# Welcome

## We're so glad you're here!

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# Acute Kidney Injury: Pathophysiology and Renal Replacement Therapy

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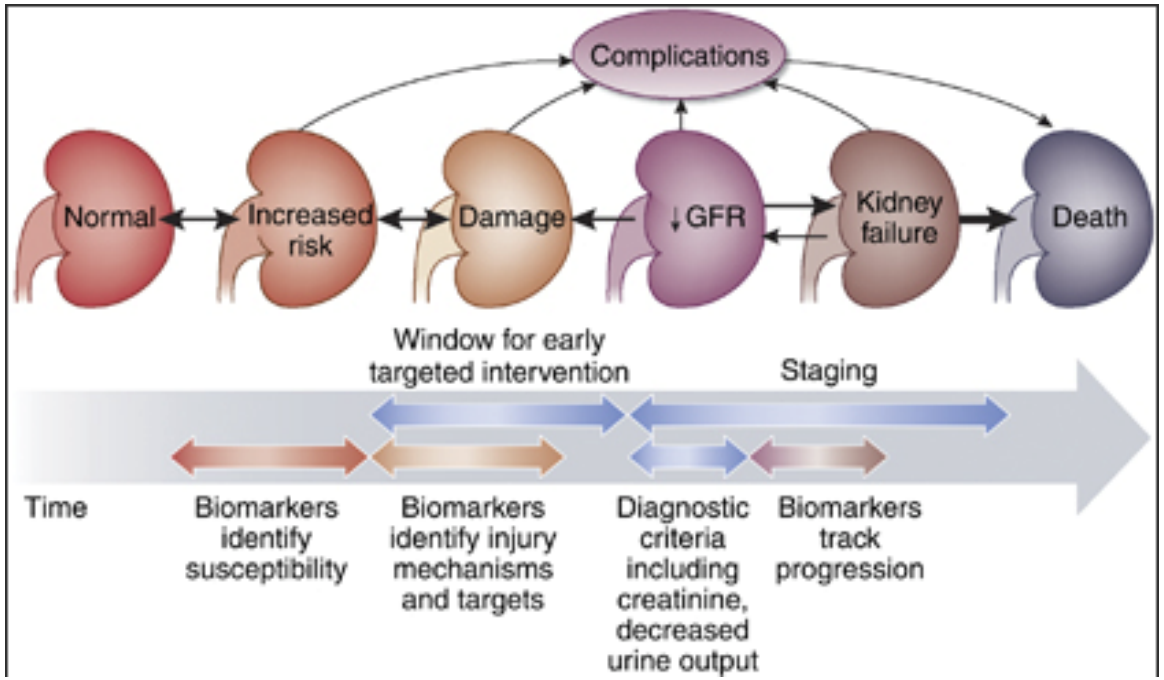
# Outline

- Pathophysiology of acute kidney injury (AKI)
- Causes of acute kidney injury
- Traditional medical therapies
- Renal replacement therapies
- Therapeutic Plasma Exchange
- Outcomes

# Acute Kidney Injury

- Occurs in 4 stages
  - Initiation
  - Extension
  - Maintenance
  - Recovery

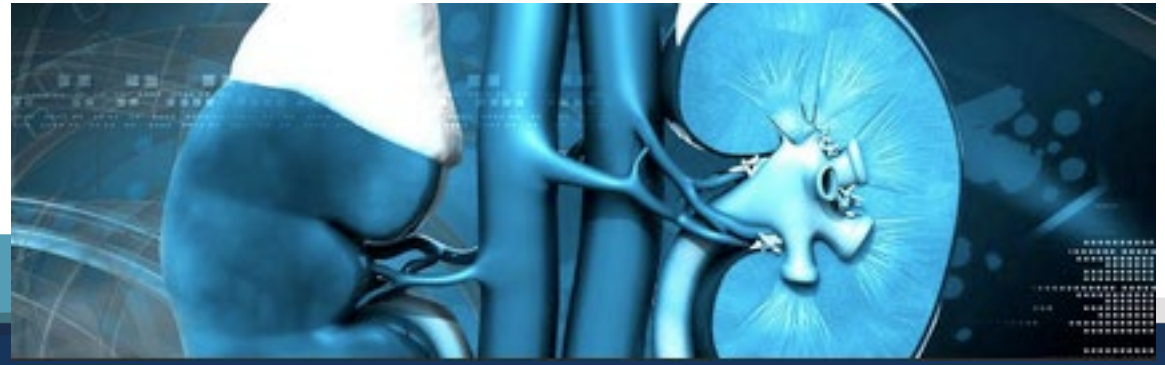


# Initiation

- Period of renal injury
- Occurs due to initial insult
  - Decreased blood flow, ischemia
- Pathologic damage is occurring
  - Dysfunctional $Na^+/K^+$ -ATPase pump
- Kidney values remain normal

# Extension

- Cellular injury progresses to cell death
- Ischemia, hypoxia continue
- Inflammation → apoptosis or necrosis
- Pro-inflammatory cytokines released



# Maintenance

- Characterized by azotemia/uremia
- May last for days to weeks
- Oliguria may occur
- Removal of the inciting cause does not reverse damage already done

# Recovery

- Repair of the damaged nephrons
- If recovery happens…
  - It may take weeks to months to occur

# Causes of AKI

- Ischemia
- Infarction
- Toxins
- Infections
- Drugs
- Hypercalcemia
- Hyperviscosity
- Sepsis
- Acute pancreatitis
  - SIRS
- MODS

# Traditional Medical Therapy

- Eliminate underlying cause
- Fluid therapy
- Frequent monitoring
  - “Ins and outs”
- Increase urine flow
  - Furosemide, mannitol, dopamine
- Supportive care

# Outcome of Medical Management of AKI

- Dogs: (Vaden et al 1997)
  - Mostly toxic or ischemic causes
  - Mortality rate ~60%
  - Hypoalbuminemia
  - Survival of >5 days
- Cats: (Worwag et al 2008)
  - Toxic, ischemic and unknown causes
  - Mortality rate ~47%
  - 50% of survivors had CKD
  - Hypoalbuminemia, hyperkalemia
- Dependent on Etiology
- Leptospirosis/Pyelonephritis
  - 56-82% survival
- Toxicities
  - EG with azotemia – Poor
  - Ischemia (NSAIDs, ACE-I) – Fair
  - Grapes - ~75% recovery
  - Lilies – Poor outcomes

# If all else fails…

Consider renal replacement therapy!

