Easy does it. Update on fluid therapy for kidney disease

Bill Saxon, DVM, DACVIM, DACVECC

IDEXX Medical Education Specialist

Disclosure:

Bill Saxon is a full-time employee of IDEXX.

VETERINARY PRACTICE GUIDELINES

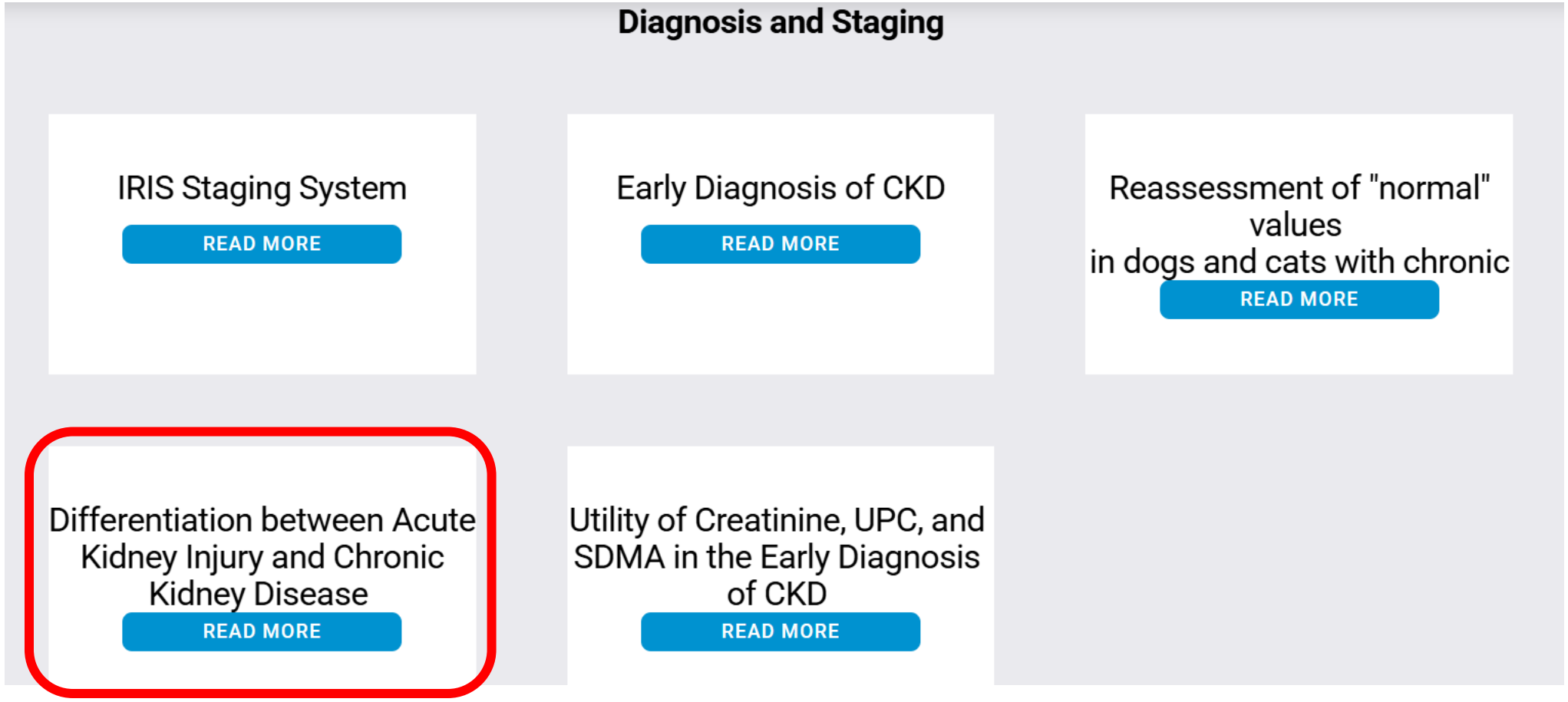
2024 AAHA Fluid Therapy Guidelines for Dogs and Cats

Mariana Pardo, BVSc, MV, DACVECC†, Erin Spencer, MEd, CVT, VTS (ECC)†,
Adesola Odunayo, DVM, MS, DACVECC, Mary L. Ramirez, DVM, DABVP (Canine and Feline),
Elke Rudloff, DVM, DACVECC, cVMA, Heidi Shafford, DVM, PhD, DACVAA, Ann Weil, DVM, MS, DACVAA,
Ewan Wolff, DVM, PhD, DACVIM (Small Animal Internal Medicine)

Why are we rethinking fluid therapy with kidney disease?
And in general?

- Recognition that hypervolemia is as dangerous as hypovolemia
- Causes increased venous pressure = impaired perfusion gradient
- Causes interstitial edema = impaired oxygen delivery
- Interstitial edema in kidney increases intrarenal pressure (rigid capsule)
- Leads to decreased renal perfusion and decreased GFR (tubules compressed)
- Causes AKI and kills pets that have it (worse than sepsis and AKI in people)
- Not all acute or chronic kidney disease is fluid responsive
  - Not all with AKI or CKD or fluid tolerant
- If azotemia doesn't improve within 12-24 hr (max) of appropriate fluids, back off

https://www.iris-kidney.com



Hallmarks of AKI v CKD

- History and physical exam
  - Acute onset – hours to days
  - Toxin exposure (lily, grapes, NSAIDs, anesthetics…)
  - Oliguria/anuria +/-
  - Renomegaly, renal pain
  - Bradycardia/hypothermia (hyperkalemia) if severe hyperkalemia
- Lab findings
  - Hyperkalemia +/-
  - Urinary granular casts, normoglycemic glucosuria, cystatin B…
- Imaging
  - Renomegaly in 70%
  - Hydroureter, pyelectasia, hydronephrosis
  - Ureteral calculi
  - Normal parathyroid gland

Tips for detecting *pre-azotemic* kidney issues

- CKD
  - Creatine, SDMA trending up but within reference interval
  - USG decreasing over time
  - Body weight decreases early with CKD in cats (up to 3 years before diagnosis)
  - Persistent renal proteinuria = proteinuric CKD (no azotemia in Stage 1)

- AKI
  - **Injury markers in urine up to 48 h before increased functional (GFR) markers in blood**
  - Complete urinalysis (cysto not necessary) evaluate for:
    - Granular casts, euglycemic glucosuria, proteinuria
    - Cystatin B

The ideal dog or cat to run a cystatin B on…

- AKI present or possible
  - Acutely ill with supportive lab results +/- non-physiologic oliguria/anuria
  - Known or possible exposure to nephrotoxin
  - Chronic NSAIDs
- Systemic disease present resulting in:
  - Renal hypoperfusion
  - Cytokine storm
- Early CKD to predict risk of progression
  - Is there a concurrent active injury component

“Fluid therapy is not the mainstay of treating azotemic patients.”

“..it is to support kidneys by correcting treatable abnormalities…so that kidneys can heal themselves.”

2024 AAHA Fluid Therapy Guidelines

What are those treatable abnormalities?

- CKD
  - Dehydration
  - Hypokalemia
  - Severe metabolic acidemia
  - Anemia

- AKI
  - Hypovolemia
  - Hyperkalemia
  - Hypoglycemia
  - Hypercalcemia

No evidence of benefit of fluids in euhydrated (and euvolemic) patients.

Fluid therapy for kidney disease – less may be more.

Fluids are drugs – avoid overdose.
They do not improve kidney function.
Hypervolemia causes AKI and kills patients that already have it.
Not every animal with kidney disease (acute or chronic) needs fluids.

Fluid tips for CKD and AKI

CKD

- Not in stable CKD patients
- SC fluids not standard care
- Correct hypovolemia
- Correct dehydration
- Trial if inappetence (subclinical dehydration)
- No forced diuresis

AKI

- Correct hypovolemia in <1-2hr
- Correct dehydration 4-6 hr
- Fluid-responsive AKI improvement within hours
  - If creatinine not normal w/in ≈12 hr not fluid responsive
- Fluids not obligatory
- No forced diuresis

Hypovolemia v dehydration

- Hypovolemia
  - Loss from intravascular space → hypoperfusion
    - Shock, hemorrhage
  - HR, pulse, CRT, mucous membranes, lactate, urine output
  - Isotonic crystalloid, e.g., LRs IV or IO
  - 10-20 ml/kg dog; 5-10 ml/kg cat over 15-30 min, x2-3, then natural colloid
- Dehydration
  - Loss from interstitial space
  - Skin turgor over rib cage, mucous membrane moisture
  - Isotonic crystalloid IV, SC, enteral via feeding tube
  - Fluid deficit in mL = BW (kg) x % dehydration (as decimal) x 1000
    - 5 kg x 0.05 x 1000 = 250 ml
  - No hypovolemia unless 10-12% dehydration

Should a patient stay on LRs for prolonged therapy?

- Maintenance fluids (*hypotonic* crystalloids)
  - For continued fluid therapy in hydrated patients with inadequate water intake
  - Meet sensible/insensible loss from urine, feces, sweat, respiration
  - Lower Na concentration than replacement fluids
  - 0.45% NaCl w/ or w/o 2.5% dextrose, Plasma-lyte 56, Normosol M
  - Homemade, 1:1 replacement fluid with 5% dextrose

  } KCl 20 mEq/L

- Incompatible (same IV line) with:
  - Blood products (citrate)
  - $NaHCO_3$

Prevent volume overload.

Goal directed fluids:
Normal perfusion parameters, normal hydration.

Monitor body weight 2-4x/day:
5% increase consider decreasing.
10% increase volume overload.

If azotaemia worsens on IV fluids consider decreasing or discontinuing fluids.

If total daily volume exceeds maintenance or if weight gain.

STOP fluids, +/- Lasix 1-4 mg/kg IV

We've probably all done this…

Box 5: Common Fluid Overload Case Scenarios

1. ***Continued IV fluid therapy in a feline patient with renal disease***. A cat is dehydrated, uremic, and anuric on presentation. Although IV fluid administration improves hydration status, uremia persists. IV fluids are continued with the misguided goal of improving GFR. However, no effective increase in GFR will occur no matter how much fluid this patient receives.
2. ***IV fluid therapy in a patient anesthetized for a lengthy procedure***. A dog receives 10 mL/kg of fluids throughout a 6 hr procedure and develops respiratory distress during anesthetic recovery.
3. ***SC fluid therapy in a cat with occult or fulminant heart disease***. A cat presents for evaluation of vomiting associated with malaise of congestive heart failure and is given SC fluids despite no evidence of dehydration.

2024 AAFP Fluid Therapy Guidelines

Now we know better:

- Once hydrated, if still inappetent no more than maintenance fluids (+ ongoing losses), with potassium prn
- Mirtazapine or capromorelin (Elura®) only when hydration normal
- Ideally NE or NG tube for hydration, nutrition

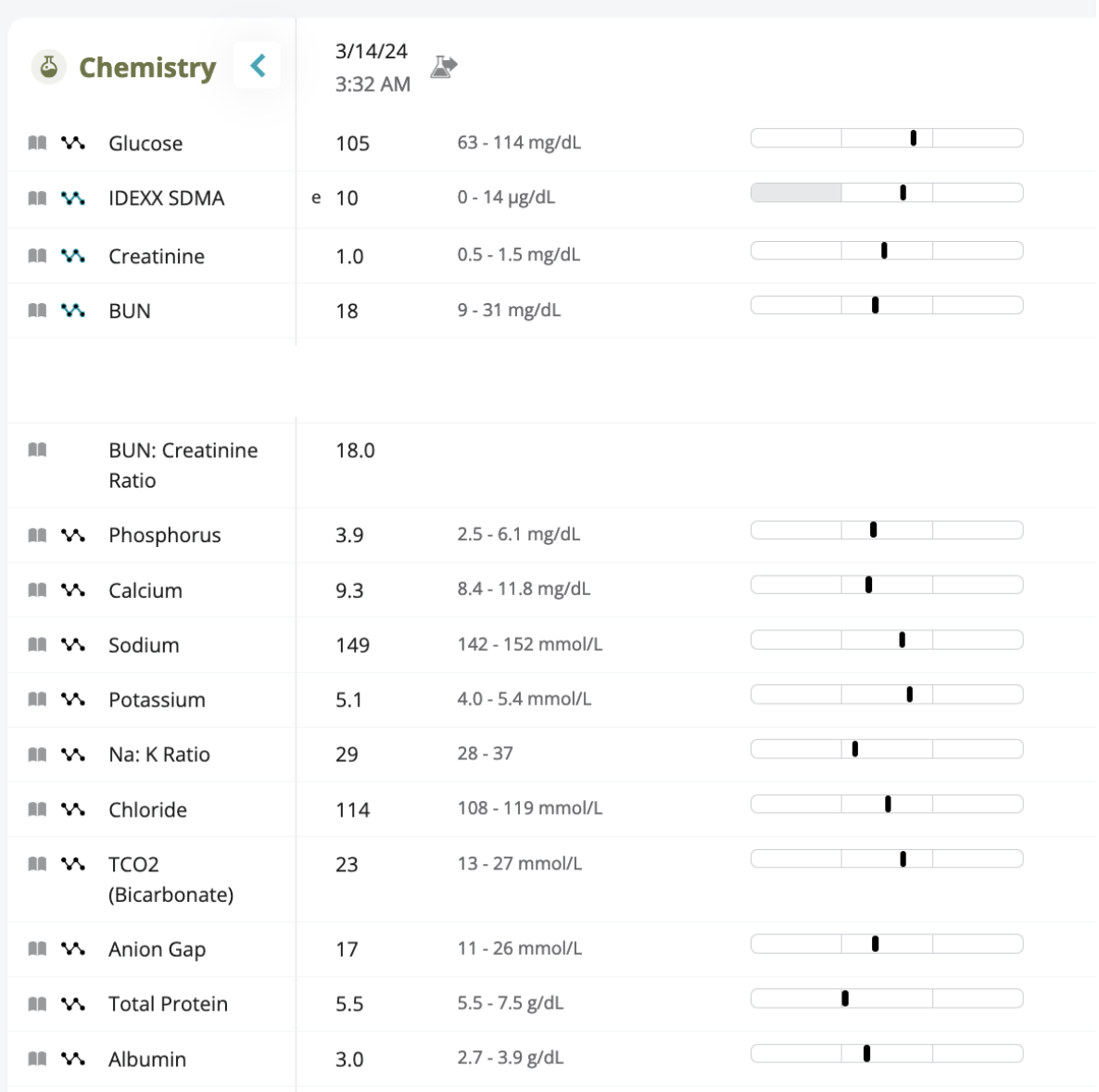
Rational fluid therapy for stable CKD

- None if eating and euhydrated
- Fluid trial if inappetent to address occult (up to 5%) dehydration
- Potassium supplementation
- As needed if acute on chronic kidney disease
- Progressive azotemia does not alone justify ‘diuresis’ (doesn’t work)

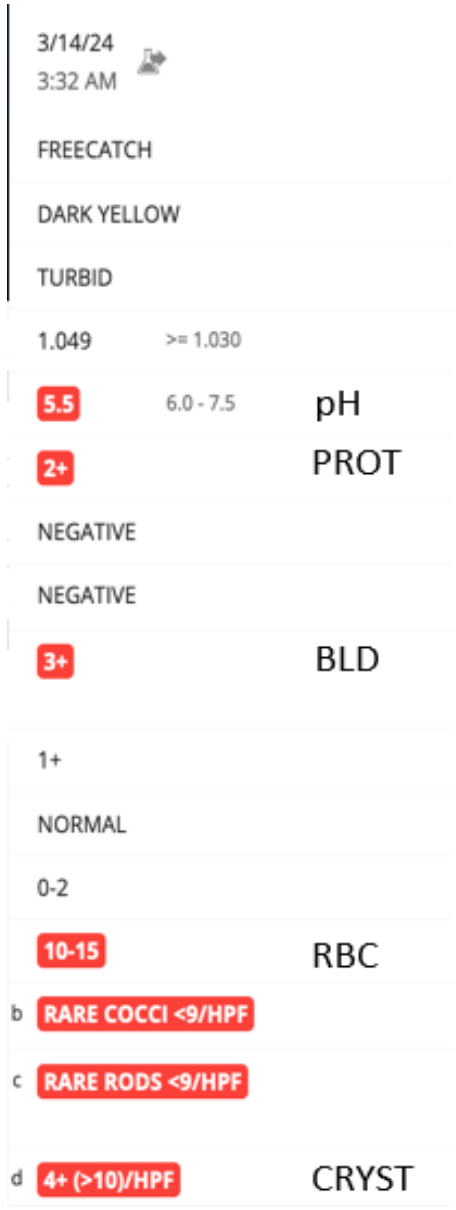
2-year-old male neutered Labrador

- Presenting complaint
  - Raisin ingestion sometime in past 8 hr (owner found empty box when returned from work)
  - No priors
  - Current on vaccination, parasite prophylaxis

