any kidney workup → even if dipstick negative for protein
  • Dipstick detects ≥ 30 mg/dL
  • UP/C detects ≥ 5 mg/dL

○ Microalbuminuria detects ≥ 2 mg/dL
  • Negative → rules out proteinuria
  • Positive → significance in dogs and cats unknown → UPC

IDEXX

Proteinuria treatment in CKD – renal diet plus…

- Benazepril or enalapril, 0.25-0.5 mg/kg q12-24h starting dose (max 2 mg/kg/d)
  - SDMA/creat 5-7d and UP/C 4-8wk after start or dose change

- Telmisartan, 1 mg/kg/d (max 2 mg/kg/d)

- Omega-3 fatty acid, 0.25-0.5 mg/kg/d EPA/DHEA

- Aspirin if albumin < 2.0 g/dl, 1-5 mg/kg/d dog; 1 mg/kg q72h cat

- Amlodipine - after maximal safe dose of ACEI/telmisartan
  - May decrease proteinuria in cats
  - Cat <4 kg 0.625 mg/cat/d
  - Cat ≥ 4 kg 1.25 mg/cat/d

IDEXX

International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats

J. Scott Weese[a,*], Joseph Blondeau[b,c], Dawn Boothe[d], Luca G. Guardabassi[e,f],
Nigel Gumley[g], Mark Papich[h], Lisbeth Rem Jessen[i], Michael Lappin[j], Shelley Rankin[k],
Jodi L. Westropp[l], Jane Sykes[l]

IDEXX

Optimal sample for urine culture

o Cystocentesis unless contraindicated
  - Ultrasound guided if small bladder, obese, pyometra, etc.

o Process immediately or refrigerate and culture within 24h

o Culture voided samples ONLY if cystocentesis contraindicated AND:
  - Cultured in house or refrigerated and processed within few hours at lab
  - Interpret w/ cytology, signs, quantity, species, +/- pure culture
  - Same for catheterized samples

IDEXX

"Sporadic bacterial cystitis"

o Bacterial infection of bladder causing inflammation **and clinical signs**.

o **Uncommon in:**

o Cats (esp. young) – feline idiopathic cystitis / urolithiasis

o Intact male dogs – prostatitis until proven otherwise

o "Recurrent bacterial cystitis"
- ≥3 episodes clinical cystitis in 12 months or ≥2 in 6 months

o Subclinical bacteriuria
- *Culture positive* bacteriuria without clinical signs

IDEXX

Treatment of bacterial cystitis

o Amoxicillin first choice
- 11-15 mg/kg PO q8-12h
- **DURATION: 3-5 days (3 may be optimal)**
- +/- treat pending culture results
- If organism not susceptible but clinical cure – no change in drug
- If no clinical response in 48h check compliance and underlying disease

o NSAIDs
- Signs are due to inflammation
- Use pending culture results or as standard therapy
- Usual precautions apply, esp. cats

o Cranberry extract, D-mannose, probiotics, bladder infusions, methanamine not recommended (no good evidence)

o Post-treatment u/a or culture not recommended if signs resolve

IDEXX

Treatment of recurrent bacterial cystitis

o Investigate for underlying cause before further antibiotics
- Endocrinopathy, CKD, uroliths, obesity, ectopic ureter…

o Empirical treatment, +/- NSAID as for bacterial cystitis

o Change antibiotic if organism resistant AND no clinical cure

o **DURATION 3-5 days**

o 7-10 days if persistent/relapsing infection, or bladder wall invasion

o Cranberry extract, D-mannose, probiotics, bladder infusions, methanamine not recommended

o Culture 5-7 d after starting long duration treatment
- If + confirm compliance and evaluate further

o Culture 5-7 d after treatment
- If + with signs further evaluation and referral for cystoscopy
- If + but no signs approach as for subclinical bacteriuria