# What is Renal Replacement Therapy?

- Removal of the patient's blood through venous access
- Purification of the blood
  - Removal of solutes (urea)
  - Removal of toxins (NSAIDs, etc)
- Return of blood to the patient
- "Artificial Kidney"

# Goals for RRT

- Removal of waste products
  - Potassium and urea
- Removal of free water
  - Fluid overload
- **Extension** of time for healing

# Indications for Hemodialysis

- Acute kidney injury
  - Some indications for chronic kidney disease
- Intoxications
  - Small, free floating molecules
- Congestive heart failure
  - Fluid overload
- Pre-surgical

# Acute Kidney Injury

- **Failure to respond to medical management**
  - **A**cidosis (pH <7.0)
  - **E**lectrolyte imbalances (hyperkalemia)
  - **I**ntoxications (ethylene glycol, drugs)
  - Fluid **O**verload
  - Severe **U**remia (oliguria/anuria)

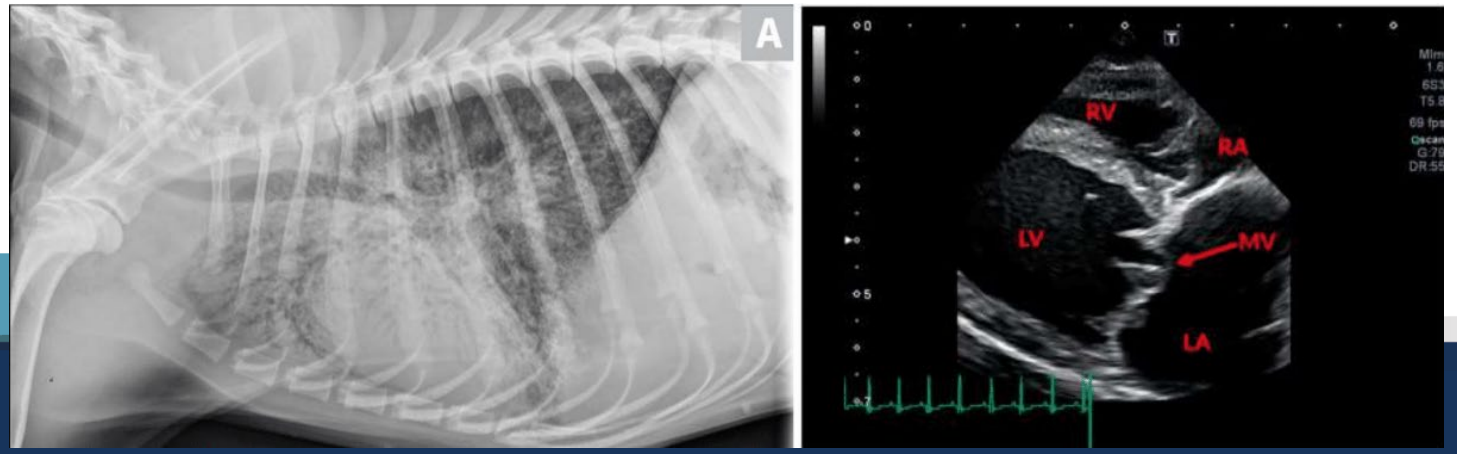
# Intoxication

- Not every toxin
- Poor protein binding
- Low volume of distribution
- Low molecular weight

- Examples of toxins that can be effectively dialized
  - Ethylene Glycol
  - Caffeine
  - Cyclosporine
  - Not all inclusive

# Congestive Heart Failure

- Patients that are refractory to diuretic therapy
- Ultrafiltration can be used to remove water and salt slowly
- May restore sensitivity of kidneys to diuretics



