

# WHEN BAD THINGS HAPPEN TO GOOD KIDNEYS

## Diagnosis and Treatment of AKI

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# OBJECTIVES

1. Diagnose AKI and identify correct etiology
2. Discuss treatment options and prognosis with owners
3. Review current literature
4. Know when dialysis or referral for intensive care would be helpful

# WHAT IS ACUTE KIDNEY INJURY?

A spectrum of disease associated with a sudden onset of renal parenchymal injury most typically characterized by generalized failure of the kidneys to meet the excretory, metabolic, and endocrine demands of the body.

- IRIS AKI Grading Guidelines

# DIAGNOSIS

- History
  - Acute illness or slow decline?
  - Previous azotemia or isosthenuria?
  - Exposure to nephrotoxins?
  - Other conditions that increase risk?
    - Diabetes, heart disease, urolithiasis, dental disease, SIRS/Sepsis, etc.

- Physical Exam

- Good body condition or skinny and muscle wasted?
- Normal, enlarged, painful kidneys or small, bumpy ones?



- Chemistry Panel
  - Clinical illness proportionate or disproportionate to degree of azotemia?
  - Potassium increased or decreased?
- Complete Blood Count
  - Normal hematocrit or non-regenerative anemia?
  - Inflammatory leukogram?
- UA/UCS
  - Active urinary sediment? Proteinuria?
  - Casts?
  - Hypersthenuric or hyposthenuric?
- Imaging
  - Pyelectasia? Ureteral dilation?
  - Full bladder or empty one?
  - Uroliths?

# ETIOLOGY

- Pre-renal
  - NSAID toxicity
  - Severe blood pressure alterations (infarct or hypertension)
  - Sepsis
  - Acute pancreatitis
  - Hyperviscosity



- Renal

- Urinary tract infection
- Aminoglycosides
- Lily toxicity (cats only)
- Renal lymphoma (mostly cats)
- Lyme nephritis (dogs only)
- Leptospirosis (dogs only)
- Grapes/Raisins (dogs only)
- Melamine contamination (dogs and cats)
- Dehydrated chicken treats (dogs only)
- Ethylene glycol
- Hypercalcemia