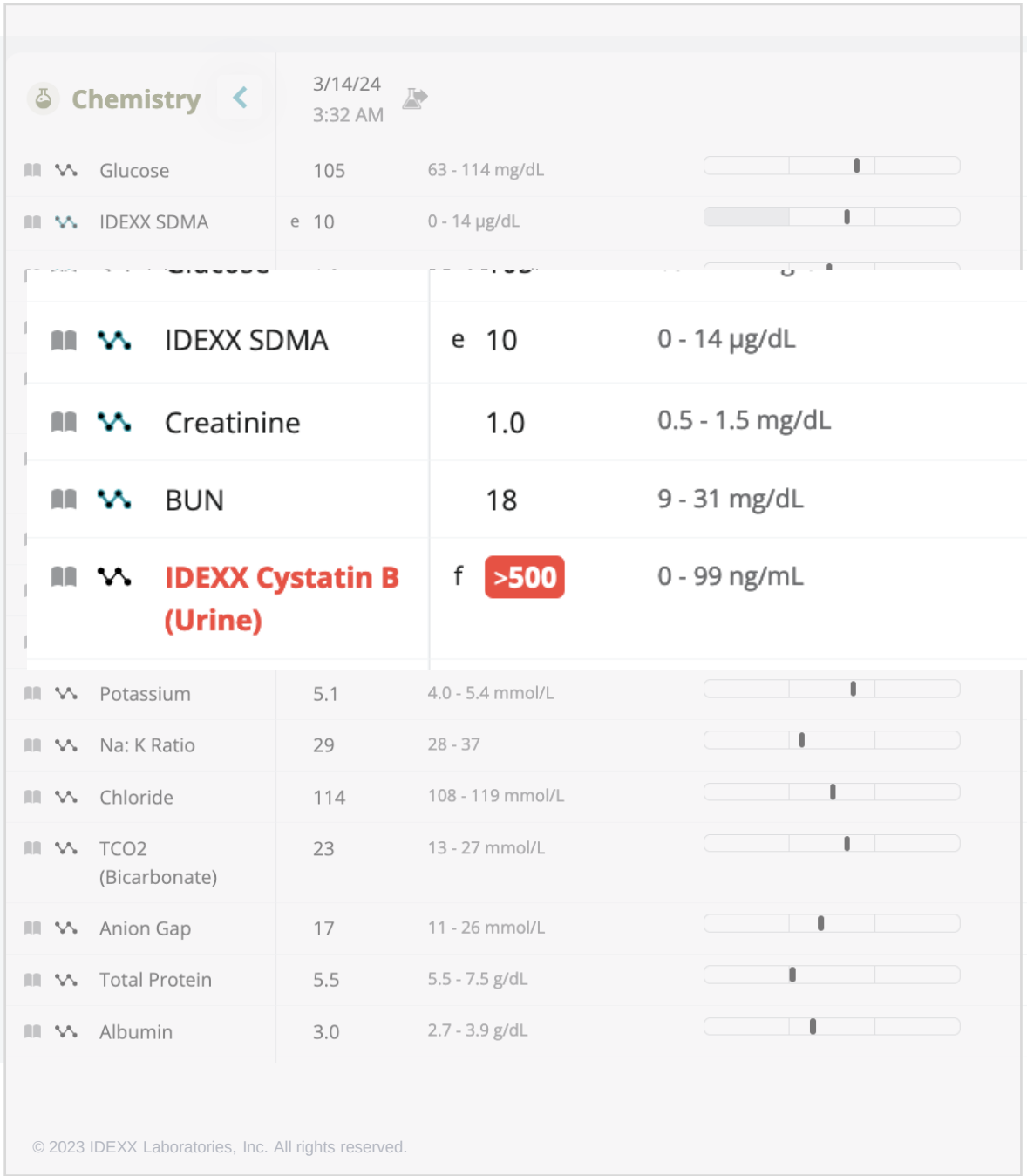
- PE
  - Vitals normal
  - No significant findings



Chemistry	3/14/24 3:32 AM		
Glucose	105	63 - 114 mg/dL	
IDEXX SDMA	e 10	0 - 14 µg/dL	
Creatinine	1.0	0.5 - 1.5 mg/dL	
BUN	18	9 - 31 mg/dL	
BUN: Creatinine Ratio	18.0		
Phosphorus	3.9	2.5 - 6.1 mg/dL	
Calcium	9.3	8.4 - 11.8 mg/dL	
Sodium	149	142 - 152 mmol/L	
Potassium	5.1	4.0 - 5.4 mmol/L	
Na: K Ratio	29	28 - 37	
Chloride	114	108 - 119 mmol/L	
TCO2 (Bicarbonate)	23	13 - 27 mmol/L	
Anion Gap	17	11 - 26 mmol/L	
Total Protein	5.5	5.5 - 7.5 g/dL	
Albumin	3.0	2.7 - 3.9 g/dL	



3/14/24 3:32 AM		
FREECATCH		
DARK YELLOW		
TURBID		
1.049	>= 1.030	
5.5	6.0 - 7.5	pH
2+		PROT
NEGATIVE		
NEGATIVE		
3+		BLD
1+		
NORMAL		
0-2		
10-15		RBC
b RARE COCCI <9/HPF		
c RARE RODS <9/HPF		
d 4+ (>10)/HPF		CRYST



Treatment options for this dog

- Cystatin B increased = *active* tubular injury
- Not azotemic, USG normal
- Hydration normal

- **Induce vomiting and give 1 dose activated charcoal**
  - **Raisins in stomach up to 24h, not rapidly broken down or absorbed by GI tract**
- Send home and recheck renal values and cystatin B in 24-48h?
- SC fluids before sending home?
  - In case further vomiting, decreased appetite?
- Hospitalize for IV fluids at maintenance rate for 48 h?
  - Fluids not beneficial euhydrated patients, don't hasten toxin excretion
- ~~Hospitalize for IV fluids at 2-4x maintenance for 48 h?~~

AKI can develop in hospital: monitor and grade daily.

Prerenal, renal, postrenal causes.

- Dehydration
- Age – very young or old
- Diuretic or nephrotoxic drug therapy
- Hypokalemia or hypercalcemia
- Sepsis
- Congestive heart failure
- Acute pancreatitis
- Systemic hypertension
- CKD

Avoid iatrogenic AKI!

Nephrotoxic drugs

Hemodynamic instability

Fluid overload

IRIS AKI grading and subgrading criteria. Apply daily.

Table 1: IRIS AKI Grading Criteria

AKI Grade	Blood Creatinine	Clinical Description
Grade I	<1.6 mg/dl (<140 µmol/l)	Nonazotemic AKI: a. Documented AKI: (historical, clinical, laboratory, or imaging evidence of AKI, clinical oliguria/anuria, volume responsiveness‡) and/or b. Progressive nonazotemic increase in blood creatinine: ≥ 0.3 mg/dl (≥ 26.4 µmol/l) within 48 h c. Measured oliguria (<1 ml/kg/h)# or anuria over 6 h
Grade II	1.7 – 2.5 mg/dl (141 – 220 µmol/l)	Mild AKI a. Documented AKI and static or progressive azotemia b. Progressive azotemic: increase in blood creatinine; ≥ 0.3 mg/dl ≥ 26.4 µmol/l) within 48 h),or volume responsiveness‡ c. Measured oliguria (<1 ml/kg/h)# or anuria over 6 h
Grade III	2.6 – 5.0 mg/dl (221 – 439µmol/l)	
Grade IV	5.1 – 10.0 mg/dl (440 – 880 µmol/l)	Moderate to Severe AKI: a. Documented AKI and increasing severities of azotemia and functional renal failure
Grade V	>10.0 mg/dl (>880 µmol/l)	

(‡Volume responsive is an increase in urine production to >1 ml/kg/h over 6 h; and/or decrease in serum creatinine to baseline over 48 h)

Table 2: IRIS AKI Subgrading

AKI Grade	Blood Creatinine	Subgrade
Grade I	<1.6 mg/dl (<140 µmol/l)	Each grade of AKI is further subgraded as: 1. Non oliguric (NO) or oligo-anuric (O) 2. Requiring renal replacement therapy (RRT)
Grade II	1.7 – 2.5 mg/dl (141 – 220 µmol/l)	
Grade III	2.6 – 5.0 mg/dl (221 – 439µmol/l)	
Grade IV	5.1 – 10.0 mg/dl (440 – 880 µmol/l)	
Grade V	>10.0 mg/dl (>880 µmol/l)	

Table 3: Illustration of IRIS AKI Grading During Hospitalization*

	Day 1	Day 2	Day 3	Day 4	Day 5
Patient 1	0.9	1.5	1.5	1.5	1.7
Patient 2	2.3 CKD	2.5 CKD	2.7	3.5	2.4
Patient 3	5.3	5.2	3.6	2.4	1.6
Patient 4	4.8	5.8	6.9	10.8	RRT
Patient 5	18.2	RRT	RRT	RRT	RRT

Non AKI · AKI Grade I · AKI Grade II · AKI Grade III · AKI Grade IV · AKI Grade V

Detect non-physiologic oliguria / anuria

- Measuring urine output **important** yet often neglected
- Indwelling urinary catheter and closed aseptic collection system optimal
  - Collection bag below patient
  - Daily disinfection of ports, visible portion of catheter, prepuce, etc.
  - Change q2-3 days
- Estimate using absorbent pads when catheterization not possible
  - Weigh before and after use
  - 1 gm = 1 ml
- Oliguria <0.5-1.0 ml/kg/hr
  - AFTER hydration and volume restored (physiologic oliguria)
  - Consider if urine production does not increase to 2-5 ml/kg/h after rehydration
  - Ensure collection system connected, patent

Treating oliguria/anuria has gotten easier.

- Furosemide - most effective
  - Loading dose 0.66 mg/kg IV then CRI at 0.66 mg/kg/h (0.5-1.0 mg/kg/h)

- Furosemide - simplest
  - 2 mg/kg IV initially
    - If no urine production within 20-40 minutes
  - 4 then 6 mg/kg IV hourly
  - Effective dose q6-8 h

- Mannitol, dopamine, fenoldopam no

- If no increase in urine production ins and outs or renal replacement therapy

Ins and outs for oliguria/anuria

- Match fluids exactly with urine produced to avoid fluid overload

- Total fluids to administer (and not a drop more) =
  Insensible loss (respiration, feces) 22 ml/kg/d +
  Sensible loss (urine) +
  Ongoing loss (vomiting, diarrhea)

- Given in 4 or 6 hr intervals

In and outs for 4 kg cat, normal hydration, no v/d

- Fluids in 6 h increments
- Insensible loss 20 ml/kg/d ÷ 4 = 5 ml/kg x 4 kg = 20 ml
- Urine production = 0 ml
- No v/d = 0 ml
- 20 ml total volume to administer over next 6 h = 3-4 ml/h

6 hours later…

Urine produced in preceding 6 h = 20 ml

Vomitus = 10 ml

Insensible loss in 6 h = 25 ml

55 ml total volume to administer over next 6 h = 9-10 ml/h

Repeat calculation every 6 hours until urine production > 1 ml/kg/h

Fluid therapy during recovery phase

- Polyuria may be profound
  - Especially with obstructive disease (or lepto in dogs)
- Higher fluid rates than any other disease
- Hypokalemia may result – spike fluids
- Monitor urine volume, body weight, perfusion and hydration parameters and keep up!
- Taper 10-25% per day once stable and continue reassessing

Adjusting drug dosages and/or frequency with AKI

- Important if excreted by kidneys
- Patient interval (hr) = normal interval (h) x serum creatinine (fluoroquinolones)
- Patient dose = normal dose / serum creatinine (penicillins)
- Creatinine serves as estimated of GFR
  - Nonlinear with creatinine > 4 mg/dL

Prognosis

- Mortality 58-73%
- Better outcomes with infectious causes
- Degree of azotemia not associated with outcome
- Poor prognostic indicators
  - Decreased urine production
  - Hypothermia
  - Hyperkalemia
  - Hypoalbuminemia
  - Decreased HCO_3 at admission
- Kidney dysfunction that lasts >3 months after AKI = CKD

Thank you!

Fluid therapy during recovery phase of AKI

- Polyuria may be profound
  - Especially with obstructive disease (or lepto in dogs)
- Higher fluid rates than any other disease
- Hypokalemia may result – spike fluids
- Monitor urine volume, body weight, perfusion and hydration parameters and keep up!
- Taper 10-25% per day once stable and continue reassessing

Fluids do not improve kidney function.

Excess fluids cause and worsen kidney disease.

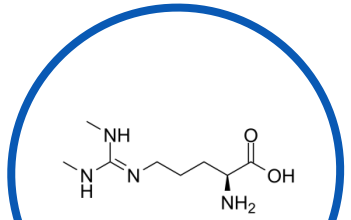
When, what type of fluid, how much, for how long?

Before we get into specifics of fluid therapy for kidney disease…

Evolution in assessing kidneys…

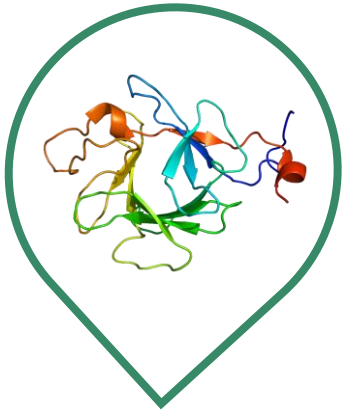
BUN early 1900s, **creatinine** 1920s, **Urinalysis** forever**.**

Yawn…
For almost 100 years!



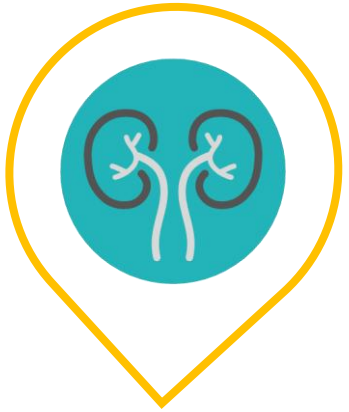
SDMA

Validated for use in dogs
2015



FGF-23

Launched for felines with chronic kidney disease
2022



Urinary Cystatin B

Detects active and acute kidney damage

Tips for early diagnosis of kidney disease

- Include all available functional (GFR) biomarkers: BUN, creat, SDMA
- Increased creat, SDMA means decreased GFR, NOT kidney disease
- Investigate prerenal, renal (intrinsic), post renal causes of decreased GFR

Investigate all causes of decreased GFR…

1

Prerenal

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

2

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

3

Postrenal

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

Tips early diagnosis of kidney disease

- Include all current functional (GFR) biomarkers: BUN, creat, SDMA
- Increased creat, SDMA means decreased GFR NOT kidney disease
- Investigate prerenal, renal (intrinsic), post renal causes of decreased GFR
- **Urinalysis (USG, dipstick, sediment) essential**

Cannot interpret SDMA, creat without USG

Both of these dogs are azotemic.

One of these dogs has a kidney problem.