# Principles of Dialysis

# Principles of Dialysis - Diffusion

- High concentration → low concentration
  - Passive movement

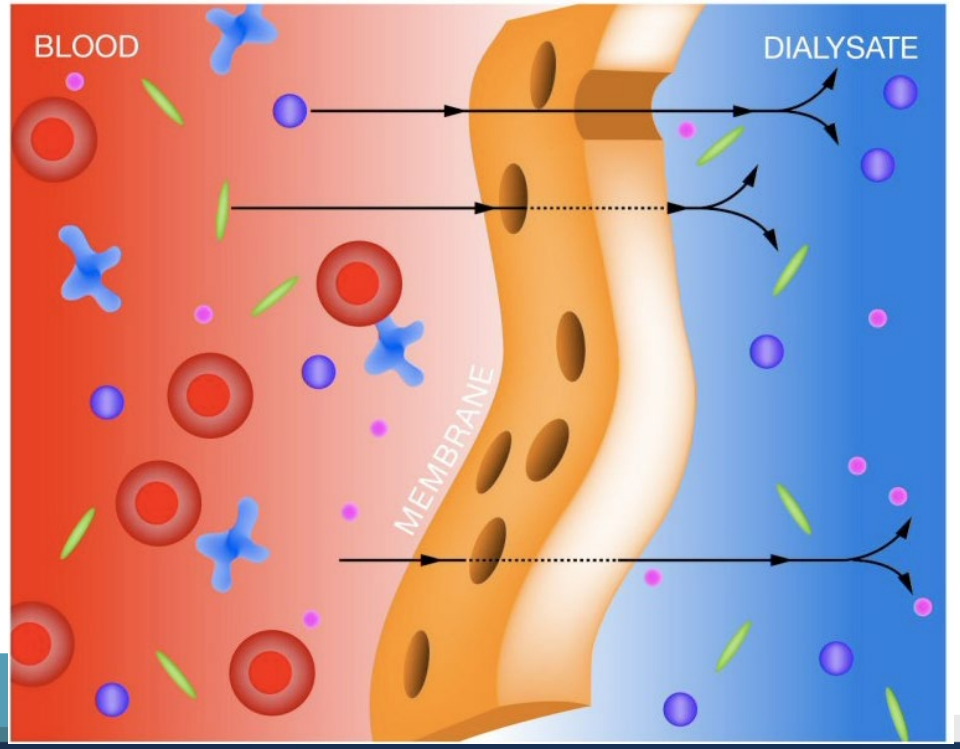
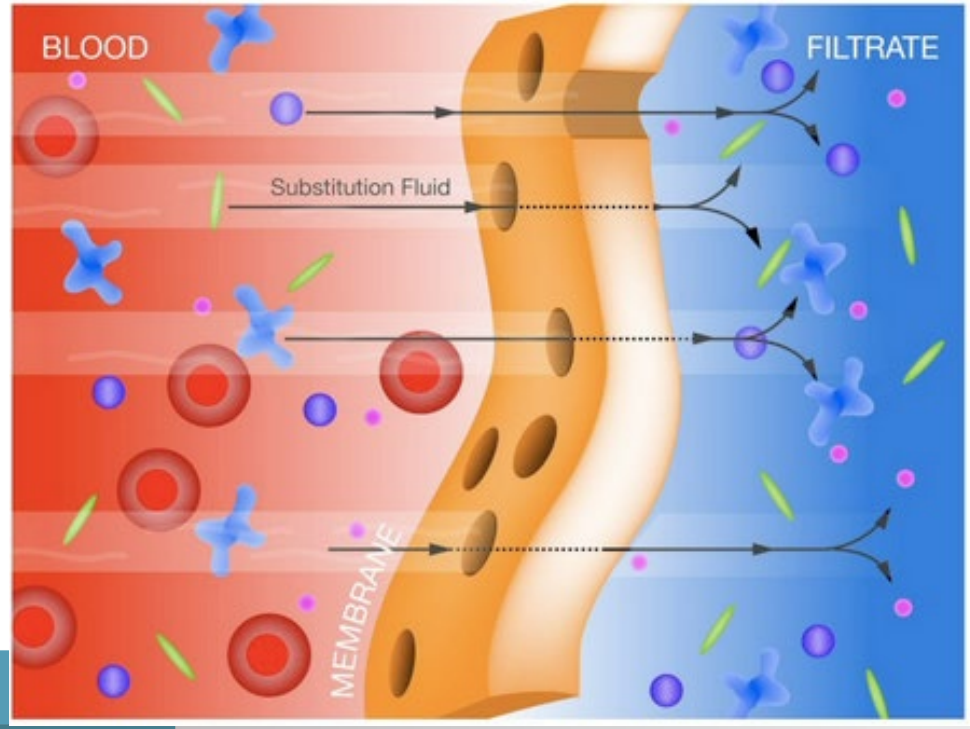



Photo from www.baxter.com

# Principles of Dialysis - Convection

- Movement of solutes with a water flow
  - “Solvent drag”

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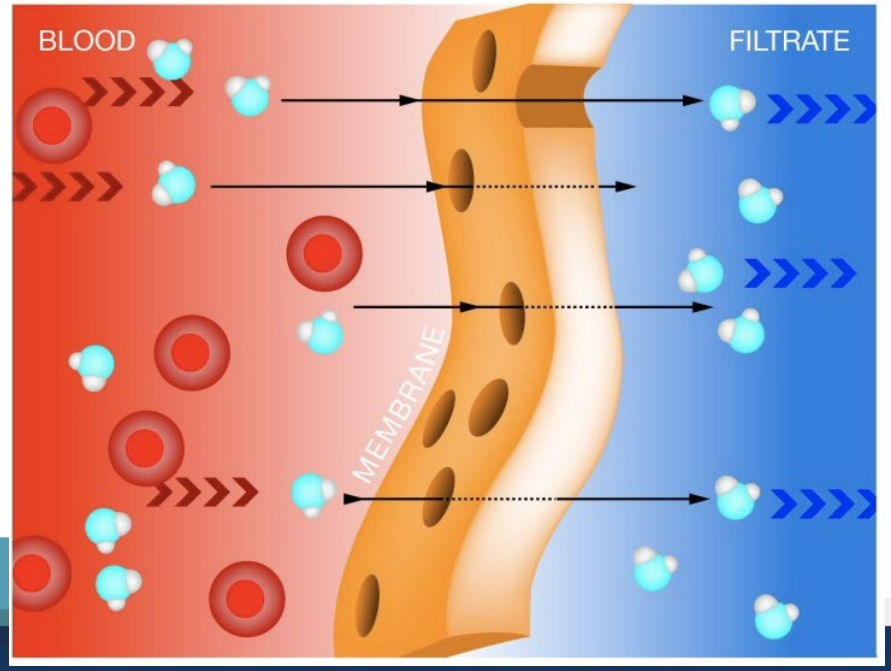
# Principles of Dialysis - Ultrafiltration

- Movement via a pressure gradient
  - Hydrostatic
  - Osmotic (impermeable solutes)