IDEXX

Pyelonephritis

o Infection of renal parenchyma from ascending infection or bacteremia

o Fluoroquinolone (or cefpodoxime)
- Enrofloxacin: **15-20 mg/kg q24h** (dog), 5 mg/kg q24h (cat)
- Marbofloxacin: 2.7-5.5 mg/kg q24h (dog, cat)
- Pradofloxacin: 3-5 mg/kg q24h (dog), 5-7.5 mg/kg q24h (cat)

o **DURATION 7-10 days**

o If no clinical improvement in 72 h reconsider diagnosis
- Subclinical bacteriuria (stop antibiotics)
- Ureteroliths, neoplasia, ectopic ureter…

o Recheck examination, labwork, urine culture 1-2 wk post treatment

IDEXX

Bacterial prostatitis

o Consider in every intact male with bacterial cystitis

o Culture and cytology of 3rd fraction of ejaculate

o Urine culture likely to yield same organism (not always)

o Screen for *Brucella canis*

o Fluroquinolone (or trimethoprim-sulfa drug 15-30 mg/kg q12h)
- Clindamycin, macrolides, fosfomycin ok based on culture
- No penicillins, cephalosporins, aminoglycosides, tetracyclines, cipro

o **DURATION 4-6 weeks**

o Drain prostatic abscesses

o Castrate as early as possible

IDEXX

Subclinical bacteriuria

o **Subclinical bacteriuria = positive culture of cystocentesis sample** with no clinical evidence of infectious urinary tract disease

o **Treatment not recommended**
   - Spontaneous resolution; MDR organisms replaced by less resistant organisms

o No evidence for risk of UTI or other infectious complications reported in dogs or cats if untreated

o Therefore few indications for urine culture in animals with no signs
   - Including those with diabetes mellitus, hyperadrenocorticism
   - **If** culture done and positive – full evaluation for causes of bacteriuria

o Repeat culture not recommended whether or not treated

IDEXX

Treatment for SBU should not be based on:

o Pyuria or other cytological abnormalities

o Bacteria number (CFU/ml)
  - >100 CFU/ml can be seen in SBU, no greater risk of disease development

o Multidrug resistance
  - MDR genes not virulence factors (organism may be LESS virulent)

o Infection control (eliminate shedding) of MDR organisms
  - Organism originate from GI tract, will recolonize bladder if treated

o Consider treating if:
  - Spinal cord injury – color/odor of urine not predictive of bacterial cystitis
  - Corynebacterium urealyticum – encrusting cystitis risk
  - Urease-producing bacteria (staphylococci) – struvite urolith risk
  - **DURATION 3-5 days** (if encrusting cystitis or urolith ruled out)

IDEXX

Ancillary treatment to prevent recurrence

o Cranberry extract → inhibit *E.coli* attachment (prevention)

o D-mannose → inhibit *E. coli* attachment (prevention)

o N-acetyl cysteine → biofilm penetration

o Glucosamine / chondroitin sulfates / antioxidants → bladder mucosal health

o Probiotic – diverse bacterial population, e.g. Proviable® → less resistant organisms
  - Dose to administer billions of colonies, e.g., 5 billion/capsule Proviable®

o **Phenylpropanolamine (female dogs)→ minimize ascending infections**

o Fecal transplantation after resolution to decrease resistance

IDEXX

Critically important antimicrobials

o 2 criteria:
- Sole or one of few agents to treat serious human disease
- Used for organisms that may be transmitted by or acquire resistance from non-human sources

o Veterinary approved
- Aminoglycosides, 3rd/4th generation cephalosporins, fluoroquinolones, macrolides

o Human
- Carbapenems (imipenem, meropenem), fosfomycin, vancomycin

IDEXX

Critical important antibiotics: doses.

o Fosfomycin, 40 mg/kg q12 h for 5-10 d

o Meropenem, 8-10 mg/kg SC q12 h 7-10 d

o (Vancomycin – absolute last resort to avoid suffering)

o Consider doxycycline (if organism susceptible)

IDEXX

Thank you!