(Normal USG >1.030 *when azotemic; >1.035 in cats.*)

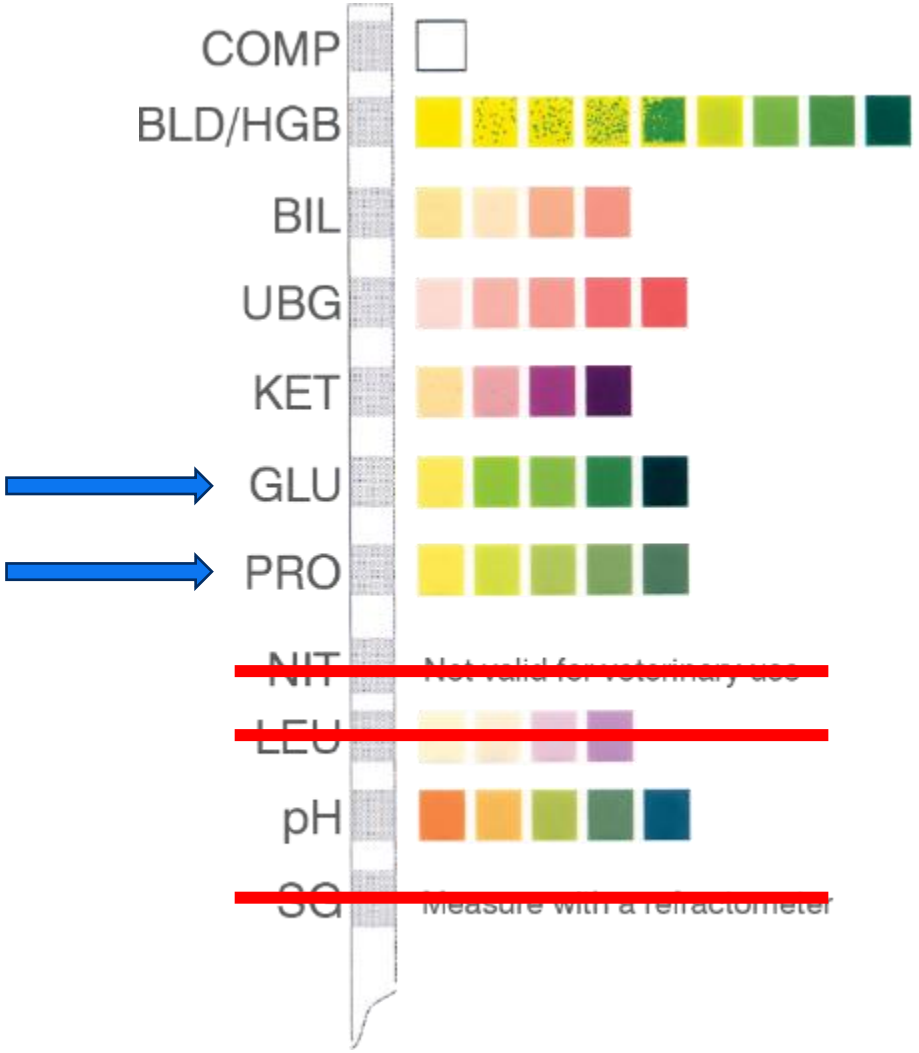
SDMA 19 ug/dL, Creat 159 umol/L

USG 1.055

SDMA 19 ug/dL, Creat 159 umol/L

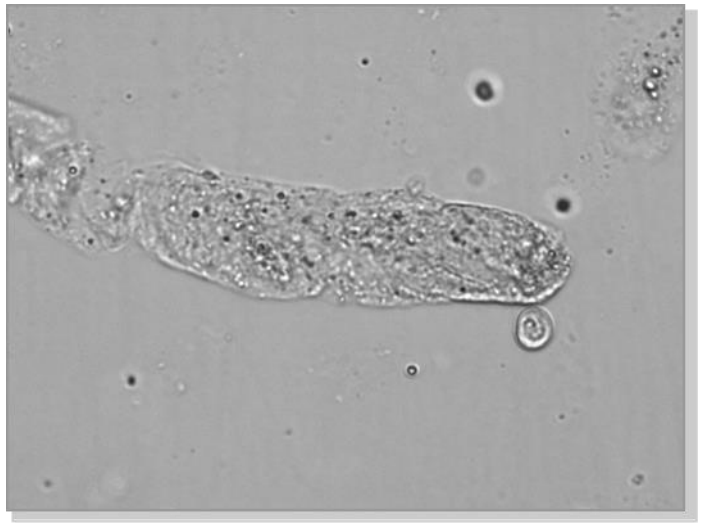
USG 1.010

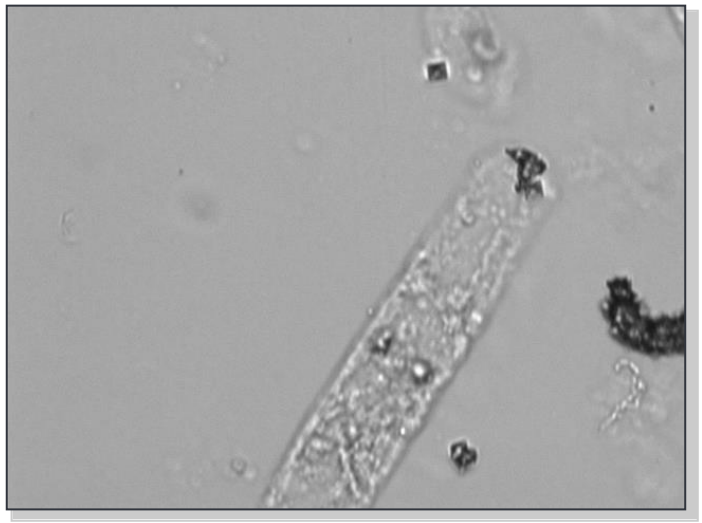
Kidney clues from dipstick?



Kidney ***injury markers*** are found ***in urine***.

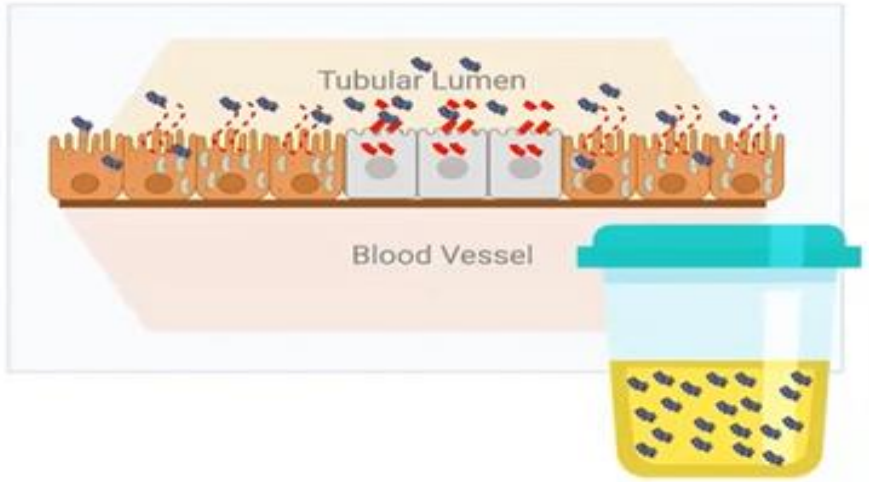
- Proteinuria
- Hematuria
- Pyuria
- Bacteriuria
- Renal epithelial cells
- Glucosuria (normoglycemia)
- + Urine culture
- Granular casts ≈16%
- Decreased urine production
- Decreased USG





Urine Cystatin B detects *active* kidney tubular damage
(ALT of the kidney)

The types of active and acute injury that can cause Cystatin B to leak into urine include both primary and secondary insults to the kidney



1
- Primary Renal Injury
  - "Acute on Chronic" Crisis
  - Toxin (grapes/raisins, lilies, ethylene glycol)

2
- Secondary Renal Injury
  - Infectious
    - Pyelonephritis
    - VBD
  - Systemic Disease (pancreatitis, vasculitis)
  - Hypo-/hypertension
  - Blood loss
  - Trauma

Tips for diagnosing kidney disease

- Include all current functional (GFR) biomarkers: BUN, creat, SDMA
- Increased creat, SDMA means decreased GFR NOT kidney disease
- Investigate prerenal, renal (intrinsic), post renal causes of decreased GFR
- Urinalysis (USG, dipstick, sediment) essential
- **Detect *pre-azotemic (early)* kidney disease or damage…**

Not all with acute or chronic kidney disease are azotemic.

Catch pre-azotemic (early) phase for better outcomes.

Tips for detecting pre-azotemic kidney issues

- CKD
  - Creatine, SDMA trending up but within reference interval
  - USG decreasing over time
  - Body weight decreases early with CKD in cats (up to 3 years before diagnosis)
  - Persistent renal proteinuria = proteinuric CKD (no azotemia in Stage 1)

- AKI
  - **Injury markers in urine up to 48 h before increased functional (GFR) markers in blood**
  - Complete urinalysis (cysto not necessary) evaluate for:
    - Proteinuria (tubular), glucosuria (w/ normal blood glucose), granular casts
    - Cystatin B

“Fluid therapy is not the mainstay of treating azotemic patients.”

“..it is to support kidneys by correcting treatable abnormalities…so that kidney can heal themselves.”

2024 AAHA Fluid Therapy Guidelines

What are those treatable abnormalities?

- CKD
  - Dehydration
  - Hypokalemia
  - Severe metabolic acidemia
  - Anemia

- AKI
  - Hypovolemia
  - Hyperkalemia
  - Hypoglycemia
  - Hypercalcemia

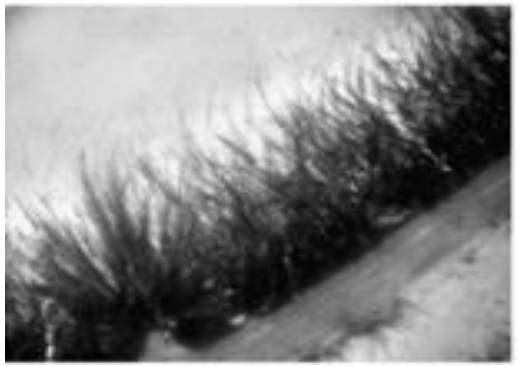
Replace rapid losses rapidly.

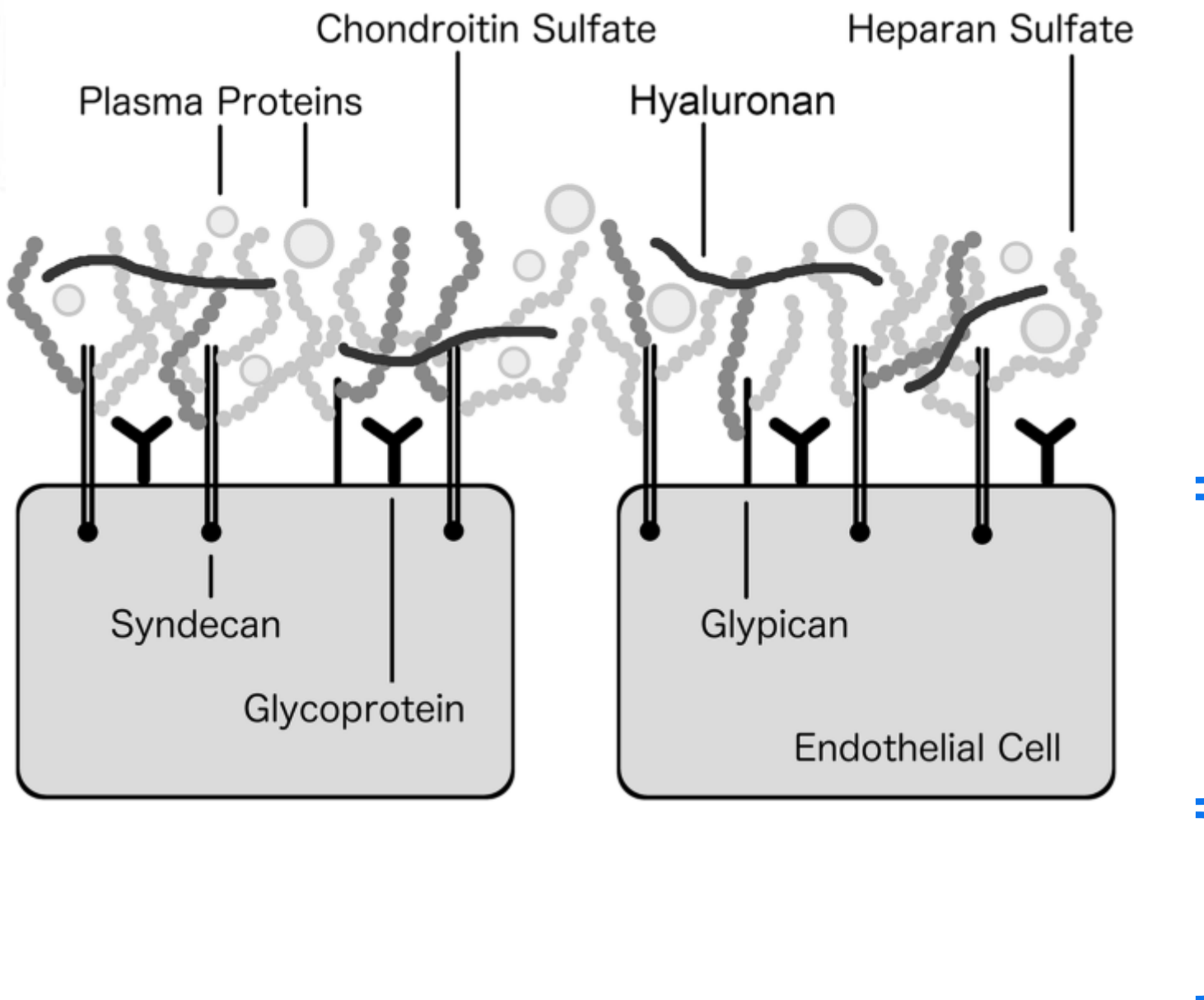
Replace gradual losses gradually.

Isotonic fluids move freely between fluid compartments.

Only ≈25% remains in intravascular space after 30 min.

Where they end up is what all the fuss is about…




Chondroitin Sulfate
Heparan Sulfate
Plasma Proteins
Hyaluronan
Syndecan
Glycoprotein
Glypican
Endothelial Cell
Lumen
Endothelium
Interstitium

EG damaged with inflammation from:

- SIRS/sepsis
- Trauma
- Ischemia-reperfusion (e.g., feline aortic thromboembolism)
- **Fluid resuscitation with large volume crystalloids**
- **Kidney disease is inflammatory**

- Results in:
  - Microcirculatory collapse (vasodilatory shock)
  - Hypercoagulability, thrombosis
  - **Capillary leakage → (interstitial) edema**
    - **Impaired oxygen diffusion (has further to go)**
    - **Increased intrarenal pressure → decreased GFR and renal blood flow**

Fluids are a drug.

Excess fluid most common drug overdose.

Increased interstitial fluid causes AKI and ↑ mortality.

Appropriate and not harmful fluid therapy:

- Restore volume fast IV, IO
- Rehydrate slower IV, SC, enteral if tube in place
- Keep up with ongoing losses (vomiting, diarrhea, extreme pu/pd)
  - 1 gm vomitus, diarrhea = 1 ml
- Provide maintenance
  - Dog 3 ml/kg/h; cat 2 ml/kg/h
- Use isotonic crystalloid with buffer
  - 0.9% NaCl acidifying, 15% drop in renal blood flow in 30 min
  - No synthetic colloids
- Weigh frequently q 6 then 8 then 12 h as improve
- No forced diuresis, e.g., 2-4x maintenance to eliminate toxins
- If creatinine, SDMA not improved within 12-24 h decrease or stop fluids

If azotemia worsens on IV fluids consider *decreasing* fluid rate.

Especially if total daily volume exceeds maintenance or if weight gain.

STOP fluids, +/- Lasix 1-4 mg/kg IV

We’ve probably all done this…

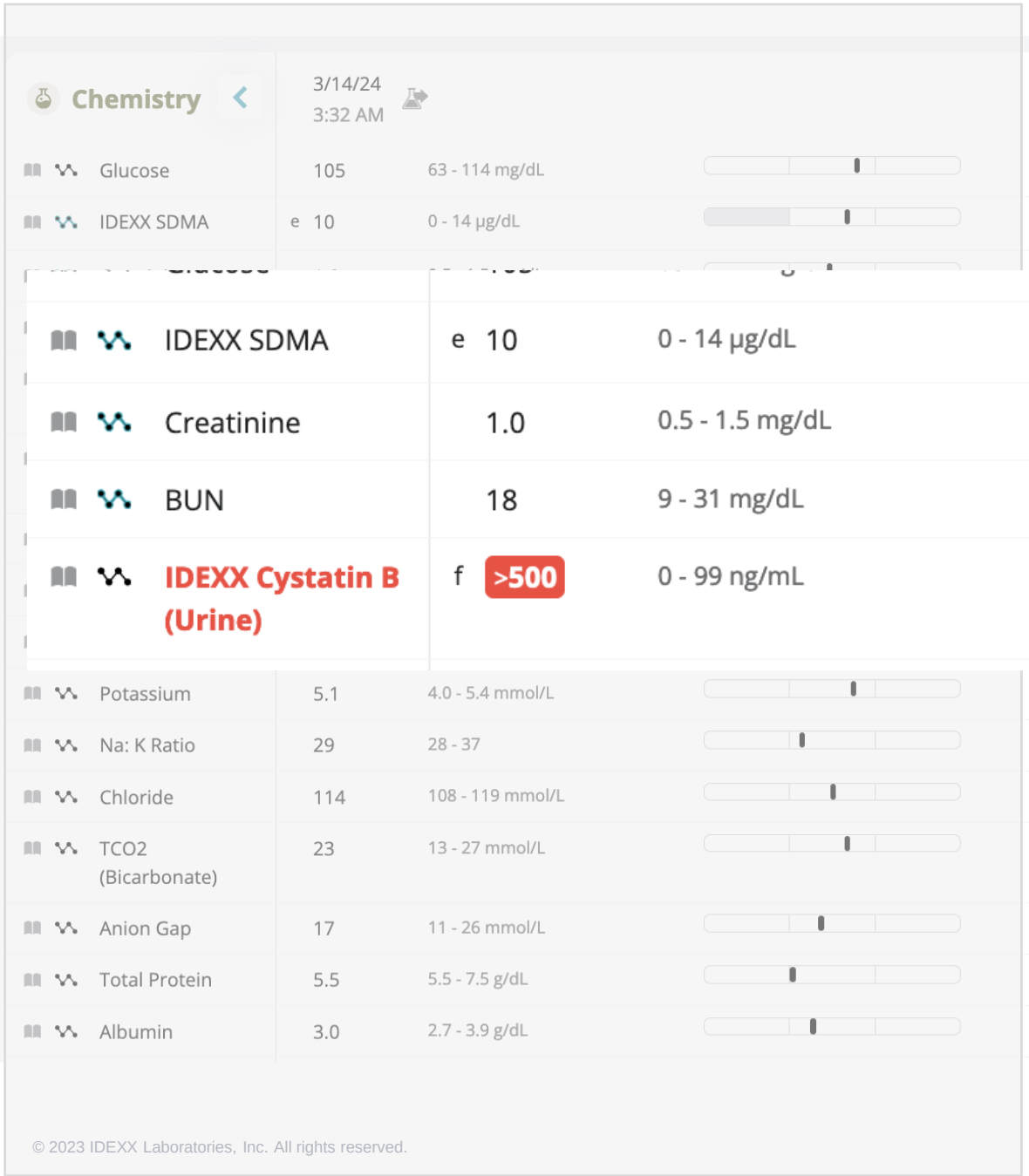
- Cat with CKD presents dehydrated, not eating, oliguric, azotemic
- We start IV fluids at 2-4 times maintenance (instead of doing math)
- After 24 hours hydration normal, urinating, still azotemic, not eating
- We continue and maybe increase IV fluids to drive SDMA and creatinine down (increase GFR) and improve appetite