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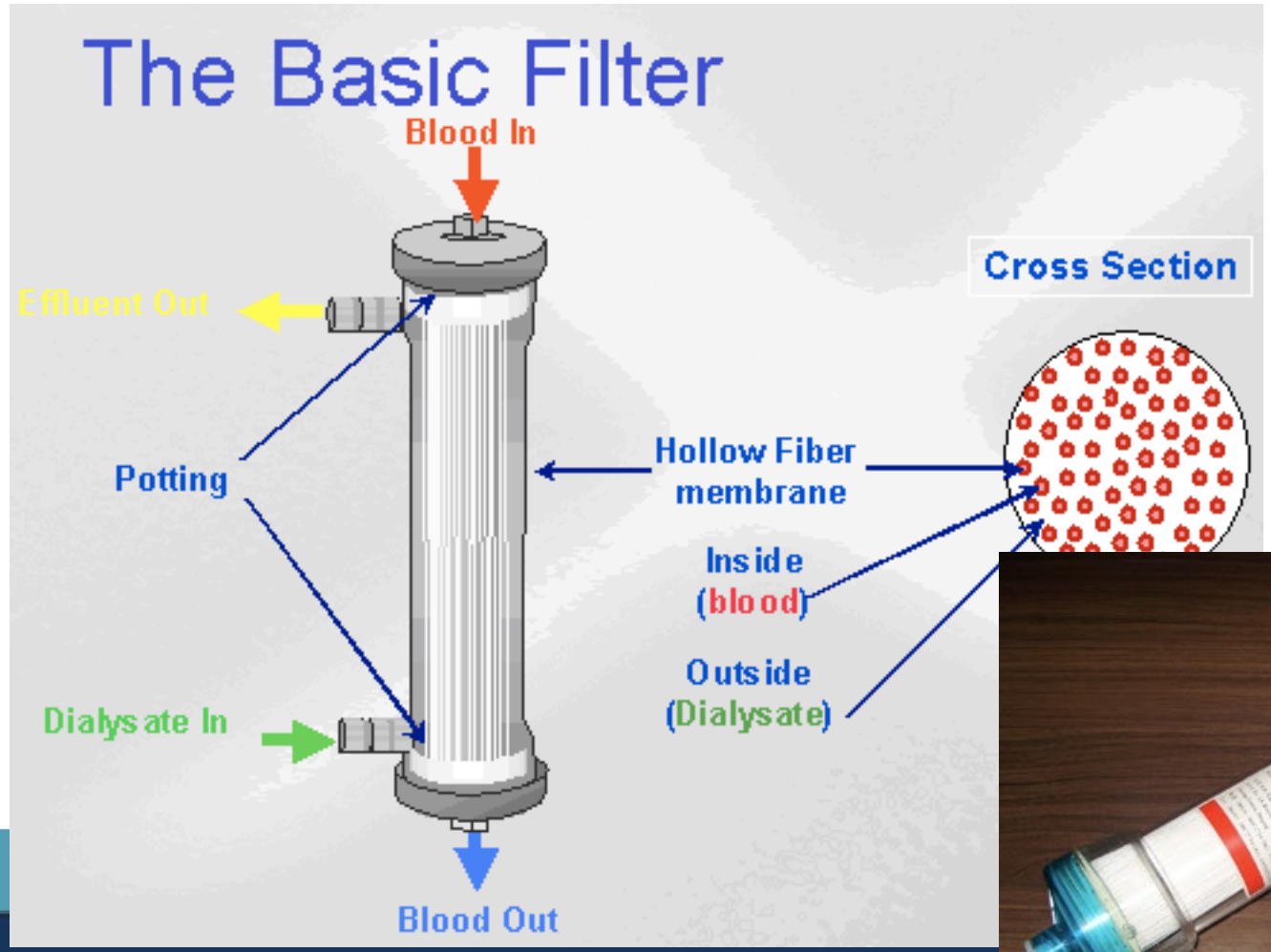
# The Hardware

- Intermittent Hemodialysis

- Continuous Renal Replacement

Images from Poeppel et al VCNA SA 2011

# Dialyzer




From Gambro.com and Ballya Health Care

# Dialysate

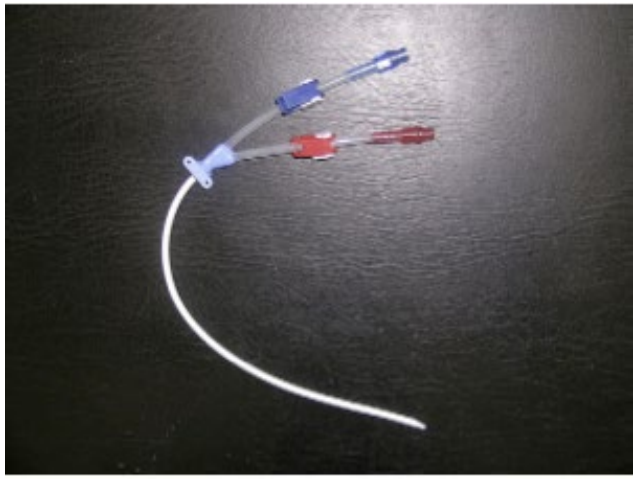
- Balanced electrolyte formula

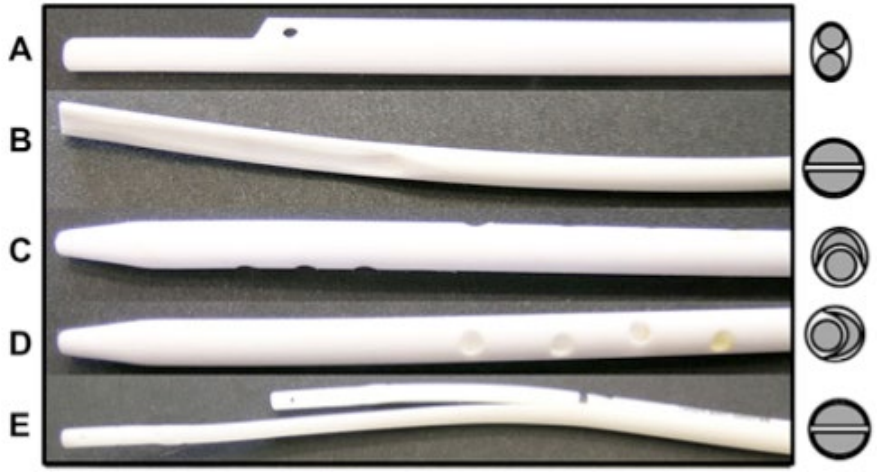
| Electrolyte | Concentration |
|---|---|
| Sodium | 140 mmol/l |
| Potassium | 1 mmol/l |
| Lactate | 45.5 mmol/l |
| Chloride | 102 mmol/l |
| Calcium | 1.6 mmol/l |
| Magnesium | 0.82 mmol/l |
| Glucose | 10.9 mmol/l |
| Osmolality | 285 mOsmol |

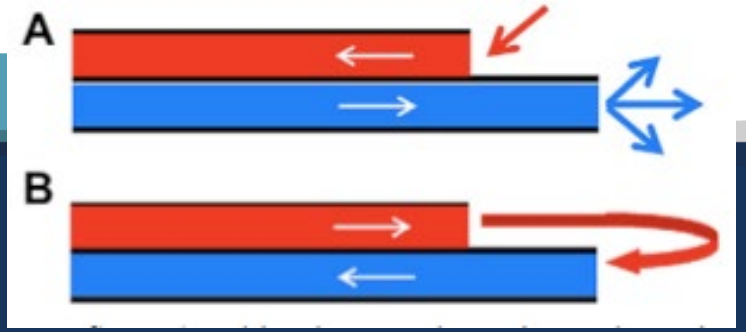
Commercially available fluid from Baxter