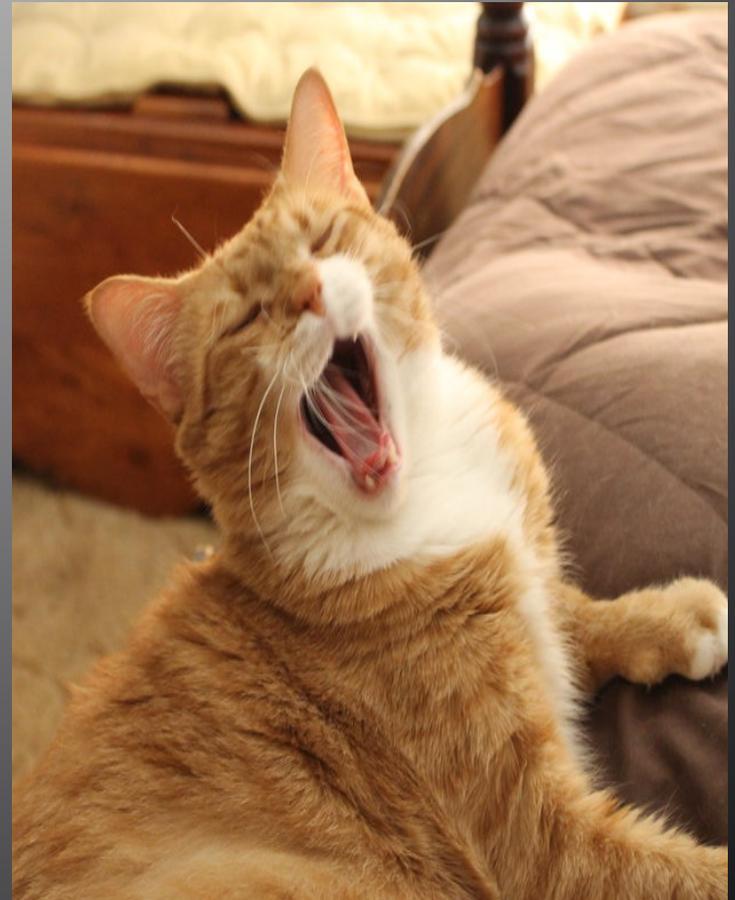
- Post-renal

- Obstruction of ureters or urethra
- Bladder rupture



# CATS: ETIOLOGY AND OUTCOME

- ACVIM Abstract (1993 – 2003): N = 119, all received dialysis
  - 1993-1998: toxicity (35%), ureteral obstruction (10%)
  - 1999-2003: ureteral obstruction (55%), toxicity (11%)
- JVIM 2013: N = 132, all received dialysis, case fatality 58%
  - Causes: ureteral obstruction (38%), ethylene glycol (9%), pyelonephritis (5%), lily (4%), unknown/other (44%)
  - Common presenting signs: anuria (55%), vomiting (47%), fluid overload (46%), dehydration (19%)
- JVIM 2013: N = 128, only hospital-acquired AKI, case fatality 66%
  - If creatinine > 1.6 mg/dl and increase from baseline > 0.3 mg/dl = 3 x higher risk of death



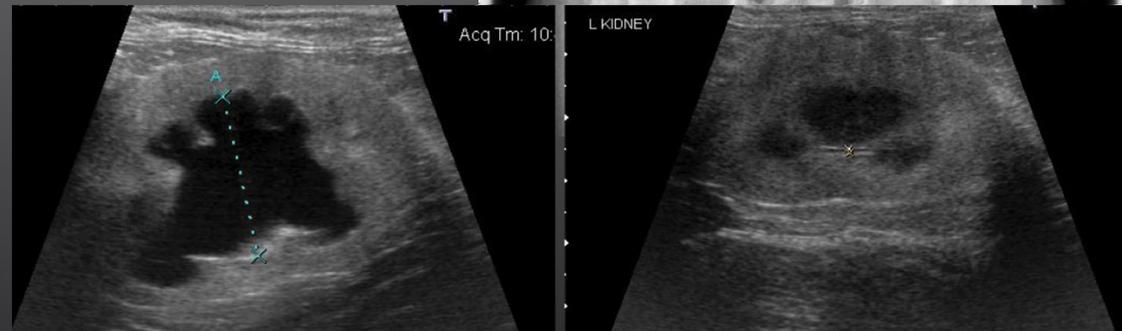
# DOGS: ETIOLOGY AND OUTCOME

- JVIM 1997: N = 99, case fatality 56%, from NCSU
  - Causes: Ischemic events (33%), toxicity (21%), Lepto (2%), pyelonephritis (2%)
- JVIM 2008: N = 182, all received dialysis, case fatality 53%, from UC-Davis
  - Causes: Lepto (30%), ethylene glycol (27%), other toxins (6%), hemodynamic (10%), unknown (26%)
  - Clinical scoring system that considered Lepto status was superior to others and correctly predicted outcome in 87% of cases
- JVIM 2013: N = 476, only hospital-acquired AKI, case fatality 62%
  - If creatinine within reference range but increased from baseline  $> 0.3$  mg/dl = 3 x higher risk of death



# URETERAL OBSTRUCTION

- Ureteral obstruction is #1 cause of AKI in cats
  - 15-20% of cats are bilaterally obstructed
  - 86-92% of obstructions caused by ureteral calculi
  - 98% of ureteral calculi in cats are calcium oxalate
  - Average number of stones per obstructed ureter = 4
  - 30% have concurrent UTI
  - Experimental occlusion of ureter for 14 days = 54% permanent reduction in GFR
- Must have > 75% loss of function to be azotemic
  - Azotemia indicates that non-obstructed kidney has to be dysfunctional
  - Act quickly to prevent permanent loss of function



# TREATMENT OPTIONS

## 1) Medical management

- 8-17% resolution rate
- 70% survive to discharge

## 2) Ureterotomy

- 75-92% survive to discharge
- 50% long-term mortality
- 43% persistent renal dysfunction
- 22-40% reobstruct
- Recent study: MST 1,519 days

## 3) Stent

- 93% survive to discharge
- 20% reobstruct
- MST 498 – 1575 days

- 4) SUB - preferred treatment
- 95% survive to discharge
  - 10% reobstruct
  - MST 762-923 days
  - Fewer complications than stent
  - Shorter surgery than stent