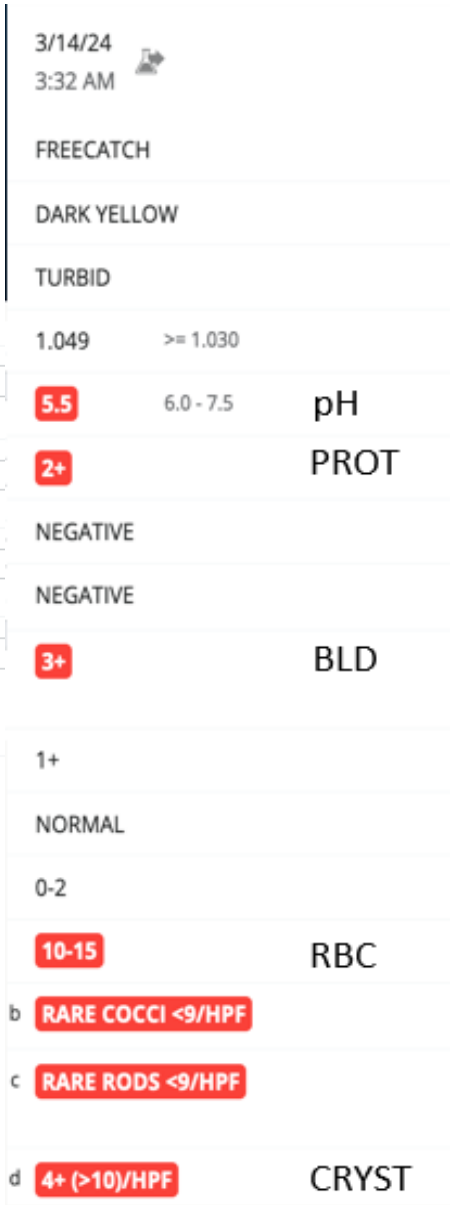
- Now we know better
  - Once hydrated no more than maintenance fluids, normalize K
  - Mirtazapine or capromorelin (Elura®)
  - Ideally NE or NG tube for hydration, nutrition

2-year-old male neutered Labrador

- Presenting complaint
  - Raisin ingestion sometime in past 8 hr (owner found empty box when returned from work)
  - No priors
  - Current on vaccination, parasite prophylaxis

- PE
  - Vitals normal
  - No significant findings





Treatment options for this dog

- Cystatin B increased = *active* tubular injury
- Not azotemic, USG normal
- Hydration normal

- **Induce vomiting and give 1 dose activated charcoal**
  - **Raisins in stomach up to 24 h, not rapidly broken down or absorbed by GI tract**
- Send home and recheck renal values and cystatin B in 2-3 d?
- SC fluids before sending home?
- Hospitalize for IV fluids at maintenance rate for 48 h?
- ~~Hospitalize for IV fluids at 2-4x maintenance for 48 h?~~

3 d later: treatment for possible UTI and IV fluids x 48 h hours

Chemistry

3/17/24
1:07 AM

IDEXX SDMA	a 8	0 - 14 µg/dL	
Creatinine	1.2	0.5 - 1.5 mg/dL	
BUN	26	9 - 31 mg/dL	
IDEXX Cystatin B (Urine)	b <50	0 - 99 ng/mL	
Ratio			
Phosphorus	5.1	2.5 - 6.1 mg/dL	
Calcium	9.5	8.4 - 11.8 mg/dL	
Sodium	148	142 - 152 mmol/L	
Potassium	5.1	4.0 - 5.4 mmol/L	
Na: K Ratio	29	28 - 37	
Chloride	114	108 - 119 mmol/L	
TCO2 (Bicarbonate)	25	13 - 27 mmol/L	
Anion Gap	14	11 - 26 mmol/L	
Total Protein	**5.1**	5.5 - 7.5 g/dL	
Albumin	2.7	2.7 - 3.9 g/dL	
Globulin	2.4	2.4 - 4.0 g/dL	

Urinalysis

3/17/24
1:07 AM

Collection	FREECATCH	
Color	DARK YELLOW	
Clarity	CLOUDY	
Specific Gravity	1.061	>= 1.030
pH	**5.5**	6.0 - 7.5
Urine Protein	**1+**	
Glucose	NEGATIVE	
Ketones	a TRACE	
Blood / Hemoglobin	**3+**	
Bilirubin	1+	
Urobilinogen	NORMAL	
White Blood Cells	0-2	
Red Blood Cells	**30-50**	
Bacteria	NONE SEEN	
Additional Bacteria		
Epithelial Cells	1+ (1-2)/HPF	
Mucus	NONE SEEN	
Casts	NONE SEEN	
Crystals	NONE SEEN	

Thank you!

Hypervolemia increases mortality.

True or False?

(Mis)conceptions with fluids for treating kidney disease

- Improve kidney function
- Speed elimination of exogenous toxins
- Reduce uremic toxins
- Fluid restriction - or no fluids - may be important with kidney disease

24 AAHA Fluid Tx Guide

Box 5: Common Fluid Overload Case Scenarios

1. ***Continued IV fluid therapy in a feline patient with renal disease.*** A cat is dehydrated, uremic, and anuric on presentation. Although IV fluid administration improves hydration status, uremia persists. IV fluids are continued with the misguided goal of improving GFR. However, no effective increase in GFR will occur no matter how much fluid this patient receives.
2. ***IV fluid therapy in a patient anesthetized for a lengthy procedure.*** A dog receives 10 mL/kg of fluids throughout a 6 hr procedure and develops respiratory distress during anesthetic recovery.
3. ***SC fluid therapy in a cat with occult or fulminant heart disease.*** A cat presents for evaluation of vomiting associated with malaise of congestive heart failure and is given SC fluids despite no evidence of dehydration.

Vigani – some AKI stuff to consider

- Hospital acquired nephrotoxic drugs, untreated hemodynamic instability, volume overload – our fault
- Type of resuscitation fluid – ongoing literature – no synthetic colloids (he says potential nephrotoxic particularly in inflammatory conditions), hi Cl drop renal blood flow shortly after administration (30 min drops 15%, no drop in balanced solution). Normal response to inc Cl in distal convoluted tubule
- Saline causes strong ion acidosis, selective extracellular acidosis, favoring efflux of K from intra to extracellular (other isotonic fluids don't)
- Prevent fluid overdose – most common drug overdose – cuz we rely on wrong markers
- Clinical status inadequate for hydration status – equal chance of saying 5% dehydration as 5% overhydration

Vigani – some AKI stuff to consider

- We consistently over estimate degree of dehydration
- Increase extracellular water CAUSES AKI – and kills those that already have it
- Positive water balance predictor of mortality
- Fluid responsive AKI should respond in a few hours, don't over do fluids
- Fluids – what they need and no more… correct hemodynamic instability. Once you achieve that, maintain it. If obvious evidence that were far above intake – dehydration (parvo) – rehydrate. If you have restored perfusion and circulation – normotensive and normovolemic – maintain for 12 h. Then 2 ml/kg/hr cat, 3 ml/kg/hr dog maintenance plus keep up losses.
- If after 12 hr no change in creatinine – non fluid responsive AKI – stop fluids.
- He doesn't use u caths in ICU to monitor urine out – monitors weight 4, 3, 2x / d the better they get
- Hosp acquired AKI dogs 9% - often we cause – fluid overload

Protecting endothelial glycocalyx in practice:
Consider fluid type and volume.

- Much yet to learn
- Mostly an issue with sepsis and trauma?
- Avoid excess crystalloids
  - Degrade EG more than protein-containing fluids
- Consider synthetic colloids in rare cases
  - May limit overall fluid volume, less crystalloids required
- Give fresh frozen plasma (or albumin?) early in resuscitation
  - Replaces lost components of EG – albumin, fibrinogen, antithrombin, syndecam-1

Assume all inappetent cats are 5% dehydrated…

Estimated dehydration	Physical examination reveals:
<5%	Not detectable
5-6%	Dry, ‘tacky’ mucous membranes
6-8%	Mild decrease skin turgor
8-10%	Obvious decrease skin turgor, retracted globes
10-12%	Persistent skin tenting, dull corneas, hypovolemia
>12%	Death due to hypovolemic shock

Formula: % dehydration as decimal x BW (kg) x 1000 = ml to administer over 4-24 hr

e.g., 5% dehydrated, 5 kg cat

0.05 x 5 = 0.25 L x 1000 = 250 ml.

CKD fluid therapy: less may be more

- *Replacement* crystalloids only for existing and ongoing losses
  - Mimic plasma composition
  - Assume and correct 5% dehydration if inappetence
  - Correct electrolyte abnormalities (hypokalemia)
  - No forced diuresis
  - E.g., LRs, Normosol-R, Plasma-Lyte A and 148, 0.9% NaCl with no additives
- *Maintenance* crystalloids once volume, hydration normal
  - Restore total body water
  - Meet sensible/insensible loss from urine, feces, sweat, respiration
  - E.g., 0.45% NaCl w/ or w/o 2.5% dextrose, Plasma-lyte 56, Normosol M
  - Homemade, 1:1 replacement fluid with 5% dextrose

} KCl 20 mEq/L

- Monitor body weight
  - Know baseline, precise scale, take into account IV catheters, bandages, e collars, etc.
  - 5% BW gain minimum threshold for clinical signs (chemosis, mild interstitial edema, regurg)
  - 10% BW gain pulmonary edema, body cavity effusion

IV fluids after nephrotoxin exposure: harmful or helpful?

- NSAIDs, lily (cat), grapes (dog)
- Fluids at 2-3x maintenance 2-3 d to induce diuresis standard recommendation
  - Diuresis may not increase toxin excretion or prevent tubular damage
  - Increases ANP which can degrade EG
  - Kidney interstitial edema → ↑ intraparenchymal pressure (rigid capsule) – ↓ perfusion/GFR
- Excessive fluid may *contribute* to AKI rather than prevent it.
- No mandatory hospitalization for IV fluids
- Use basic principles
  - Correct dehydration/hypovolemia, replace losses from V/D, maintenance if inappetence
  - Discharge when eating and drinking normally w/o excessive losses

All cats with CKD benefit from fluid therapy.
True or false?

FALSE!

No evidence that SC fluids in hydrated patients is helpful.

Be aware of ‘occult’ dehydration, <5% body weight.

24 AAHA Fluid Tx Guide

- Using replacement fluids as long term main fluids may lead to hyperNa and hypoK – no evidence that using replacement for maint has short term detrimental effects…but know what you're doing
- Total fluid requirement = replacement + rehydration (including ongoing losses) + maintenance

24WSAVA Hem Shock Boyd

- PCV 30 cut off – above more crystalloid, below lower volume
- He said Hartmanns
- Clear fluids = isotonic crystalloid, hypertonic crystalloids, synthetic colloid
- LRs/Hartmann – buffered, sm amt Ca
- P-148/Norm-R – buffer, no Ca, actetate vasodilatory
- 0.9 NaCl – acidifying, no advantages
- Ca-free crystalloid during resusc can cause low Ca
- Hypertonic cryst – no evid in vivo of hypocoag, in vitro studies show some effect of hemodilution – esp in lg dogs or TBI, hi Cl fluid so promotes acidosis
- Synthetic colloids – hydroxyethel starch or gelatin – strong evidence that worsen coagulopathy via viscoelastic tests (decreases clot strength)

24 AAHA Fluid Tx Guide

- Hypovolemia = reduced vol of circulating blood resulting in dec tissue perfusion (water and lytes lost – as w dehydration (lose more than take in).
- Dogs 15-20 ml/kg, cat 5-10 ml/kg IV over 15-30 min
- Correct hypovol rapidly IV or IO
- Correct dehyd 12-24 hr, SQ or IV or enteral
- Fluid def in mL = BW kg x % dehyd (as decimal)

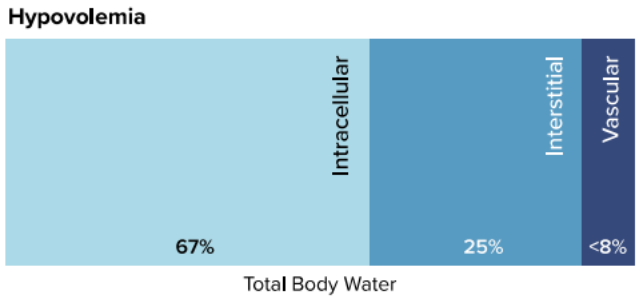


FIGURE 3

Hypovolemia results in a decreased volume within the vascular space. Acute hypovolemia primarily affects this compartment. As the severity and duration of hypovolemia persist, it can affect other compartments as well.

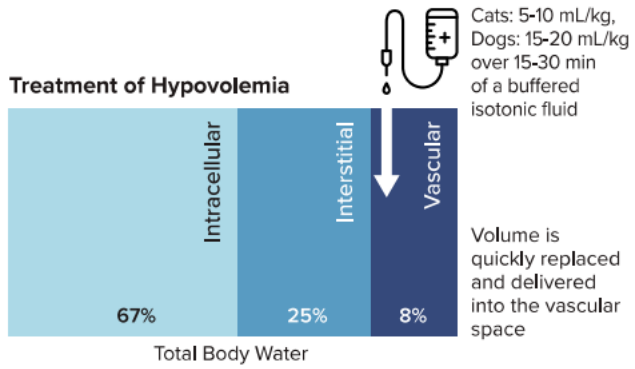


FIGURE 4

Treatment of hypovolemia requires rapidly delivering fluid into the vascular space to restore the effective circulating volume.

AKI specialist Webinar – Alessio Vigani

- Creatinine generation rate not consistent – drops by 50% in septic humans, similar in dogs/cats probably
- Thus don’t see creat inc even if significant decrease in GFR
- He says creatinine soley eliminated by GFR – not excreted or reabsorbed – BUT generation rate not consistent.
- Also – in some septic patients muscle activity/creat generation rate low – so just as likely to see decrease in creat as increase in kidney dz
- Creatinine decrease same predictive risk of mortality as creatinine increase
- Functional markers delay 2 days after injury markers
- Thus v small increases in creat should get you v worried – exponential increase in creat masked by decreased generation
- The sicker the patient, the more significant a smaller increase in creat

AKI specialist Webinar – Alessio Vigani

- 99.8% reabsorption of filtrate done at tubules
- If reabsorptive function decreases – will remain polyuric
- Thus urine output even worse than creat as GFR predictor
- Urine output has no correlation with GFR
- But trending / tracking of urine output valuable – persistent drop in production for 6 hr is predictive of creat increase in hosp patients.
- But our patients have endocrine alteration or intervention the effects normal reabsorption – interfering with ADH – so correlation drops
- Inappropriate ADH release – ADH increase post op/general anesthesia – affects urine output independent of tubular function
- Lepto – high high urine output with high creatinine – thus urine output not a proxy for function

AKI specialist Webinar – Alessio Vigani

- 4 ml/kg/h of urine production even if lost 99% GFR – polyuria possible even with 1% GFR
- W 99% loss GFR no way good concentration / reabsorption ability
- 2 ml/kg/h even if lost only half of normal GFR – definition of pu
- Other functional markers – similar to creatinine – he says no advantage over creat
- Advantage of SDMA – earlier development of CKD in cats, largely independent of mm mass (better renal function indicator in CKD as BCS becomes impaired)
- Renal blood flow increases in sepsis though function decreases
- Hospital acquired nephrotoxic drugs, untreated hemodynamic instability, volume overload – our fault
- Around 3% AKI postop – renal blood shunted from cortex to medulla - normally ischemia associated

AKI specialist Webinar – Alessio Vigani

- Attempt to maintain O2 support to areas w highest extraction rate – med thick ascending loop extraction rate normally is 80% - reason flow is shunted there
- Type of resuscitation fluid – ongoing literature – no synthetic colloids (he says potential nephrotoxic particularly in inflammatory conditions), hi Cl drop renal blood flow shortly after administration (30 min drops 15%, no drop in balanced solution). Normal response to inc Cl in distal convoluted tubule
- He found no diff in type of fluid re incidence of AKI
- Saline causes strong ion acidosis, selective extracellular acidosis, favoring efflux of K from intra to extracellular (other isotonic fluids don't)
- Prevent fluid overdose – most common drug overdose – cuz we rely on wrong markers
- Clinical status inadequate for hydration status – equal chance of saying 5% dehydration as 5% overhydration

AKI specialist Webinar – Alessio Vigani

- We consistently over estimate degree of dehydration
- Increase extracellular water CAUSES AKI – and kills those that already have it
- Positive water balance predictor of mortality
- Need higher Lasix dose bc tubular secretion required to work (transporters effected, organic anions/ab's accumulate, same transporter as Lasix – need much higher dose for same degree of natriuresis – so text dose needs to be 6-8 mg/kg for same diuretic effect as normal patient.
- Fluid responsive AKI should respond in a few hours, don't over do fluids
- Arginine avoid in AKI patients – precursor of NO – vasodilates – decreased GFR, contraindicated in sepsis (vasoplegia) – OVERsupplementation (minimum requirements fine)

AKI specialist Webinar – Alessio Vigani

- Cys b cats – v little data
- Fluids – what they need and no more… correct hemodynamic instability. Once you achieve that, maintain it. If obvious evidence that were far above intake – dehydration (parvo) – rehydrate. If you have restored perfusion and circulation – normotensive and normovolemic – maintain for 12 h. Then 2 ml/kg/hr cat, 3 ml/kg/hr dog maintenance plus keep up losses.
- If after 12 hr no change in creatinine – non fluid responsive AKI – stop fluids.
- AKI diet – liquid diet via feeding tube – regular diet, recovery diet unless can't tolerate fat causing GI signs. Nasogastric for CRI of diet – 100 RER, no multiplier, if don't tolerate give fraction of RER they tolerate. Less nausea with decompression, trickling if dilated pylorus still possible. If not – trophic feeding 10-15% CRI. Only cisapride for promotility – metoclopramide no good in his hand.