# Venous Access

- Large bore double lumen catheters
  - Cut-down vs. percutaneous
  - Temporary vs. permanent





# Coagulation and RRT

- Systemic anti-coagulation
  - Heparin IV
  - Monitor ACT
- Regional anti-coagulation
  - Calcium citrate in the circuit
  - Administer calcium in venous circuit

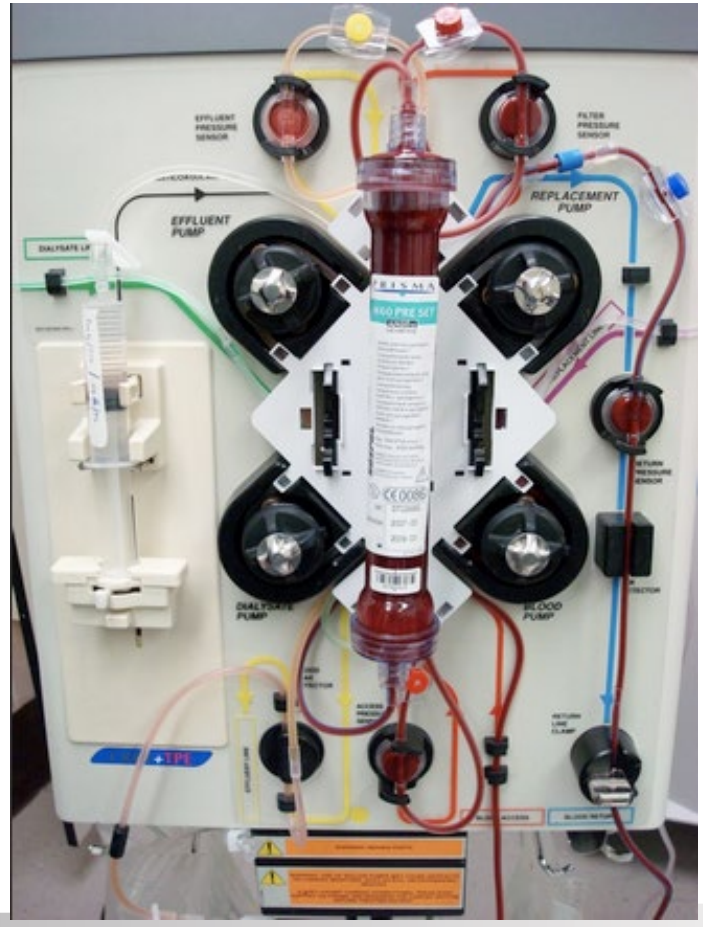
# Available Modalities for RRT

- Continuous renal replacement therapy (CRRT)
- Intermittent hemodialysis (IHD)
- Therapeutic Plasma Exchange (TPE)

# Continuous Renal Replacement Therapy (CRRT)

# Continuous Renal Replacement Therapy (CRRT)

- Continuous
- Removes solutes and fluids
- Slow flow rates
- Filters medium size molecules
- May be useful in sepsis

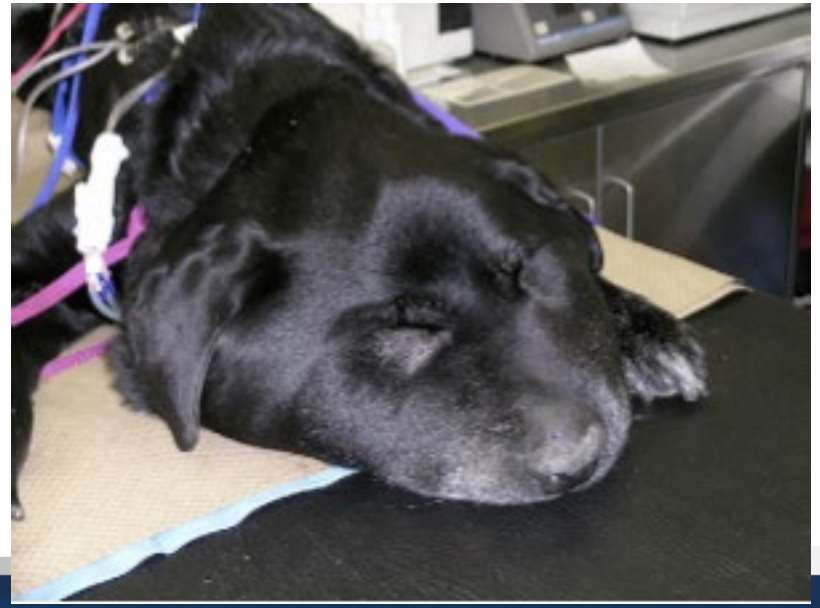


# Modalities of CRRT

- Slow continuous ultrafiltration (SCUF)
- Continuous veno-venous hemofiltration (CVVH)
- Continuous veno-venous hemodialysis (CVVHD)
- Continuous veno-venous hemodiafiltration (CVVHDF)