# NSAIDS

- Pharmacodynamics:
  - Ibuprofen: renal toxic dose = > 175 mg/kg (dog), 88 mg/kg (cat), T1/2 = 4-hours (dog)
  - Rimadyl: renal toxic dose = 40 mg/kg, T1/2 = 8-18 hours (dog), 20-36 hours (cat)
  - Naproxen: renal toxic dose = 10-25 mg/kg, T1/2 = 74 hours (dog)
- Treatments:
  - Decontamination: Emesis ONLY in first 2 hours, activated charcoal up to every 6 hours
  - Fluid diuresis: 120 ml/kg/day for 48 hours. For longer half-life drugs 72 hour diuresis.
  - Gastroprotectants:
    - Proton-Pump Inhibitors: Pantoprazole (1 mg/kg/day), omeprazole (1-2 mg/kg/day)
    - Famotidine (0.5 mg/kg BID)
    - Sucralfate (dogs: 0.5-1 g TID, cats 0.25-0.5 g TID) – separate from other medications by 2 hours
    - Misoprostol (dogs: 1-5 mg/kg TID, not recommended in cats)
    - Antiemetics as needed
  - IV Lipid Infusion – JAAHA (2014, ibuprofen, case report), JVECS (2015, naproxen, 3 cases)
  - Dialysis
- Prognosis:
  - Variable; depends on dose, timing of intervention, type of intervention
  - Anuria or oliguria is most important negative prognostic indicator



# GRAPES/RAISINS

- Toxic dose: 0.32-0.65 oz/kg (1/2 grape or 1 raisin per kg)
- Delayed onset: 2-24 hours after ingestion
- Treatment:
  - Emesis up to 2 hours after ingestion
  - Fluid diuresis 48 hours
  - Monitor creatinine for 72 hours
- Prognosis:
  - JVIM 2005: Azotemic on presentation. 53% survival.
    - Elevated calcium and Ca:Phos negative prognostic indicators
    - Recovery over 15 days in survivors
  - ASPCA – APCC: 50/140 cases symptomatic, 7/140 died.



# LILY TOXICOSIS

- Toxic dose: unknown, but ingestion of less than 1 petal associated with AKI
- Treatment:
  - Emesis first 2 hours after ingestion
  - Decontamination
  - Diuresis 48 hours
  - Recheck renal values 24, 48, 72 hours
- Outcome:
  - JAVMA 2003: 50% mortality rate, all survivors developed CKD and died within 1.5 years
  - JAAHA 2011: 5% mortality rate, 5% chronic renal disease, 73% owners unaware of danger
  - JAVMA 2013: 100% survived, 26% developed azotemia, 9% chronic renal disease



# DIALYSIS

- Dialysis
  - Exchange of solutes and water across semipermeable membrane
- Hemodialysis
  - Extracorporeal exchange of solutes and water between blood and a prepared solution, dialysate.