AKI specialist Webinar – Alessio Vigani

- >1 kcal/ml allows less volume – concentrated diet
- AKI w CHF (cardiorenal syndrome) – extracorporeal therapy – fluid removal – worse than CHF who develops pyelonephritis
- Monitor volume – hands, eyes, stethoscope, pocus (prune bad, mushroom good, atrium 2-3 times size volume overloaded) – not crazy about volume via ultrasound in awake patients
- Euvolemia is clinical call – lactate normal, not tachycardiac, CRT, etc…
- Evaluated renal recovery – same parameters as for dx – creatinine, clinical response…rise in urine output before drop in serum creatinine, med functionality returns beforer glomerular filtration
- He doesn’t use u caths in ICU to monitor urine out – monitors weight 4, 3, 2x / d the better they get

AKI Alessi Vigani

- Small inc in creat associated with worse prognosis
- AKI mortality plateaus at grade 3 – creat >4, ie 5 is as bad as 10
- Long term mortality higher after AKI in hosp compared to critical illness unrelated to kidney
- IRIS grade survival between grades unknown, known for AKI v no AKI
- He says no need to go about grade 3
- AKI 1-3 less likely to survive to discharge JVECC 2011
- Acute on chronic – survival less if CKD prior to AKI – talk to owners – 50% survival at 180 days (equal to HSA)
- AKI independent predictor of mortality (not bystander)
- AKI**nsufficiency** if we use functional markers (not injury)

AKI specialist Webinar – Alessio Vigani

- Prognosis – serial cys b for prognosis? -- he doesn't know but interested in finding out.
- Once creat inc we know insufficiency is present but don't if injury just occurred or occurred prior, fxn'al markers lagging indicators unless damage is massive
- Actual damage occurs up to 48 hr prior to inc serum creat
- Always a delay if use functional markers to detect injury
- Biomarker of injury – damage of cells that constitute functional tissue of organ we can id early (right away)
- Creat generation rate decreases – drops 50% in sepsis – with illness
- So don't see increase even w sig alteration in GFR b/c generation by body proportionally decreased as decreased GFR can't see inc (experimental animals, and people)

AKI specialist Webinar – Alessio Vigani

- Less metabolic fxn in muscle of sick people (presume animals)
- In crit illness a drop in creat same affect on risk of mortality as increase in creatinine
- Thus small inc in creat in critical illness could indicate v severe dec fxn
- Degree of inc creat does not correlate with potential reversibility – that depends on cause of injury
- Normal urine output does not exclude severe renal injury – ie lepto – profound urine output, sky high creat, lungs full of hemorrhage/edema
- Patient w 1% GFR can be polyuric
- IF you dx AKI w functional markers you're 2 days late
- Clinical phases – early recognition of extension phase is where we are, need to id onset with injury markers

AKI specialist Webinar – Alessio Vigani

- NGAL same in normal dogs as w AKI
- NGAL:cr ratio not different from NGAL concentration – no benefit in it's specificity for AKI
- Septic shock – NGAL predictive at 24 hr of development of AKI however many had sig inc in NGAL despite not developing inc creat over 5 days (histopath did not correlate at all w NGAL or creat)
- Cys C ubiquitous all epi cells in body – surrogate of filtration like creat – urine levels due to filtration of increased serum levels
- Renal Cys B specific to tubule cells
- Healthy below 25, confirmed AKI high v controls, clusterin behaves like cys B
- No correlation between cys B and grade of AKI
- Best use in AKI of cys b would be to predict/anticipate rise in creatinine – eg would avoid nephrotoxic drugs (ag, iodinated contrast, NSAIDS), monitor more closely - unknown

AKI specialist Webinar – Alessio Vigani

- Ibuprofen in 2 cats - sky high creats and also severe glomerular component – resolved w rez of creatinine (10 d) -- UPC 25 – 1. Protein losses were all glomerular (albumin)
- Hosp acquired AKI dogs 9% - often we cause – fluid overload
- Goal of therapy – optimize hemodynamics
- Addisonian – std treatment – w/in 12 hr creat will be normal
- But what about fluid-responsive azotemia - creat not where we want it within 12 hr we keep going w fluids
- Fluid-responsive azotemia – will see response w'in hours
- RBF drops by 15% if excess Cl – normal response w Inc cl in distal convoluted tubule – in clinical trial buffered crystalloid v saline no difference in AKI – probably not that important

AKI specialist Webinar – Alessio Vigani

- But inc chloride does cause strong ion acidosis – extracellular acidosis, efflux of K into extracellular space
- Clinical assessment of hydration status inaccurate – even dehydrated v overhydrated difficult to distinguish – equally likely to call it 5% dry v 5% overhydrated using same scale.
- Clinical assessment consistently overestimates the degree of dehydration
- Mortality proportional to degree of increase of extracellular water
- Overload causes AKI and increases mortality in patients that have it
- Positive fluid balance negative prognostic indicator – dialysis or not
- You don’t flush a clogged toilet
- Volume overload increases risk of mortality more than sepsis with AKI

AKI specialist Webinar – Alessio Vigani

- Lasix only drug that increases O2 partial pressure in medulla (not mannitol) – area where tubular necrosis occurs – sparing energy from tubular system
- May be nephroprotective
- Tub secretion required for Lasix to work, other organic anions accumulate (sulfate) – transported through same transporter (blocked) so much higher dose Lasix require for equal degree of natriuresis / diuresis
- Thus test dose of Lasix – 6-8 mg/kg (same effect as in normal patient)
- When to stop fluids –
- He rarely measures UO – relies on BW
- Don’t know if cys b predictive of later decrease in function or anticipatory as improvement of GFR 2 days later (if cys b drops does it mean creat will come down so we can celebrate)

Fluids are a drug.

Overdosing fluids is as harmful as underdosing.

Fluid therapy for kidney disease

- Does not improve kidney function
  - May increase urine *volume*
  - Forced diuresis is *over*
- Excess can *cause or exacerbate* kidney damage
  - Endothelial glycocalyx degradation
  - Interstitial edema

- Apply basic principles
  - Correct dehydration
  - Restore volume
  - Replace losses from V/D
  - Provide maintenance if inappetence

Assume all inappetent cats are 5% dehydrated…and correct

Estimated dehydration	Physical examination reveals:
<5%	Not detectable
5-6%	Dry, ‘tacky’ mucous membranes
6-8%	Mild decrease skin turgor
8-10%	Obvious decrease skin turgor, retracted globes
10-12%	Persistent skin tenting, dull corneas, hypovolemia
>12%	Death due to hypovolemic shock

Formula: % dehydration as decimal x BW (kg) x 1000 = ml to administer over 4-24 hr

e.g., 5% dehydrated, 5 kg cat

0.05 x 5 = 0.25 L x 1000 = 250 ml.

IV fluids after nephrotoxin exposure: harmful or helpful?

- NSAIDs, lily (cat), grapes (dog)
- Fluids at 2-3x maintenance 2-3 d to induce diuresis standard recommendation
  - Diuresis may not increase toxin excretion or prevent tubular damage
  - Increases ANP which can degrade EG
  - Kidney interstitial edema → ↑ intraparenchymal pressure (rigid capsule) – ↓ perfusion/GFR
- Excessive fluid may *contribute* to AKI rather than prevent it.
- No mandatory hospitalization for IV fluids
- Use basic principles
  - Correct dehydration/hypovolemia, replace losses from V/D, maintenance if inappetence
  - Discharge when eating and drinking normally w/o excessive losses

If azotemia worsens on IV fluids consider *decreasing* fluid rate.

Especially if total daily volume exceeds maintenance or if weight gain.

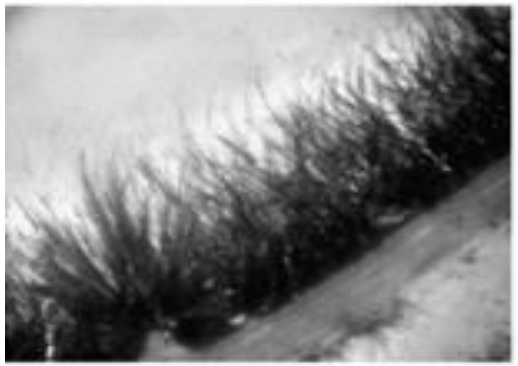
STOP fluids, +/- Lasix 1-4 mg/kg IV

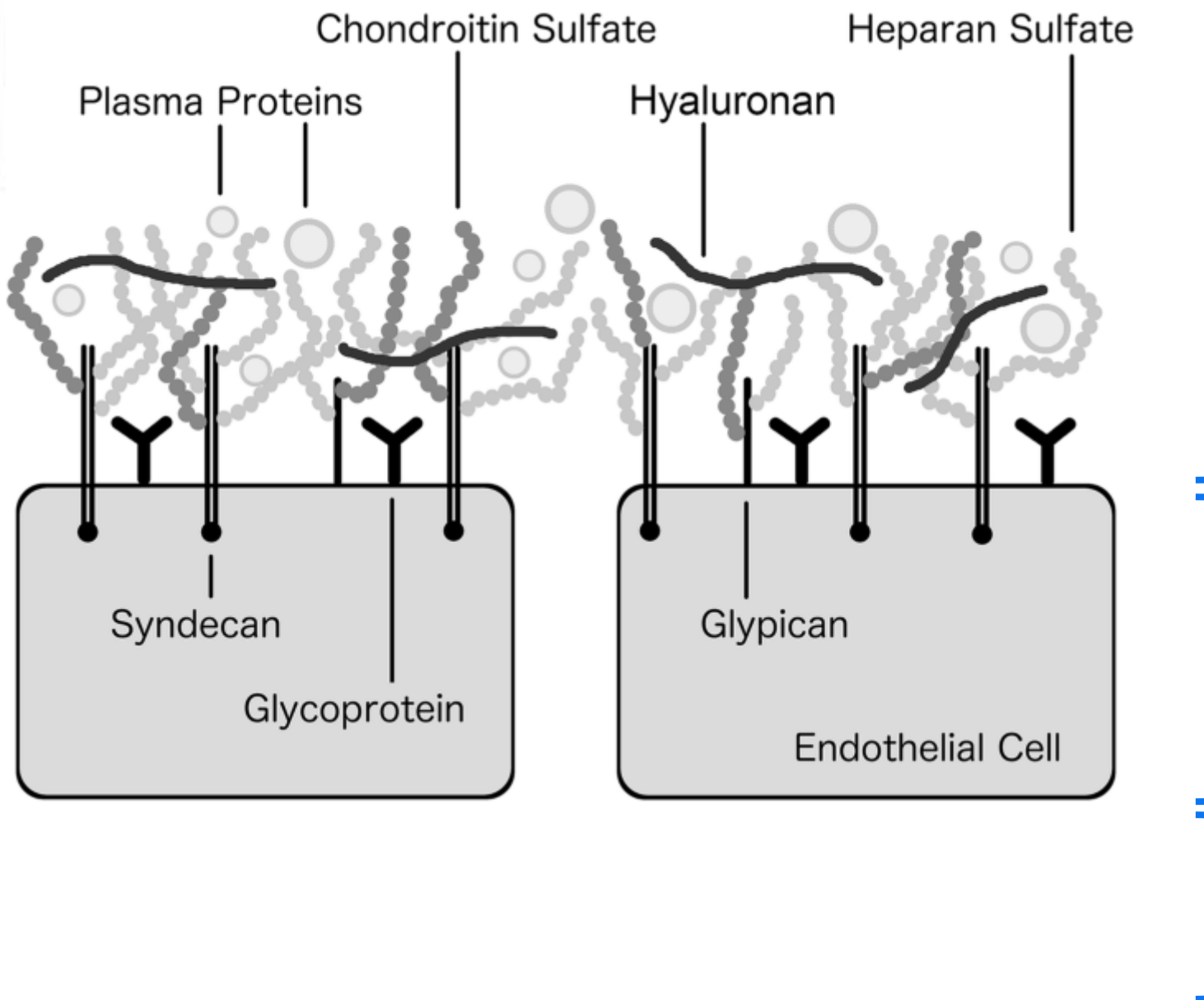
Fluids are a drug – avoid overdose.

Rethinking fluid therapy for kidney disease

- Fluids do not improve kidney function
  - May increase urine *volume*
- Excess more likely to cause harm than improve kidney function
  - Endothelial glycocalyx degradation
  - Interstitial edema
- Forced diuresis is over

- Apply basic principles
  - Correct dehydration
  - Restore volume
  - Replace ongoing losses, e.g., vomiting, diarrhea…
  - Provide maintenance until eating and drinking normally




Chondroitin Sulfate
Heparan Sulfate
Plasma Proteins
Hyaluronan
Syndecan
Glycoprotein
Glypican
Endothelial Cell
Lumen
Endothelium
Interstitium

IV fluids for AKI

- Avoid excess fluid
  - Decreased GFR and RBF due to increased renal interstitial pressure
  - Tissue hypoxia due to impaired O2 diffusion
- Aim for euvolemia and euhydration
  - CRT, membranes, HR, pulses, mentation, lactate, base excess = perfusion parameters
- Balanced crystalloid with calcium
  - LRs, Hartmann’s
  - Normosol-R, Plasma-Lyte 148 no Ca, acetate vasodilatory (?)
- Not 0.9% NaCl even if hyperkalemia
  - Acidifying
  - Afferent arteriolar constriction

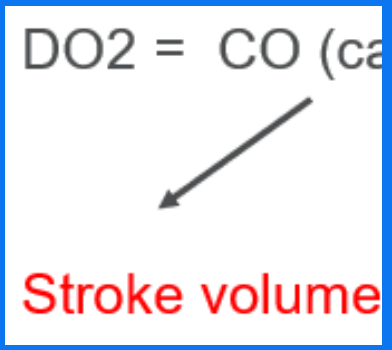
IV fluids for AKI, cont'd.

- Correct dehydration in 4-6 hr
  - Body weight (kg) x estimated % dehydration x 1000 = fluid deficit in milliliters
- Provide maintenance and keep up with ongoing losses
  - 44-66 ml/kg/d
- Switch to lower sodium fluid for longer maintenance therapy
  - LRs half-strength with 2.5% dextrose, 0.45% NaCl in 2.5% dextrose
  - Home made: 1:1 dilution of LRs and 0.5% dextrose
- Monitor body weight
  - Know baseline, precise scale, take into account IV catheters, bandages, e collars, etc.
  - 5% BW gain minimum threshold for clinical signs (chemosis, mild interstitial edema, regurgitation)
  - 10% BW gain pulmonary edema, body cavity effusion

IV fluids after nephrotoxin exposure: help or hurt?

- NSAIDs, lily (cat), grapes (dog)
- Fluids at 2-3x maintenance 2-3 d to induce diuresis standard recommendation
  - No evidence that increases toxin excretion or prevents tubular damage
  - Increases ANP which can degrade EG
  - Kidney interstitial edema → ↑ intraparenchymal pressure (rigid capsule) – ↓ perfusion/GFR
- Excessive fluid may *contribute* to AKI rather than prevent it.
- No mandatory hospitalization for IV fluids
- Use basic principles
  - Correct dehydration/hypovolemia, replace losses from V/D, maintenance if inappetence
  - Discharge when eating and drinking normally w/o excessive losses

What's new in fluid therapy?