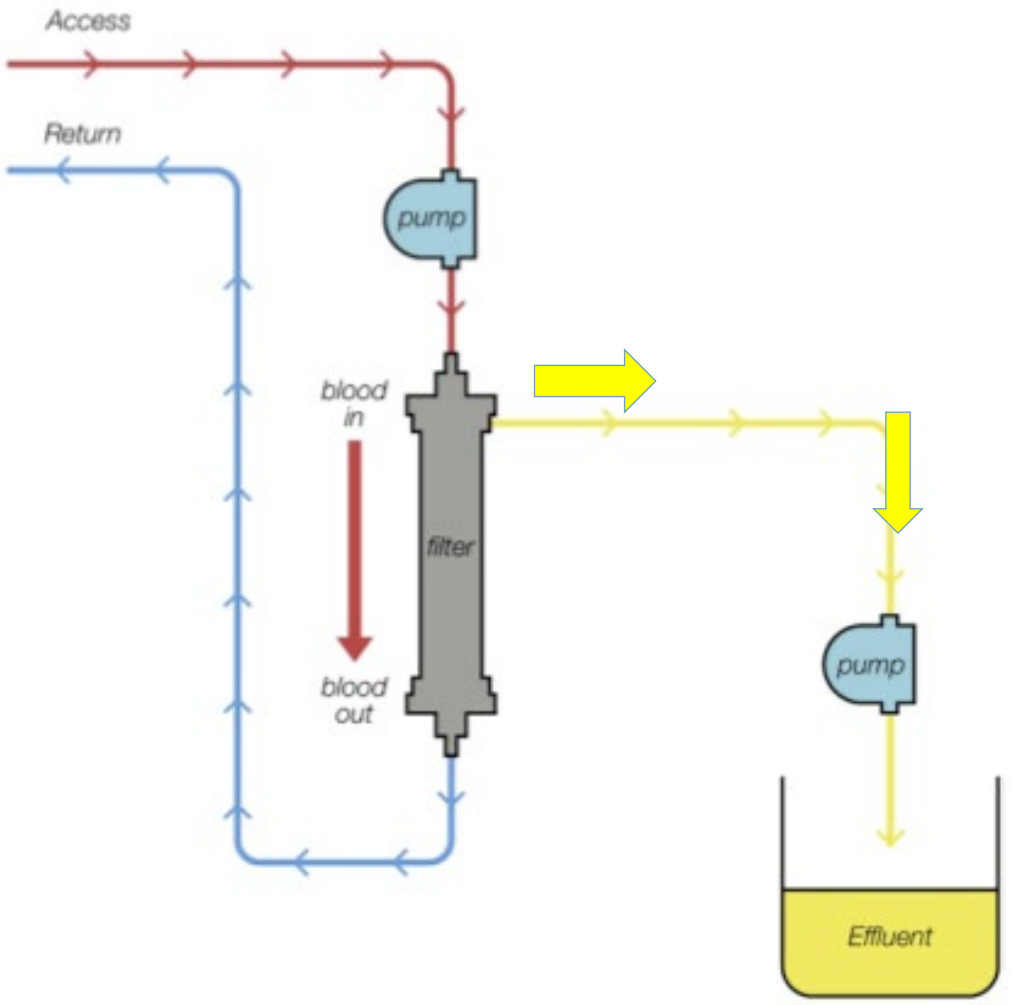
# Slow Continuous Ultrafiltration (SCUF)

- Slow removal of fluid via ultrafiltration
- Poor removal of solutes due to slow rates
- May be useful in:
  - Fluid overload
  - Congestive heart failure



From Calhoub et al VCNA 2011

# Slow Continuous Ultrafiltration (SCUF)

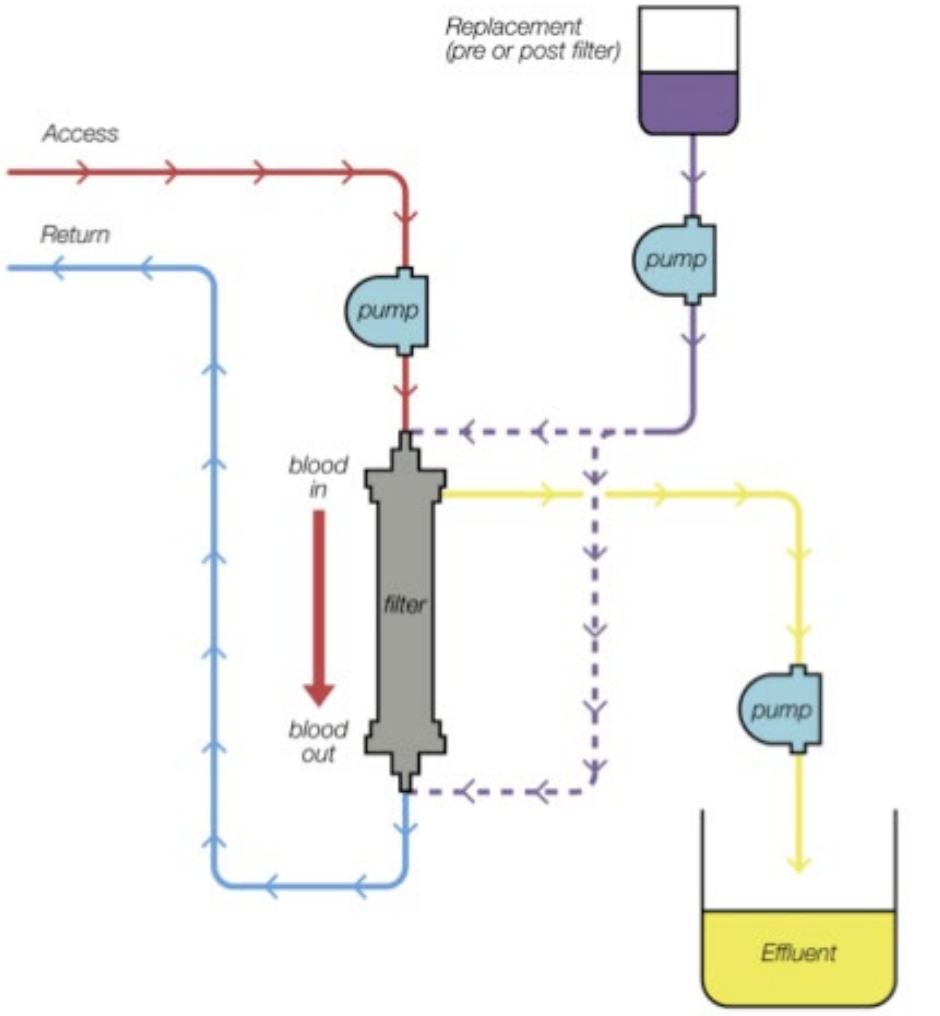



Adapted from Acierno M. 2011 VCNA-SA

# Continuous Veno-venous Hemofiltration (CVVH)

- Resultant solute drag (convection)
- Hemofiltration removes large amounts of fluid and solutes
- Replacement fluid necessary
  - Several liters daily