Blood Flow

Filter

DIFFUSION

HCO<sub>3</sub>

K

HCO<sub>3</sub>

K

HCO<sub>3</sub>

HCO<sub>3</sub>

K

K

Concentration Gradient

HCO<sub>3</sub>

K

K

K

HCO<sub>3</sub>

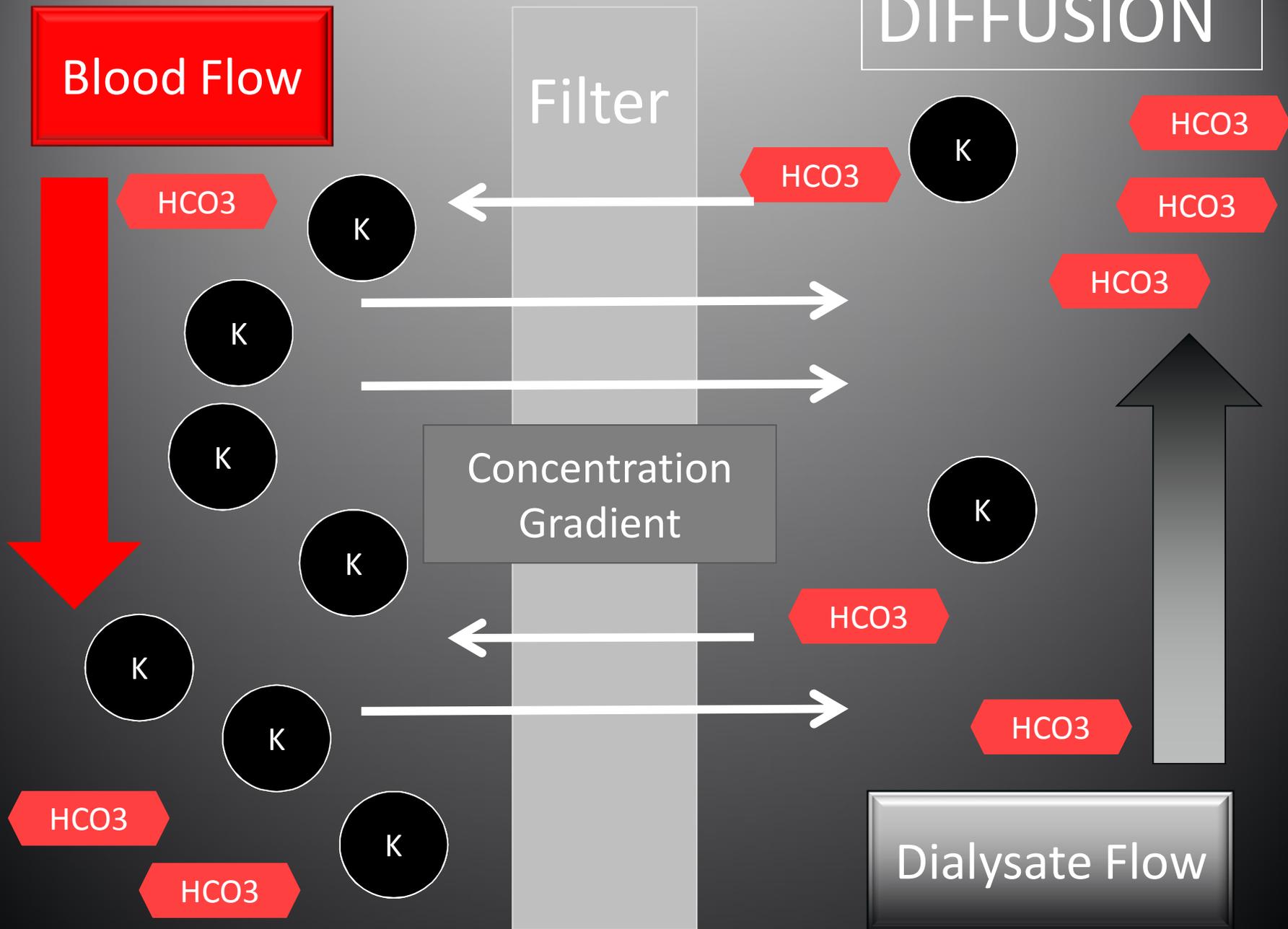
HCO<sub>3</sub>

HCO<sub>3</sub>

HCO<sub>3</sub>

K

Dialysate Flow



Blood

Dialysate

Filter

High Pressure

Transmembrane Pressure Gradient

Low Pressure

Water

Water

Water

Water

Ultrafiltration

Water

Water

Water

# WHEN?

- Progressive azotemia
- Anuria
- Hyperkalemia
- Acidemia
- Volume overload
- **Toxins**