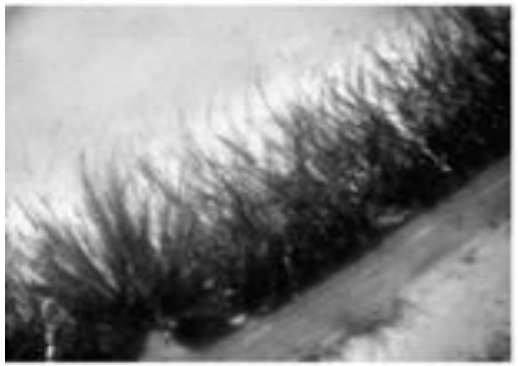


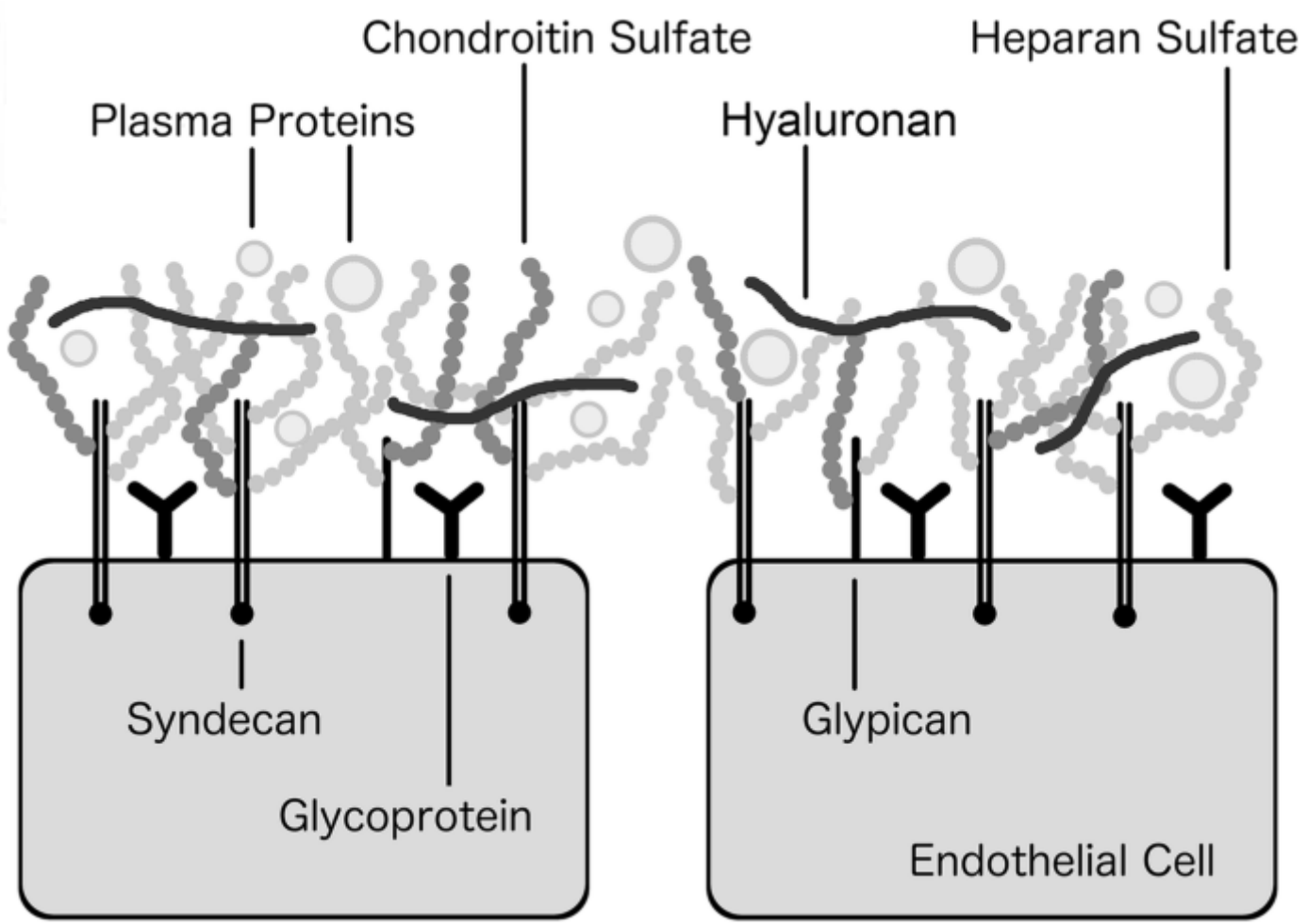
H*yper*volemia increases complications, morbidity, and mortality.

Filtration organs affected first – gut, kidneys.

First signs might be regurgitation, worsening kidney function.

Protect the endothelial glycocalyx.





EG damaged by:

- Sepsis/SIRS
- Trauma
- Ischemia-reperfusion (e.g., feline aortic thromboembolism)
- *Fluid resuscitation with larger volume crystalloids and rapid rate of infusion*
  - *Even given to healthy dogs under anesthesia at 5-10 ml/kg*

- Results in:
- Microcirculatory collapse (vasodilatory shock)
- **Tissue edema**
- Proinflammatory state
- Hypercoagulability, thrombosis

Basic principles of fluid therapy to avoid hypervolemia:

- Restore normal blood volume (resuscitation) within 30-60 min
- Correct dehydration over 4-24 hr
- Keep up with ongoing losses (vomiting, diarrhea, polyuria)
- Provide maintenance fluids until eating and drinking normally

- **THEN STOP**

- Weigh frequently – precise gram scale
  - 5% gain → consider adjusting
  - 10% gain → volume overload
- Watch for regurgitation, worsening kidney function, respiratory signs

Fluid therapy revamp: less may be more.

- Fluids are drugs – avoid overdose
- Restore volume, hydration, ongoing losses, maintenance – then stop
- LRS almost always preferred initial fluid – has buffer, Ca, anti-inflammatory
  - Normosol-R, Plasmalyte-148 – no Ca, acetate vasodilatory(?), magnesium
  - 0.9% NaCl – acidifying, high chloride causes renal vasoconstriction
- Hypertonic saline if critical especially large dog, traumatic brain injury…
- Use natural colloid, i.e., plasma, canine-specific albumin
- Avoid synthetic colloids unless no other options
- **Switch to maintenance fluid once resuscitated**
  - **0.45% NaCl in 2.5% dextrose, 1:1 dilution LRs with D5W, K supplementation prn**

Which fluids?

- LRS almost always preferred initial fluid – has buffer, Ca, anti-inflammatory
  - Normosol-R, Plasmalyte-148 – no Ca, acetate vasodilatory(?), magnesium
  - 0.9% NaCl – acidifying, high chloride causes renal vasoconstriction
- Hypertonic saline if critical especially large dog, traumatic brain injury…
- Use natural colloid, i.e., plasma, canine-specific albumin
- Avoid synthetic colloids unless no other options
- **Switch to maintenance fluid once resuscitated**
  - **0.45% NaCl in 2.5% dextrose, 1:1 dilution LRs with D5W, K supplementation prn**

EG-sparing resuscitation: low and slow

Isotonic crystalloid 10-15 ml/kg dog, 5-10 ml/kg cat x 2-3
(over 15-30 minutes)

Hypertonic saline 7.2% 4 ml/kg once if critical

Then fresh frozen plasma, canine specific albumin
FFP 10-20 ml/kg
Canine-specific albumin 16%, 1 g/kg

Hypervolemia causes AKI and increases morality in those that have it.

If azotemia worsens on IV fluids consider *decreasing* fluid rate.

Especially if volume given exceeds maintenance or if weight gain.

STOP fluids, +/- Lasix 1-4 mg/kg IV

Treat life-threatening hyperkalemia

- Hypothermia *and* bradycardia indications to treat
- 10% calcium gluconate
  - Cardioprotective, buys time
  - 0.5-1.5 ml/kg over 10-15 minutes
- Regular insulin and 50% dextrose
  - ¼ U/kg with 2 gm 50% dextrose/U of insulin
- HCO3 rarely necessary
  - Consider if pH<7.1, HCO3<12 mmol/L
  - BW (kg) x 0.3 x (24 – HCO3) = mEq HCO3 deficit
  - Give ½ deficit IV over 30 minutes
  - If pH not >7.2 remainder in IV fluids over 2-4 hr

Assume all inappetent cats are 5% dehydrated…and correct

Estimated dehydration	Physical examination reveals:
<5%	Not detectable
5-6%	Dry, ‘tacky’ mucous membranes
6-8%	Mild decrease skin turgor
8-10%	Obvious decrease skin turgor, retracted globes
10-12%	Persistent skin tenting, dull corneas, hypovolemia
>12%	Death due to hypovolemic shock

Formula: % dehydration as decimal x BW (kg) x 1000 = ml to administer over 4-24 hr

e.g., 5% dehydrated, 5 kg cat

0.05 x 5 = 0.25 L x 1000 = 250 ml.

Bottom line:

- Consider pancreatitis in any dog or cat with:
  - Chronic or intermittent GI or nonspecific signs of illness
  - Acute vomiting, lethargy, fever/hypothermia, pain
  - Unexplained increase in liver enzymes
- Assume pain present with any form of pancreatitis
- Palpable abdominal mass in ≈25% cats with pancreatitis

Dog or cat?

No breed, age, or sex predisposition.

Risk factors for acute pancreatitis in dogs: updated.

No common risk factors in cats.

Traditional

- Yorkie, Min Schnauzer, Poodle
- Breed predisposition / genetic
- Overweight
- Dietary indiscretion
- High fat diet
- Hypertriglyceridemia
- Endocrine diseases
- Drugs
- Chemotherapeutics
- Hypercalcemia

Updated

- All small breeds equal risk
- No proven genetics for pancreatitis
- Overweight 1.3x risk
- Garbage 13.2 OR (unusual 6.1, scraps 2.2)
- Keto (57% fat), struvite dissolution (26% fat)
- ≈850 5x risk (<500 no increased risk)
- Diabetes mellitus (12.4x risk)
- KBr *and* phenobarbital
- Azathioprine, L-asparaginase
- Ionized hypercalcemia

Pancreatitis can develop in cats with:

- Recent anesthesia 6.4%
- Trauma 3.8%
- Poor hemodynamics
  - CHF, urethral obstruction, GI foreign body 2.5%
- Organophosphate toxicity 1%

Maintain perfusion:
IV fluids, oxygen, blood pressure support.

- Idiopathic in 136/157 cats (87%)

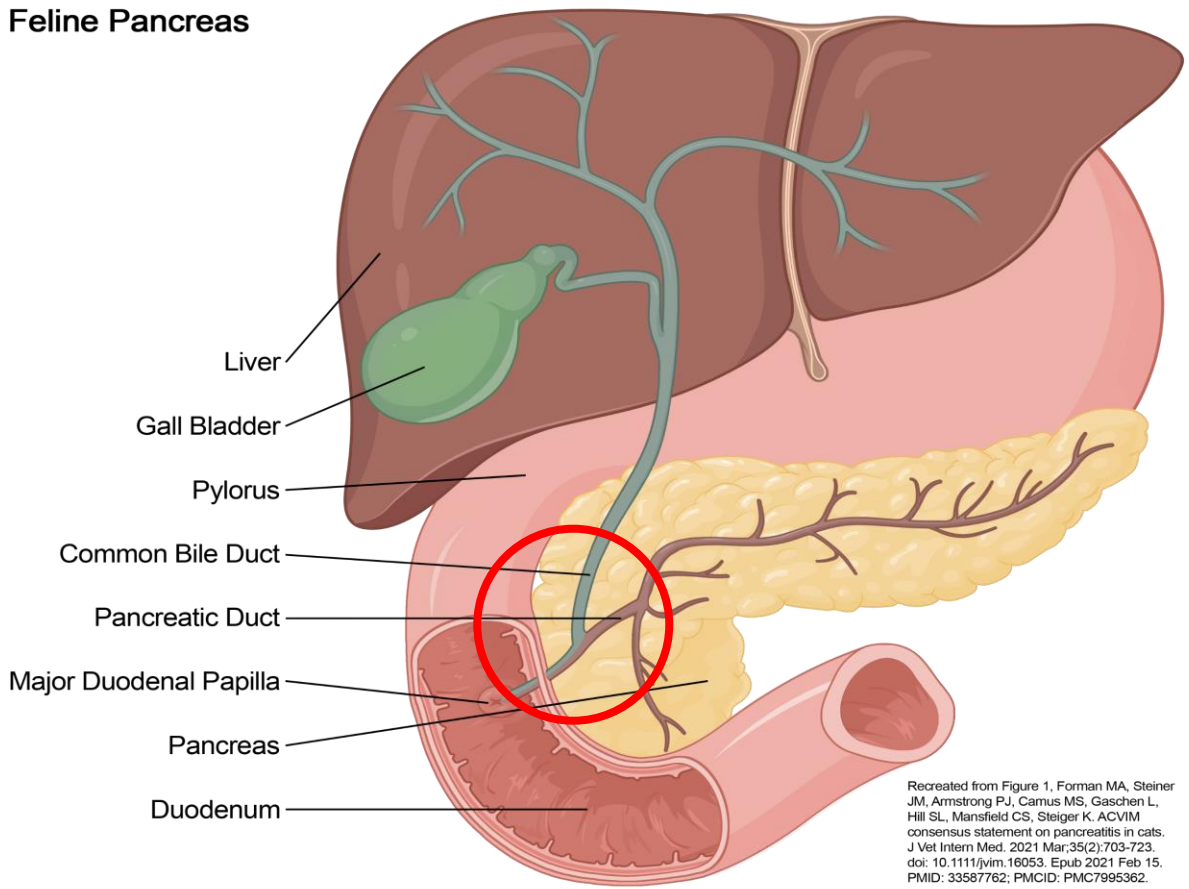
Nivy R, Kaplanov A, Kuzi S, et al. A retrospective study of 157 hospitalized cats with pancreatitis in a tertiary care center. Clinical, imaging and laboratory findings, potential prognostic markers and outcome. J Vet Intern Med 2018:32:1874-1885.

Dog or cat?

Concurrent GI and liver disease common.

2/3+ of cats with pancreatitis have concurrent illness

It’s the ducts.



Recreated from Figure 1, Forman MA, Steiner JM, Armstrong PJ, Camus MS, Gaschen L, Hill SL, Mansfield CS, Steiger K. ACVIM consensus statement on pancreatitis in cats. J Vet Intern Med. 2021 Mar;35(2):703-723. doi: 10.1111/jvim.16053. Epub 2021 Feb 15. PMID: 33587762; PMCID: PMC7995362.

- **Cholangiohepatitis**
- **Chronic enteropathy**
- **Biaditis / triaditis**
- **Hepatic lipidosis**
- **Diabetes mellitus**
  - **SGLT2 inhibitors contraindicated**

Dog or cat?

Combination of clinical findings, pancreatic lipase immunoreactivity (PLI) and ultrasound provides most reliable diagnosis.

Diagnostic criteria for acute pancreatitis in literature…

- 2 or more of the following clinical signs:
  - Abdominal pain, diarrhea, vomiting, anorexia/hyporexia
- Abdominal ultrasound reveals no other cause of signs
- Increased SNAP cPL test

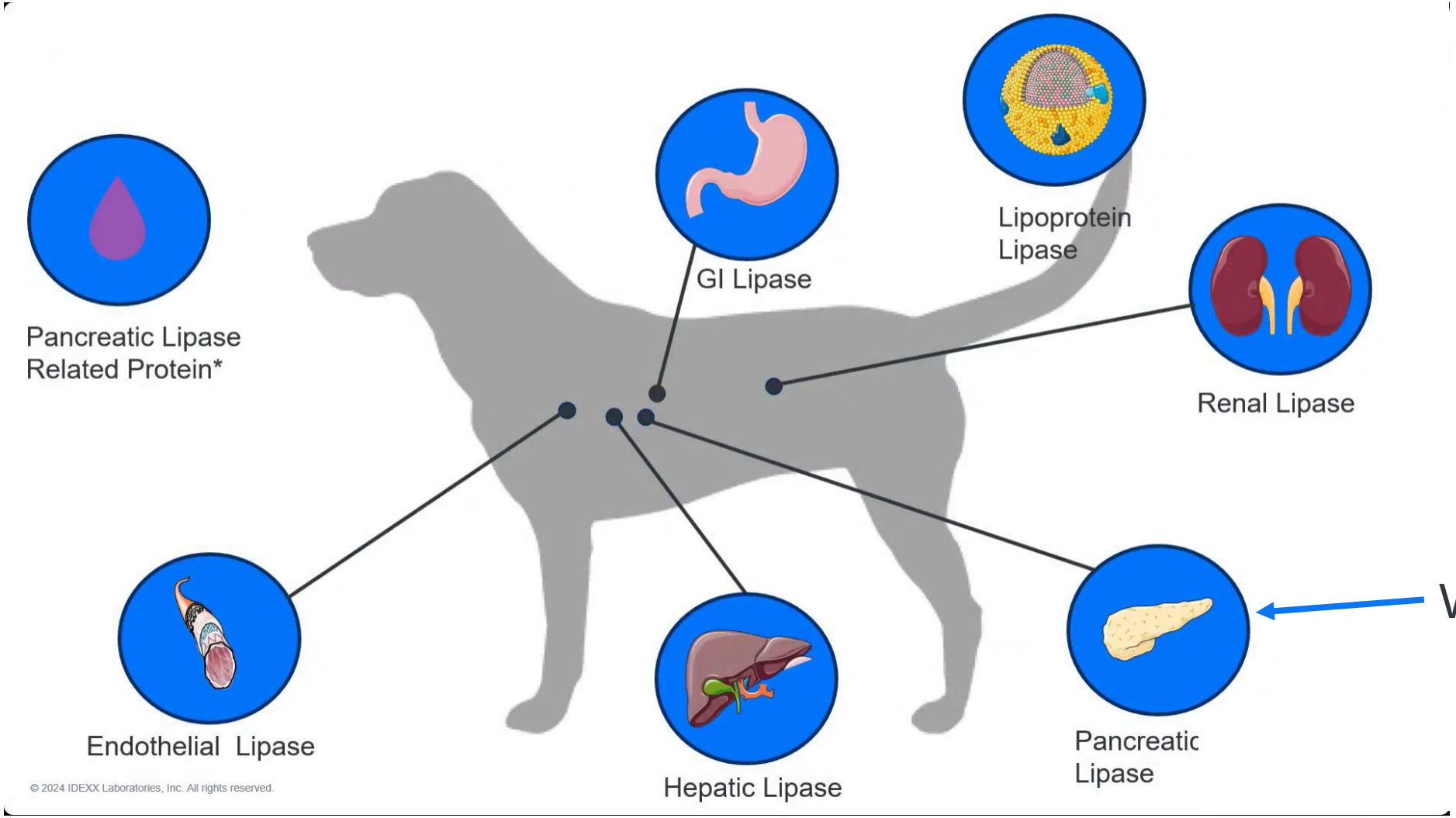
Gori E, et al. Vet Journal 2019

Serum amylase and lipase fall short

- Not sensitive or specific for pancreatitis
- Ignore amylase in dogs and cats
- Ignore lipase in cats
- Lipase slightly better in dogs but not sufficient to diagnose pancreatitis

Why does serum lipase fall short?