# Continuous Veno-venous Hemofiltration (CVVH)

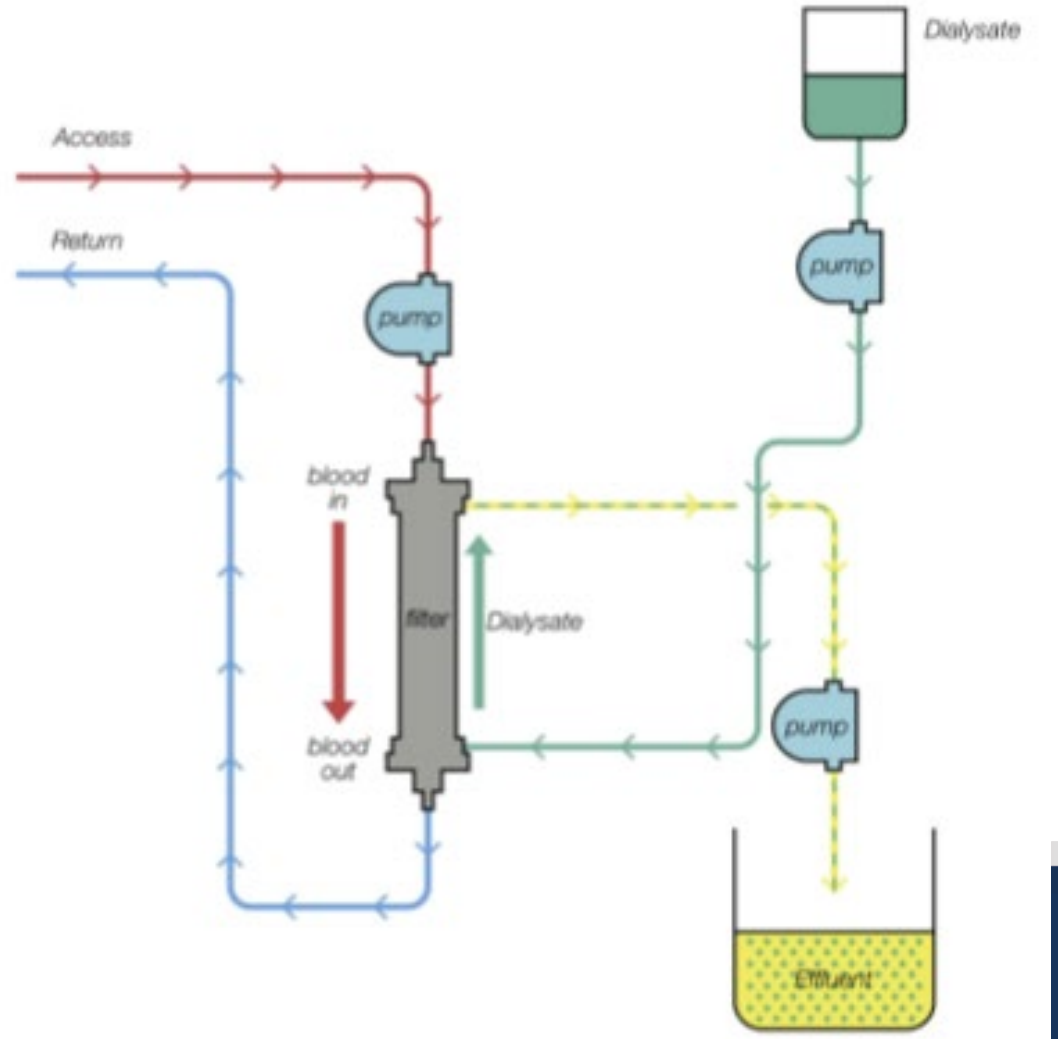



Adapted from Acierno M. 2011 VCNA-SA

# Continuous Veno-venous Hemodialysis (CVVHD)

- Uses diffusion to remove solutes
- Dialysate solution creates countercurrent mechanism
- Filters out toxins and allows bicarbonate in
- Slow rate of flow