# DIALYSIS GOALS

Uremic toxin removal

Correct fluid balance

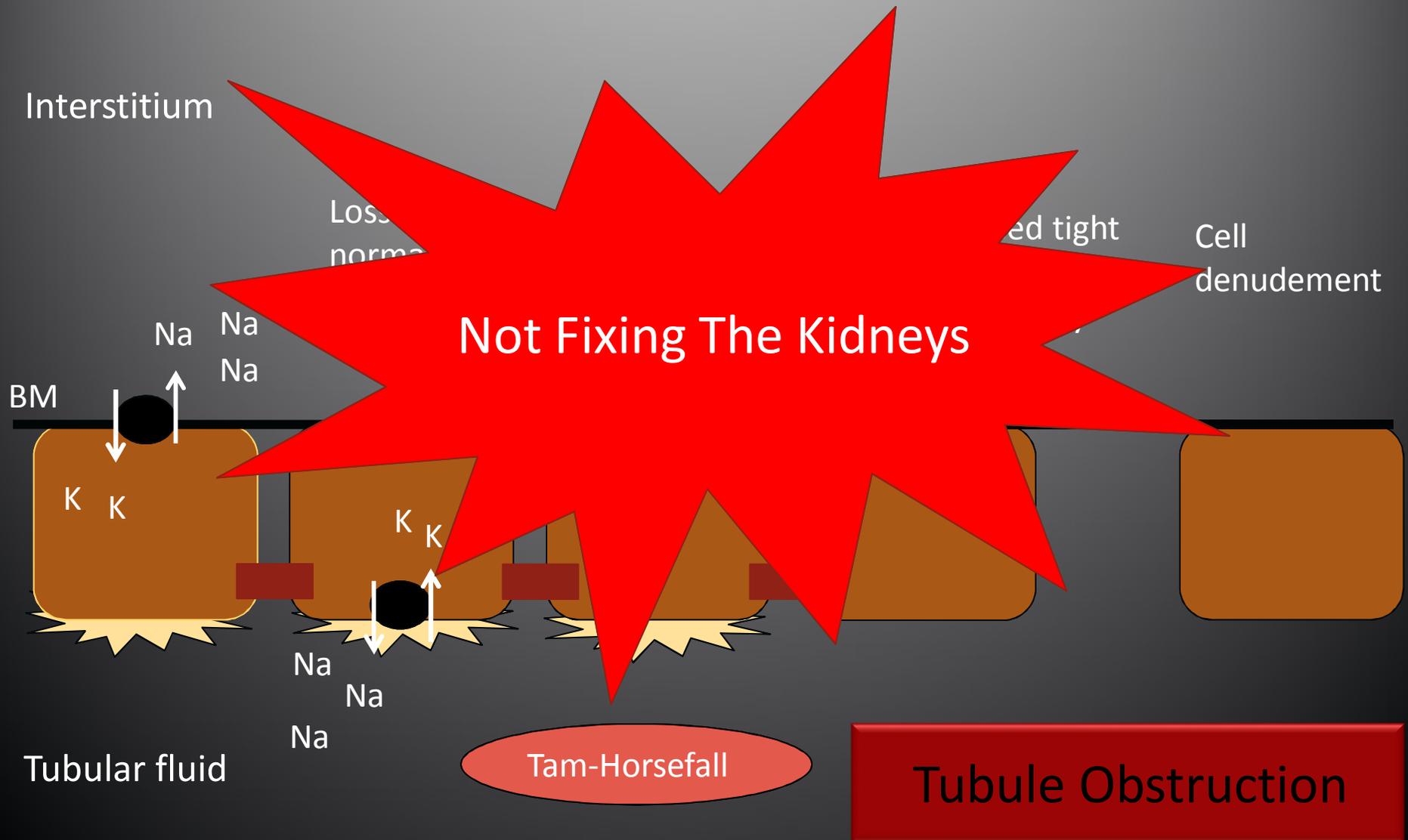
Correct electrolyte balance

Correct acid base balance

Stabilize for surgery

Allow TIME for intrinsic repair

# Actin Cytoskeleton

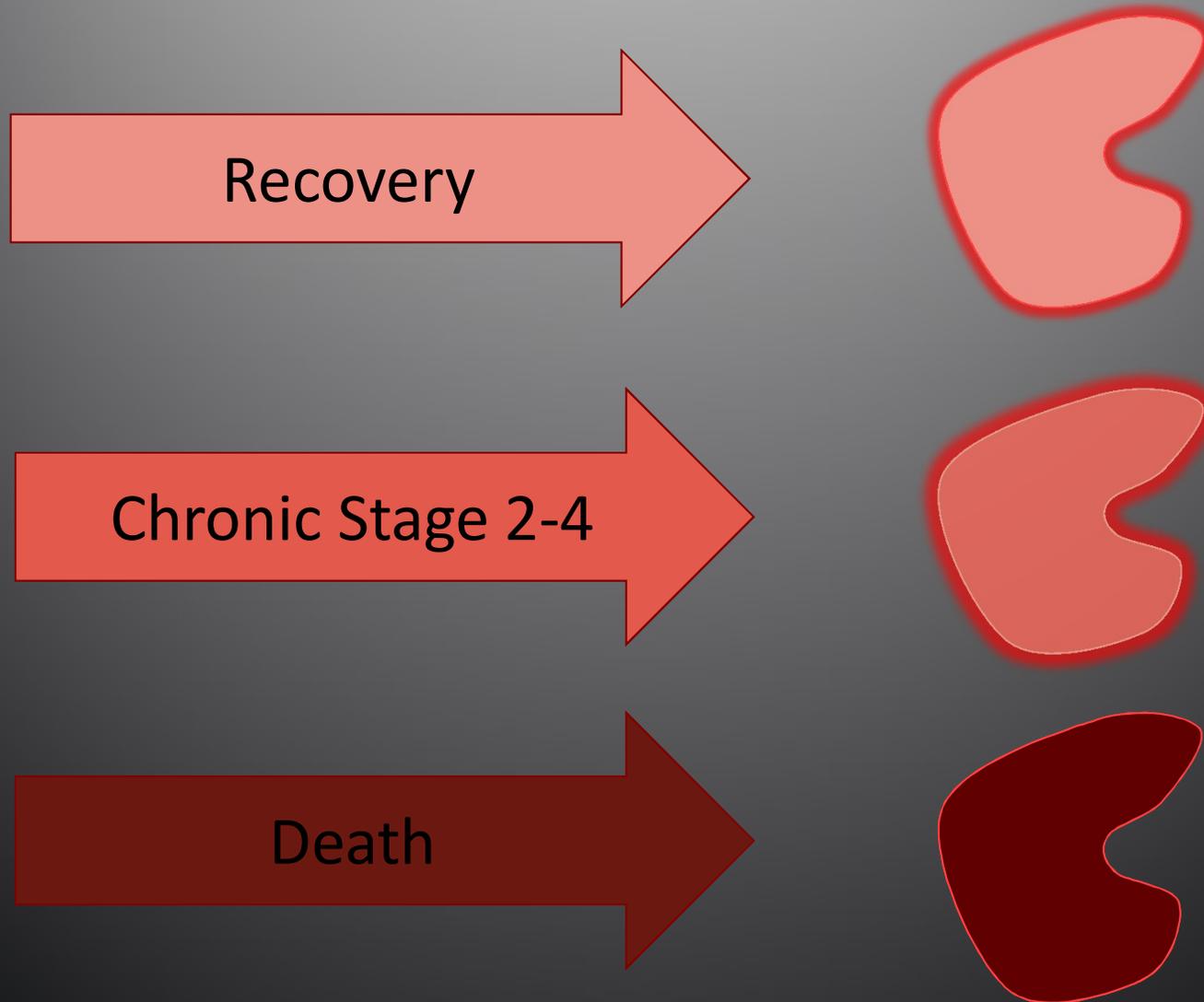


# IRIS

Grade	Creatinine (mg/dl)	Description
I	< 1.6	<ul style="list-style-type: none"><li>• Non azotemic</li><li>• Some reason to suspect (historic, imaging)</li><li>• &gt; 0.3 mg/dl rise in creatinine in 48 hr</li><li>• Oliguric/anuric over 6 hours</li></ul>
II	1.7-2.5	<ul style="list-style-type: none"><li>• Azotemic</li><li>• &gt; 0.3 mg/dl rise in creatinine in 48 hr</li><li>• Oliguric/anuric over 6 hours</li></ul>
III	2.6-5	Increasing severity of azotemia
IV	5.1-10	
V	> 10	