≈100 lipases in dogs and cats.



We only care about

We need a lipase test that detects *only* pancreatic lipase

- Immunoassays most specific for pancreatic lipase
  - Use antibodies that *only* detect lipase from pancreas, no cross reaction with others
  - No cross reaction with other lipases
  - SNAP cPL/fPL, Spec cPL/fPL, cPLI/fPLI

- Enzymatic assays
  - None inherently specific for pancreatic lipase
  - Can’t distinguish between lipases from different sources
  - Amylase, lipase

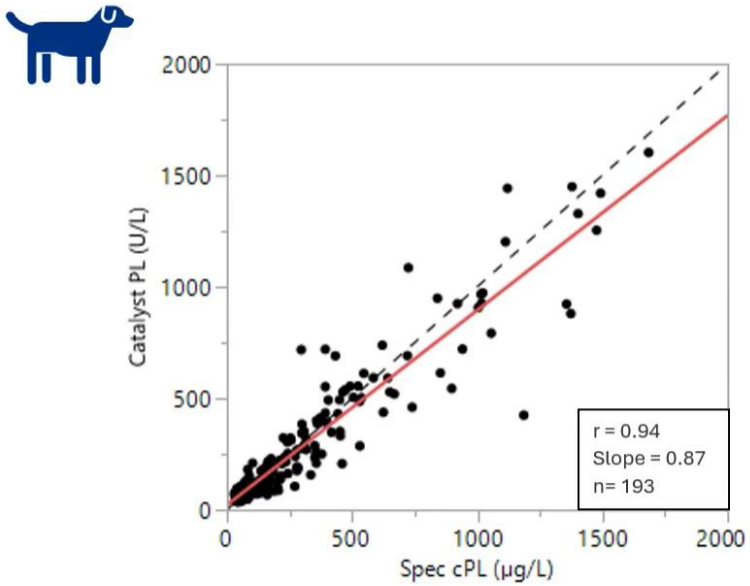
CONFIRMING pancreatitis now possible in clinic

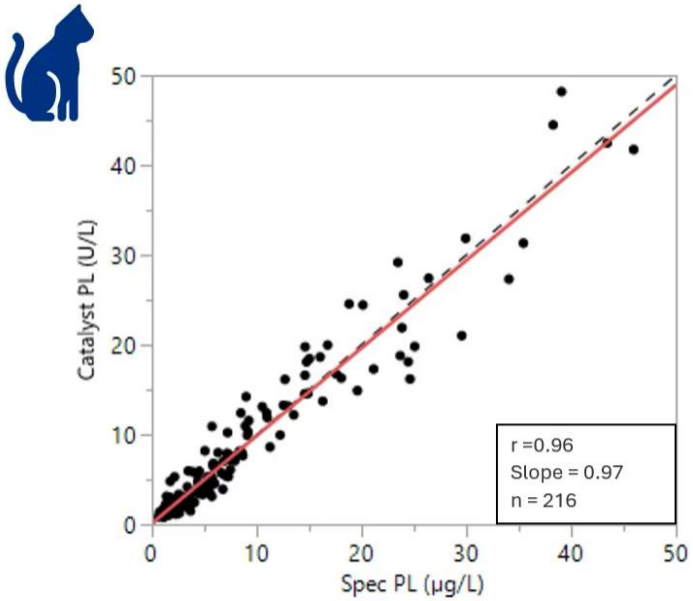
- SNAP cPL/fPL
  - Screening test, negative result rules OUT pancreatitis (SnOUT)
  - Positive result *could* be pancreatitis, must confirm
  - Spec cPL/fPL (send out test) to confirm, quantitative

- Catalyst pancreatic lipase
  - DGGR assay engineered (pH, temperature) to only detect pancreatic lipase
  - Undetectable in dogs with pancreatic acinar atrophy (EPI), i.e., specific for pancreatic lipase
  - Excellent correlation with Spec cPL/fPL*
  - Precision (5.2%) and reproducibility (6.6% dog, 6.1% cat) well below 10%*
  - Icterus, lipemia, hemolysis minimal/no interference
  - Quantitative result within minutes

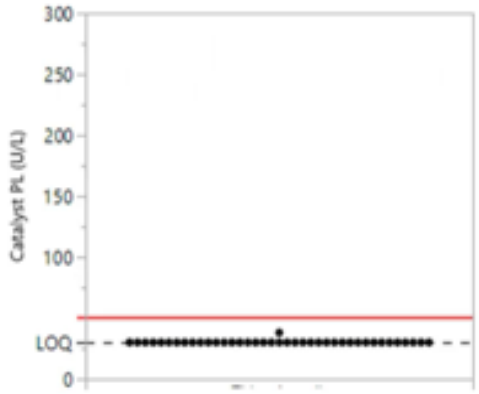
*Internal and external validation

Correlation between qPL and Spec PL excellent



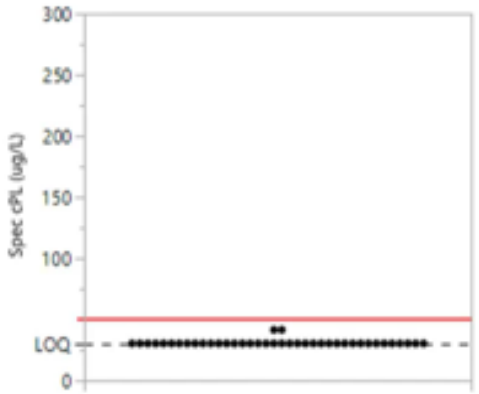


Dogs with EPI prove specificity of qPL for pancreatic lipase



Catalyst PL

3 samples > 30 U/L
0 samples > 50 U/L



Spec cPL

5 samples > 30 ug/L
0 samples > 50 ug/L

Dog or cat?

CBC, biochemical profile, and urinalysis are essential for determining severity and prognosis.

Use routine labs for support in diagnosis, severity, prognosis.

- **CBC**
  - Anemia variable
  - WBC count variable
    - ↑ band neutrophils +/-
  - **Thrombocytopenia**
  - Decreased RETIC-HB
    - Inflammation

- **Biochemistry**
  - ↑ ALT, ALP, bilirubin
  - ↑ SDMA, creatinine
  - **↑ CRP (dogs only)**
  - ↑ or ↓ glucose
    - **Hypoglycemia**
  - Hypercholesterolemia
  - Hypercalcemia
    - Risk factor
    - **Hypocalcemia**

Normal in up to 33% cats with acute pancreatitis.

- **Urinalysis**
  - Bilirubinuria
  - **AKI**

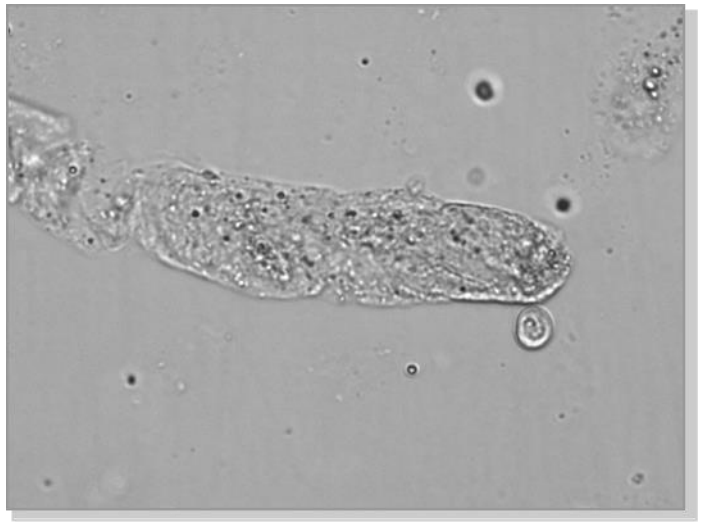
Pancreatitis↔AKI

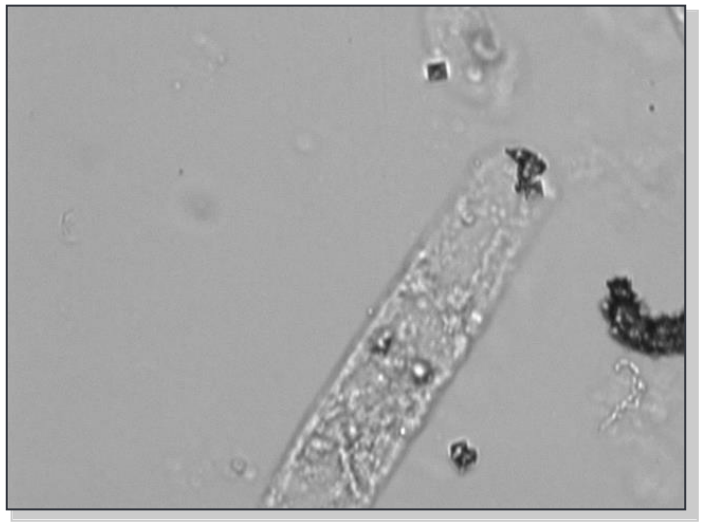
Red = negative prognostic indicator

IDEXX

Pancreatitis → AKI: earliest evidence in URINE.

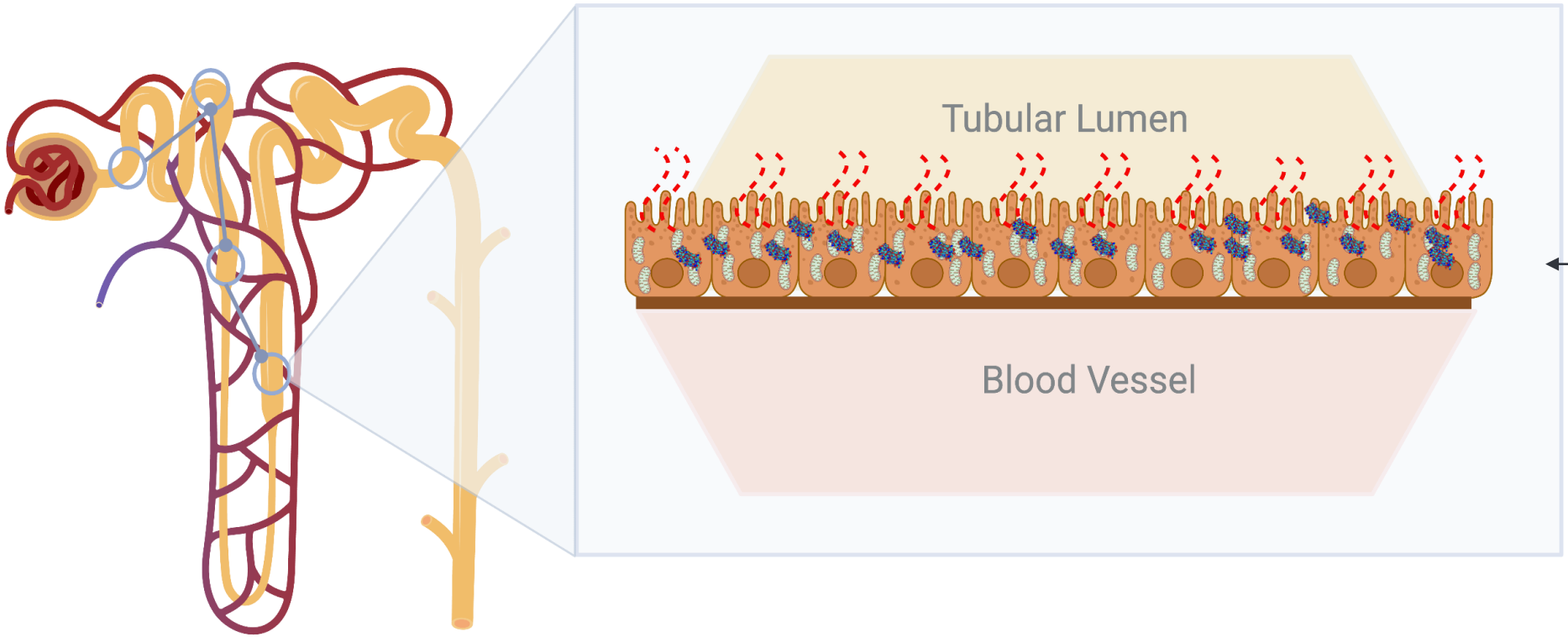
- Proteinuria
- Hematuria
- Pyuria
- Bacteriuria
- Renal epithelial cells
- Glucosuria (normoglycemia)
- + Urine culture
- Granular casts ≈16%
- Decreased urine production
- Decreased USG





Urine Cystatin B detects *active* kidney tubular damage

(ALT of the kidney)

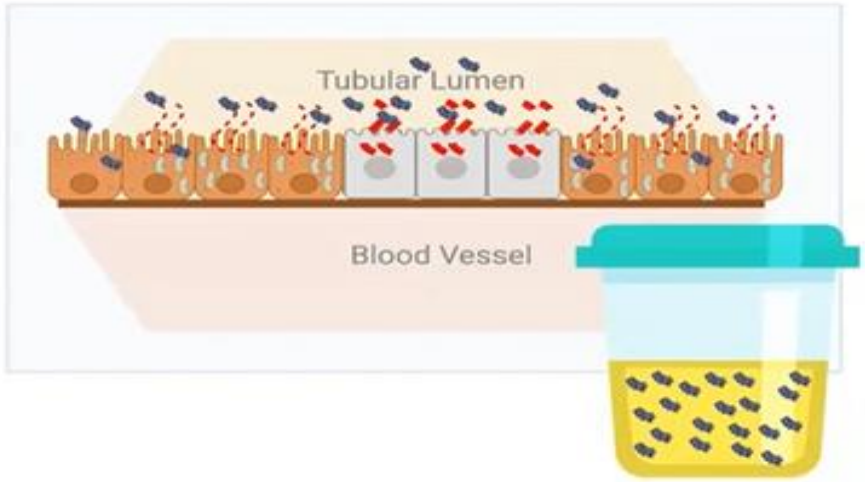


Cystatin B leakage from injured or necrosed tubular epithelial cells

Harjen HJ, Anfinsen KP, Hultman J, et al. Evaluation of urinary clusterin and cystatin B as biomarkers for renal injury in dogs envenomated by the European adder (Vipera berus). Top Companion Anim Med. 2022;46:100586. doi:10.1016/J.TCAM.2021. 100586

Starybrat D, Jepson R, Bristow P, et al. Prospective evaluation of novel biomarkers of acute kidney injury in dogs following cardiac surgery under cardiopulmonary bypass. J Vet Emerg Crit Care. 2022; 32(6):733-742. doi:10.1111/VEC.13250

The types of active and acute injury that can cause Cystatin B to leak into urine include both primary and secondary insults to the kidney



1

- Primary Renal Injury
  - "Acute on Chronic" Crisis
  - Toxin (grapes/raisins, lilies, ethylene glycol)

2

- Secondary Renal Injury
  - Infectious
    - Pyelonephritis
    - VBD
  - Systemic Disease (pancreatitis, vasculitis)
  - Hypo-/hypertension
  - Blood loss
  - Trauma

Ultrasonography and radiology

- Radiographs
  - Abdomen – obstruction/intussusception, wide duodenal angle/gas, mass effect, fluid
  - Chest – pleural effusion, pneumonia

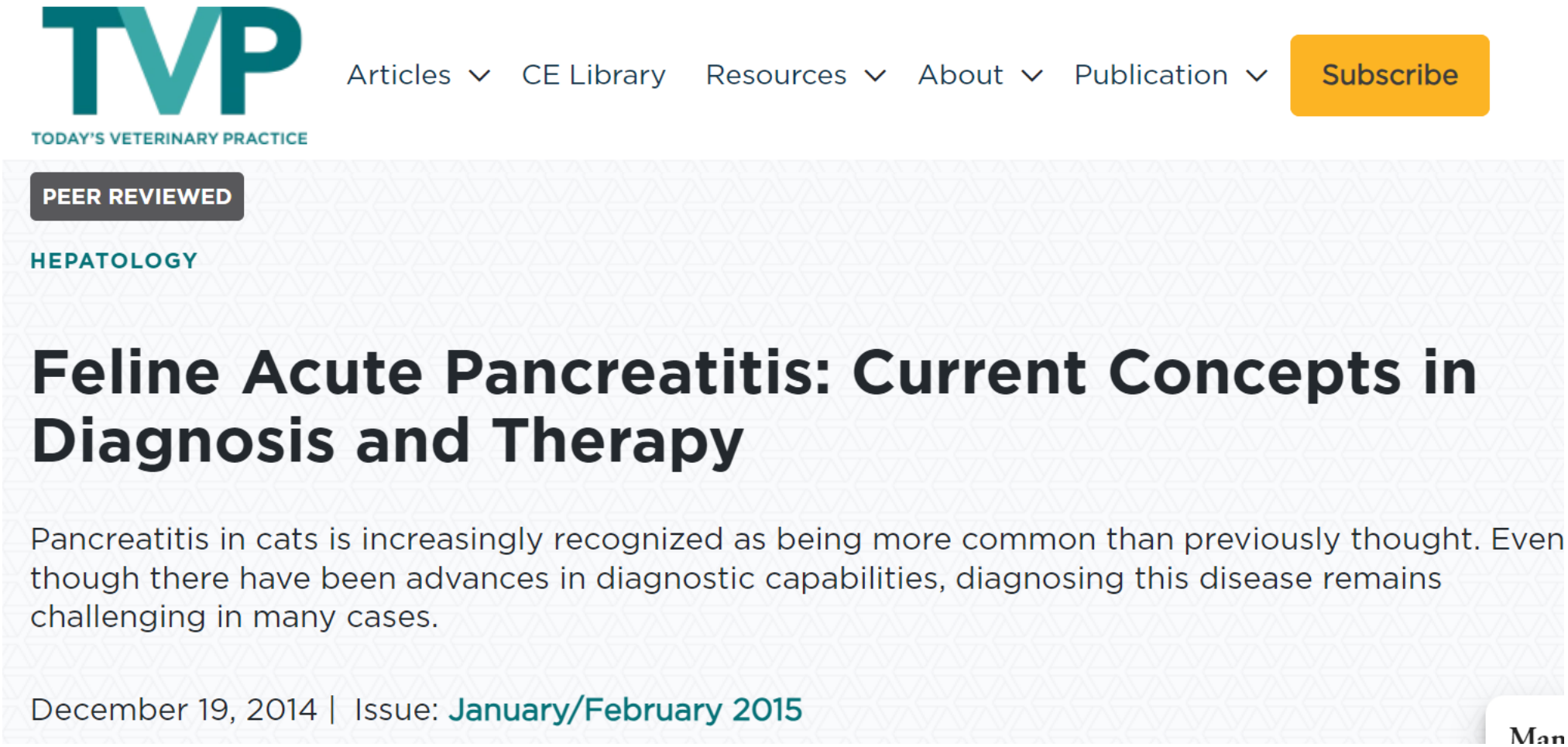
- Abdominal ultrasound
  - **Rule out other causes of signs**
  - Evaluate size, echogenicity, pancreatic/bile duct, portal vein, fluid
  - *Serial – 64% positive admission, another 27% positive 2 d later* (dogs)*
  - *Sensitivity in cats 11%-68%, higher with more severe disease*

*Gori et al, Vet Journal 2019

Treatment:

- Fluid therapy
- Analgesia
- Vomiting, nausea control
- Enteral nutrition within 48 hours (Panoquel® (Ceva) – dogs)

Good treatment chart with dosages…



IV fluids:

Which?

How much?

Fluids are a drug – avoid overdosing.

LRs best initial fluid for acute pancreatitis (almost anything)

- Good first choice in general
  - Isotonic, composition similar to plasma
  - Contains buffer (lactate) → non-acidifying, non-vasodilating
  - Contains Ca
  - Trivial amount of K → safe with hyperkalemia
- With pancreatitis (vs 0.9% NaCl)
  - Lactate has anti-inflammatory effects
  - Less SIRS, lower CRP and cytokines
  - Decreased progression moderate to severe disease by 50%

How much fluid and how fast

- If lose fluid fast replace fast – 30-60 min with hypovolemia
  - 10-15 ml/kg dog, 5-10 ml/kg cat over 15-30 minutes, repeat x2-3
  - Mucous membranes, capillary refill time, HR, pulse strength, lactate, urine production
- If lose fluid slowly replace slowly – 6-24 hr with dehydration
  - BW (kg) x % dehydration as decimal x 1000 = mLs to deliver
- Keep up with ongoing losses and provide maintenance
- Frequent body weight, accurate gram scale
  - 5% increase → consider adjusting
  - 10% increase → volume overload

Resuscitation: low and slow

Isotonic crystalloid 10-15 ml/kg dog, 5-10 ml/kg cat x 2-3
-over 15-30 minutes

Hypertonic saline 7.2% 4 ml/kg once if critical

Then fresh frozen plasma, canine specific albumin
FFP 10-20 ml/kg
Canine-specific albumin 16%, 1 g/kg

Analgesics in all: opioids based on pain severity:

- Mild or *clinically nonapparent*
  - Buprenorphine
  - Methadone
- Moderate to severe
  - Morphine
  - Fentanyl
- Adjunct
  - Lidocaine CRI, ketamine
  - Local anesthetic, dilute 1:1 with saline, roll patient, lasts 72 hr

Maropitant: antiemetic with benefits...

- Antiemetic, visceral analgesia, anti-inflammatory, antinausea
  - Safe for chronic long-term use without washout period
  - Visceral analgesia equal to morphine +/-
  - Minimizes pain-induced vomiting

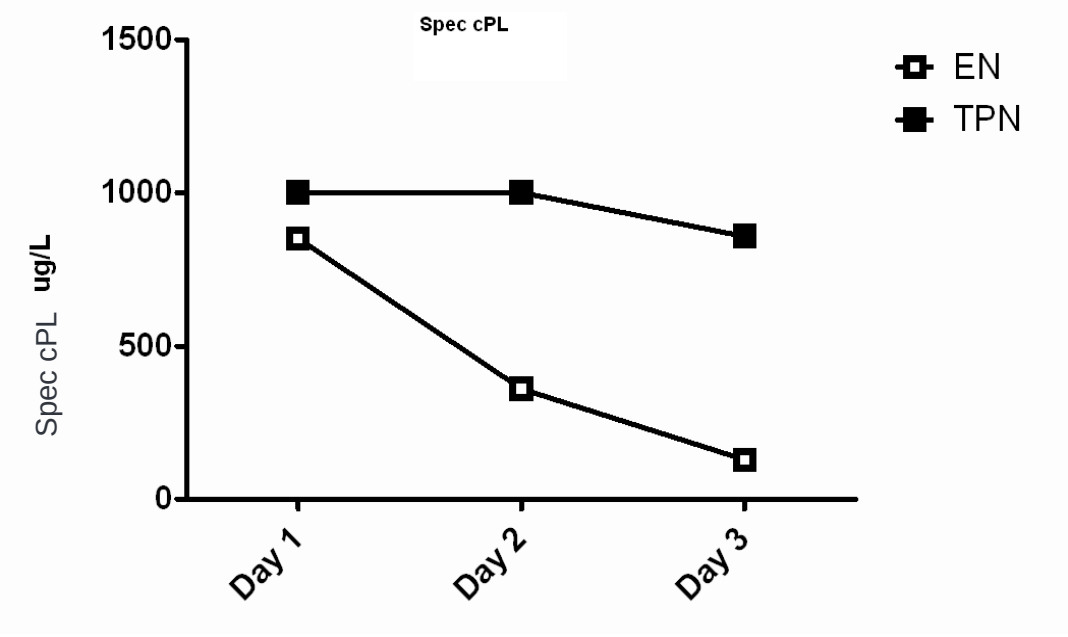
- 1 mg/kg q24h PO, SC, IV over 1 minute
  - Refrigerate *may* decrease SQ injection pain
  - Decrease dose 50% with liver disease (?)

Reduce nausea and functional ileus

- Mirtazipine in cats: ↓ nausea, ↓ vomiting, ↑ appetite
  - 1.88-3.75 mg/cat q2-3d PO
  - 3.75 mg Lipoderm gel transdermal q2d
- Ondansetron (with maropitant prn)
  - 0..5-1.0 mg/kg IV q12-24h
- Reduce ileus and gastric distention if present
  - Metoclopramide 0.2-0.4 mg/kg SC or PO q6-8h, 1-2 mg/kg/d IV constant rate infusion
  - Naso**gastric** tube suction - effective, also allows physiologic hydration (water) and enteral nutrition

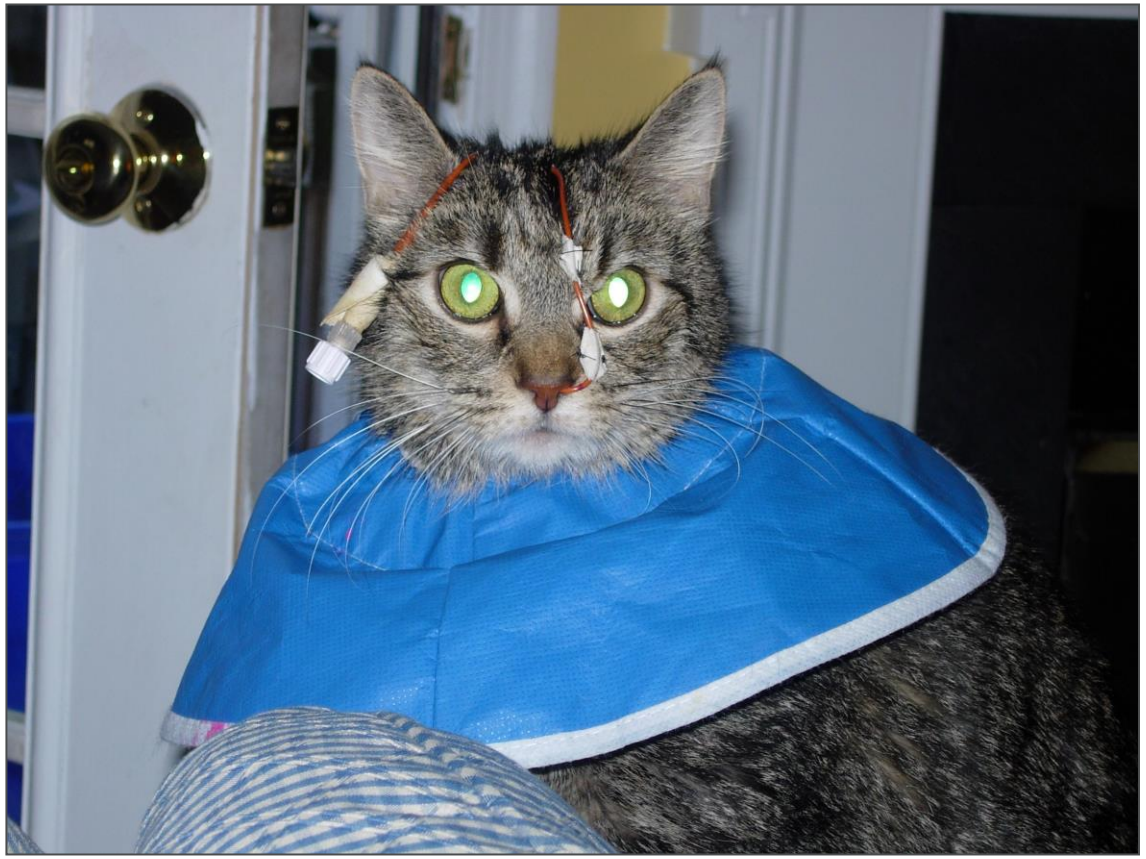
Enteral nutrition within 48 hours *of onset of signs.*
(Does not make pancreatitis worse)

- Include time prior to presentation
- Control vomiting w maropitant to allow feeding
  - No force feeding (creates aversion)
  - Metoclopramide if functional ileus
- ENTERAL (not parenteral) nutrition[1,2]
  - GI mucosal regeneration
  - Decreased cytokines
  - Decreased catabolism
  - Maintains plasma protein levels
  - Faster recovery (vs parenteral nutrition)



EN = Enteral nutrition
TPN = Total parenteral nutrition
Mansfield CS et al. J Vet Intern Med 2011;25:419-425.

1. Datz C. Nutritional Approach to Pancreatitis. ACVIM 2109 Proceedings.
2. Jensen KB, *et al*. Nutritional management of acute pancreatitis in dogs and cats. *J Vet Emerg Crit Care*. 2014;24:240–250.



Enteral nutrition specifics

- RER = 30 x BW (kg) + 70 (between 2 and 30 kg)
  - 70 x BW $(kg)^{0.75}$
- Feed 1/3 RER day 1, 2/3 RER day 2, RER day 3-5
  - Just get some calories in…
- Maropitant 1 mg/kg q24h SC, IV (and gastric suction) if vomiting
- Metoclopramide CRI (cat 1-2 mg/kg/d, dog 2-4 mg/kg/d) if ileus
- Water via tube to maintain hydration

Additional treatments…

- Antibiotics
  - Only if sepsis (hypoglycemia), concurrent disease (cholangitis, pneumonia), abscess…
  - Ampicillin-sulbactam, clavulanate-ticarcillin, 3rd gen cephalosporine, fluoroquinolone
- GI protectants
  - Only if other risk factors for GI erosion/ulceration
- Corticosteroids – do not cause pancreatitis
  - Cats with chronic pancreatitis, concurrent IBD, cholangitis/cholangiohepatitis
    - Prednisolone 0.5-2.0 mg/kg q12-24h, taper
    - 2.5-5 mg/cat q48-72h (chronic, intermittent, relapsing pancreatitis)
  - Dogs with acute or acute-on-chronic pancreatitis (0.5-1.0 mg/kg/d)
    - Good evidence for reduced histologic severity
    - Fair evidence for reduced CRP and shorter hospitalization
    - CRP decreased earlier, mortality rate significantly lower v no prednisone*
    - Given early may be beneficial**

*Okanishi H, Nagata T, Nakdane S et al. Comparison of initial treatment with and without corticosteroids for suspected acute pancreatitis in dogs. J Small Anim Pract. 2019;60:298-304.
**Bjørnkjær-Nielsen and Bjørnvad Acta Vet Scand (2021) 63:28 https://doi.org/10.1186/s13028-021-00592-0

Cobalamin: cats w/ pancreatitis at risk for deficiency

- Pancreas sole source of intrinsic factor (also stomach in dogs)
  - Concurrent chronic enteropathy(cobalamin absorbed in ileum)
- Supplement if <400 ng/L
- Injectable preferred in acute patients
  - 250 ug/week SC for 7 weeks
  - Recheck cobalamin 1 month later
- Oral effective (some absorption along entire GI tract)
  - 250 ug/day for 12 weeks
  - Recheck cobalamin 1 week later

Approved drug for canine acute pancreatitis

PANOQUELL®-CA1 (fuzapladib sodium for injection) (Ceva)

- Leukocyte function associated antigen-1 activation inhibitor
- Prevents neutrophil extravasation and release of proteases and chemokines
- Decreases reactive oxygen species (hydroxyl radical, peroxide, superoxide)
- Clinical severity scores*, cPLI, CRP improved faster v placebo
- Dose 0.4 mg/kg IV SID x 3 days, bolus over 15-60 seconds
- Inpatient or outpatient
- NOT CATS (license loser)

Monitor for sequelae

- Chronic pancreatitis, exocrine pancreatic insufficiency (Cocker Spaniel)
- Bile duct obstruction/icterus ≈1 week after resolution of acute pancreatitis
  - Transient – NOT surgical
- Abscess, cysts
- AKI
  - Urine protein, cells, granular casts, normoglycemic glucosuria
  - Urine cystatin B
  - Creat increase ≥ 27 mmol/L in 48 hr, <1 ml/kg/hr urine over 6 hr
- Serial examination, labs tailored to patient
  - CBC, biochemistries, urinalysis with sediment exam, CRP, Spec cPL/fPL, imaging

Thank you!

Additional treatments…

- Antibiotics
  - Only if sepsis (hypoglycemia), concurrent disease (cholangitis, pneumonia), abscess…
  - Ampicillin-sulbactam, clavulanate-ticarcillin, 3rd gen cephalosporine, fluoroquinolone
- GI protectants
  - Only if other risk factors for GI erosion/ulceration
- Corticosteroids – do not cause pancreatitis
  - Cats with chronic pancreatitis, concurrent IBD, cholangitis/cholangiohepatitis
    - Prednisolone 0.5-2.0 mg/kg q12-24h, taper
    - 2.5-5 mg/cat q48-72h (chronic, intermittent, relapsing pancreatitis)
  - Dogs with acute pancreatitis (?) - improved outcomes in one study*
    - Prednisolone 1 mg/kg/day
    - CRP decreased earlier, mortality rate significantly lower v no prednisone

*Okanishi H, Nagata T, Nakdane S et al. Comparison of initial treatment with and without corticosteroids for suspected acute pancreatitis in dogs. J Small Anim Pract. 2019;60:298-304.