Subgrade oliguric or non-oliguric

# OUTCOME



# POTENTIAL LIMITATIONS

Hypotension

<2.5 kg

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Coagulopathy

Aggressive

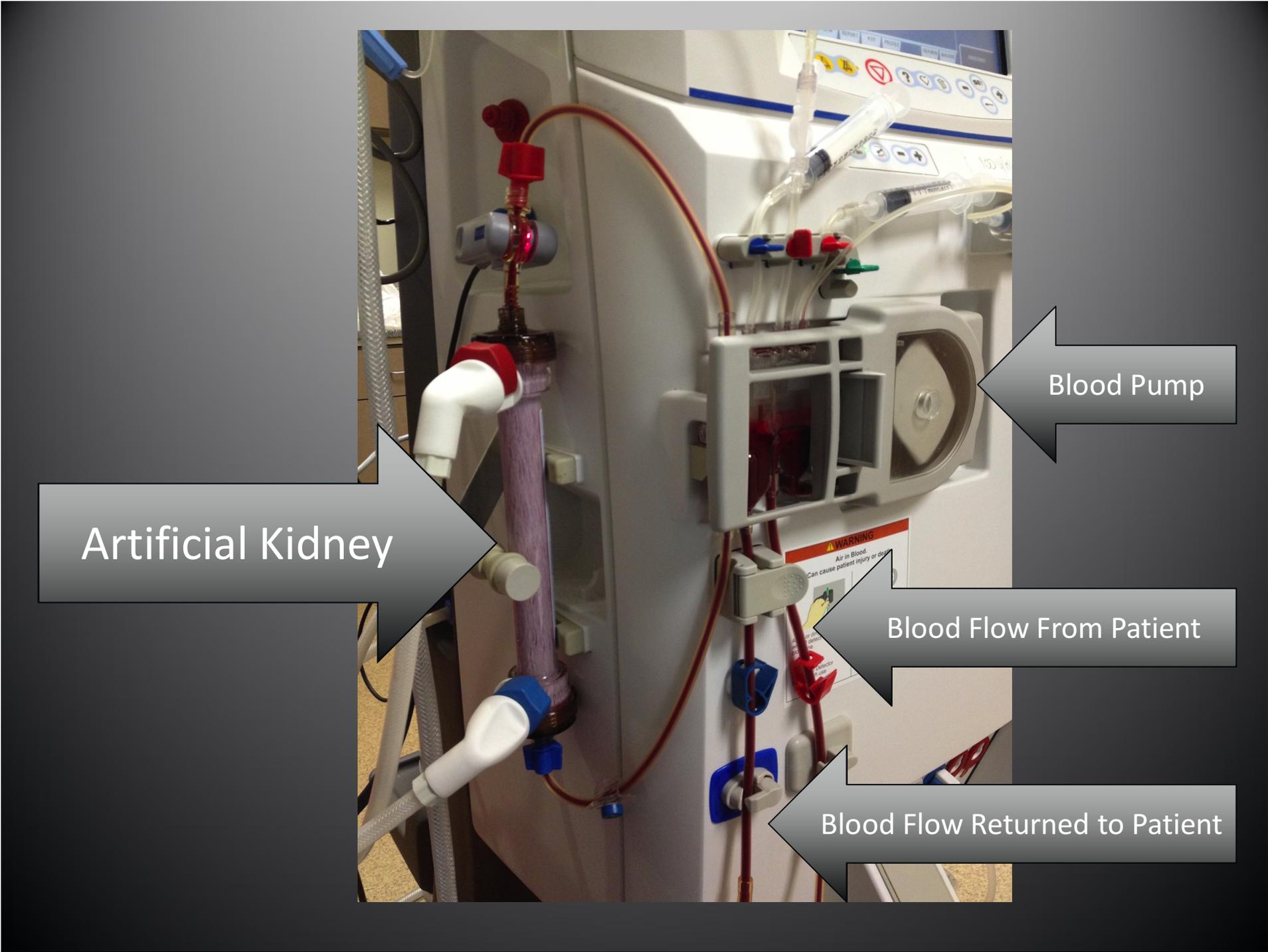


# THE PROCESS

- History
- Review records and current therapy
- Assess hydration status
- Place dialysis catheter
- Dialyze
  - Usually 3 days on
  - Then 3x week or EOD







Artificial Kidney

Blood Pump

Blood Flow From Patient

Blood Flow Returned to Patient

# COMPLICATIONS

- Catheter Dysfunction
- Hypotension
- Clotting
- Dialysis Disequilibrium
- Infection

# **A Retrospective Study of Acute Kidney Injury in Cats and Development of a Novel Clinical Scoring System for Predicting Outcome for Cats Managed by Hemodialysis**

G. Segev, R. Nivy, P.H. Kass, and L.D. Cowgill

132 cats

42% HD  
free

28% died

30% euth

# Long-term outcome of cats and dogs with acute kidney injury treated with intermittent hemodialysis: 135 cases (1997–2010)

Adam E. Eatroff, DVM, DACVIM; Cathy E. Langston, DVM, DACVIM;  
Serge Chalhoub, DVM, DACVIM; Karen Poeppel; Eleonora Mittelberg

JAVMA, Vol 241, No. 11, December 1, 2012

Species	Survival to discharge	Survival to 30 d	Survival to 1 yr	HD continued after discharge
Cats	50%	48%	38%	7%
Dogs	53%	42%	33%	23%

Cats with obstruction  
survived longer

# IMPORTANT CHARACTERISTICS

## **Solute**

- Size
- Molecular charge
- Protein binding
- Lipid solubility
- Volume of distribution
- Cellular seclusion

## **Membrane**

- Thickness
- Surface area
- Number of pores
- Size of pores

# HEMOPERFUSION



- NSAIDs
- Ibuprofen
- Barbiturates
- Vincristine
- Amanita

ADSORPTION



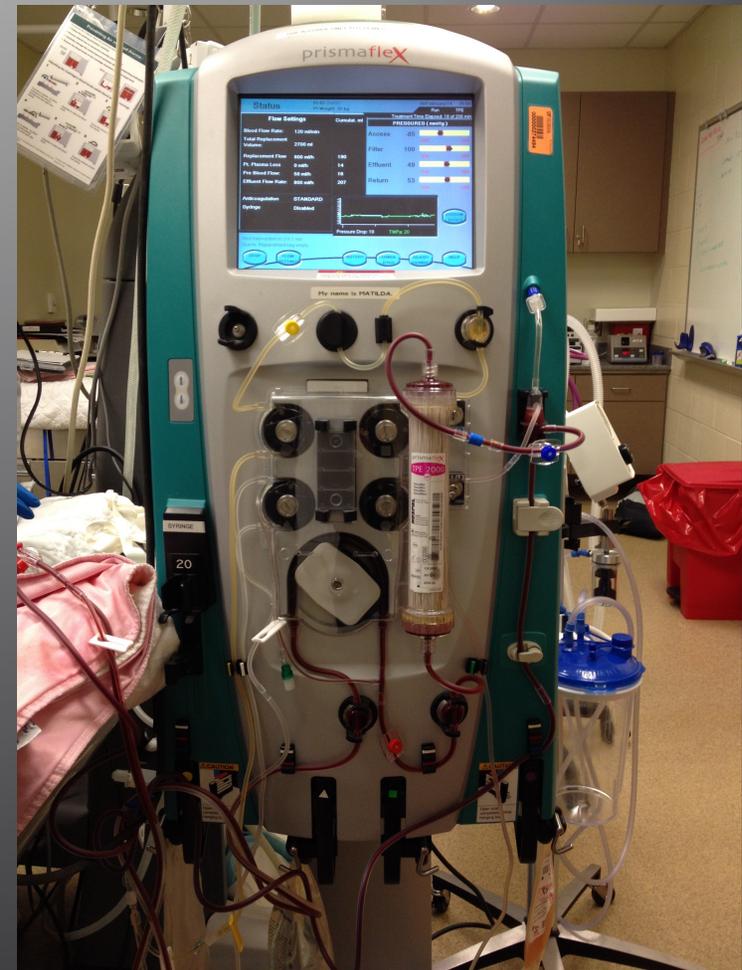
# COMPLICATIONS

- Thrombocytopenia
- Leukopenia
- Clotting
- Hypotension

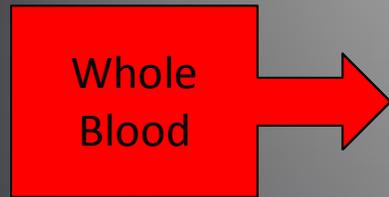
Usually only one treatment

# THERAPEUTIC PLASMA EXCHANGE

- Indications:
  - Immune mediated Disease
    - IMHA
    - Myasthenia Gravis
    - Pemphigus
  - TOXINS



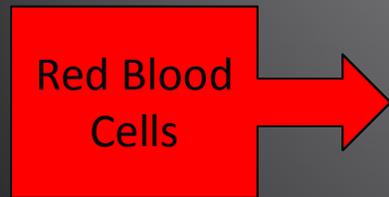
# HOW IT WORKS



Blood enters dialyzer



Plasma fraction is separated out



Cells returned to patient



Plasma volume is replaced

# BENEFITS

- Removal of:
  - Highly protein bound substances
  - Low volume of distribution
- Does not become saturated
  - Charcoal
- May have immunomodulatory effects

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Slide 6:

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