# Continuous Veno-venous Hemodialysis (CVVHD)

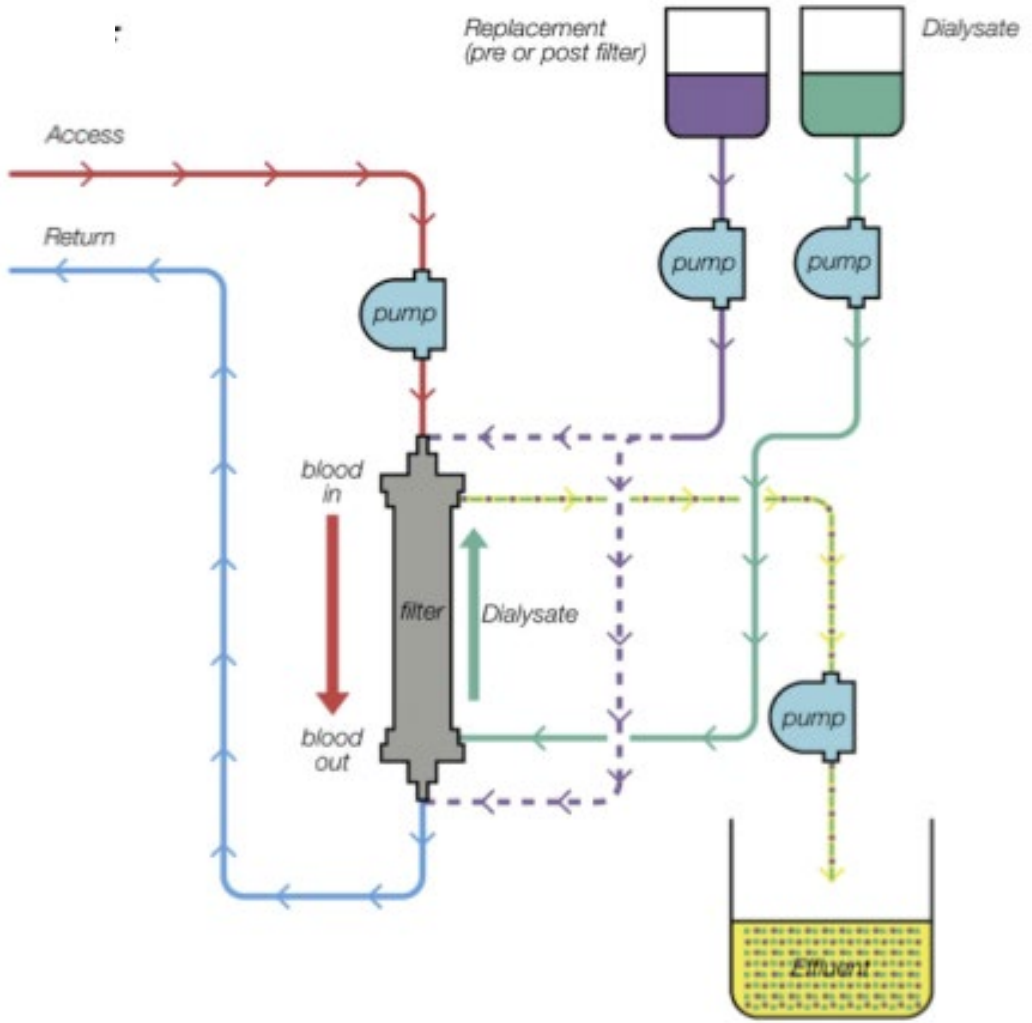



Adapted from Acierno M. 2011 VCNA-SA

# Continuous Veno-venous Hemodiafiltration (CVVHDF)

- Combines ultrafiltration, convection and diffusion
- Large amounts of replacement fluids needed
- Specialized dialysate fluid also used
- Potentially more effective than IHD or CRRT alone

# Continuous Veno-venous Hemodiafiltration (CVVHDF)

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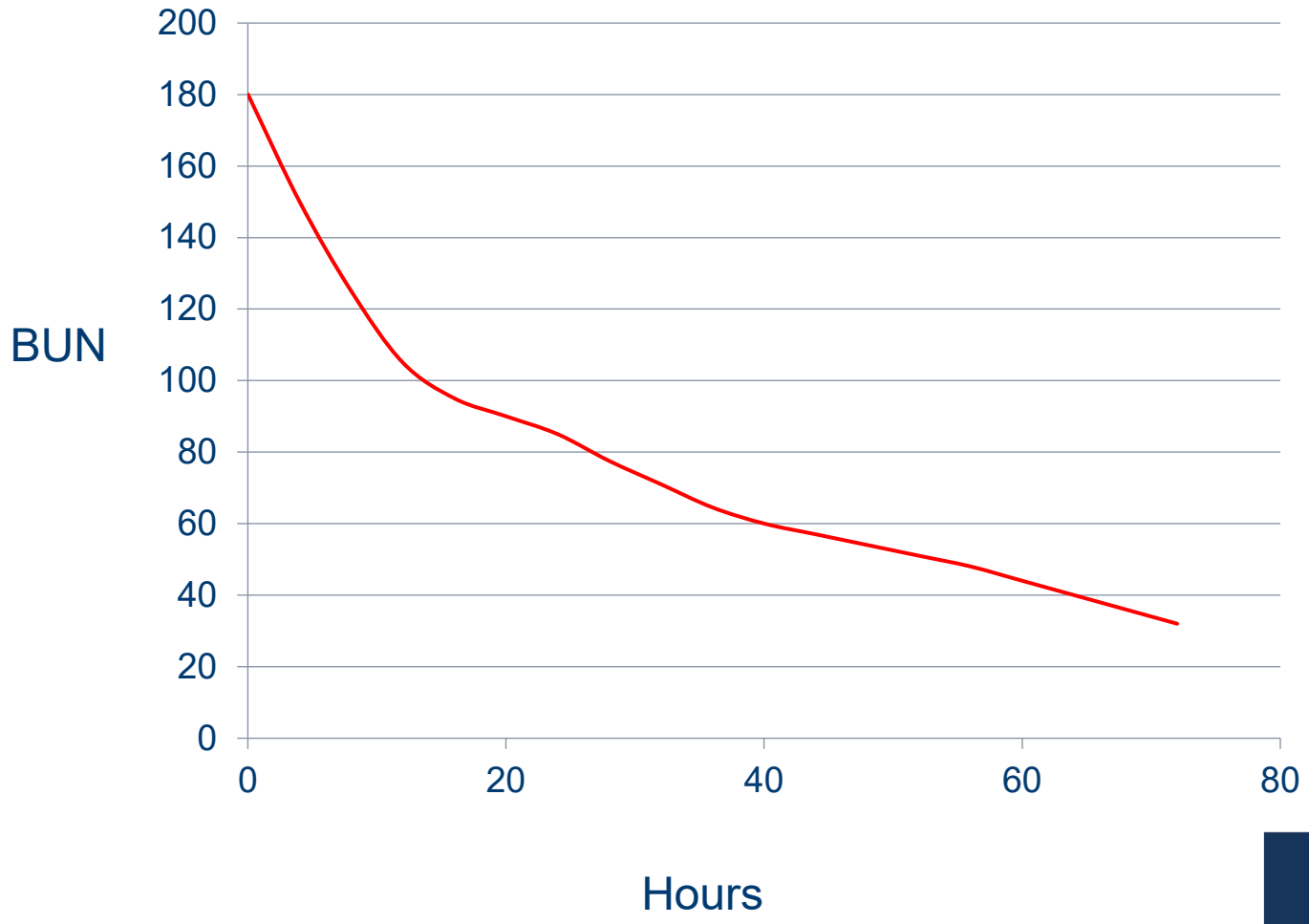
# Elimination of Solutes with CRRT

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# Complications of RRT

- Clotting of the filter
- Bleeding due to anti-coagulation
- Hemodynamic instability
- Disequilibrium syndrome

# Outcome with CRRT

- **Depends on underlying cause**
- Survival 40-60%
- Readily reversible causes have better outcomes
- Diehl S et al. 2008
  - CRRT decreased BUN, creatinine effectively
  - 41% dog survival, 44% cat survival

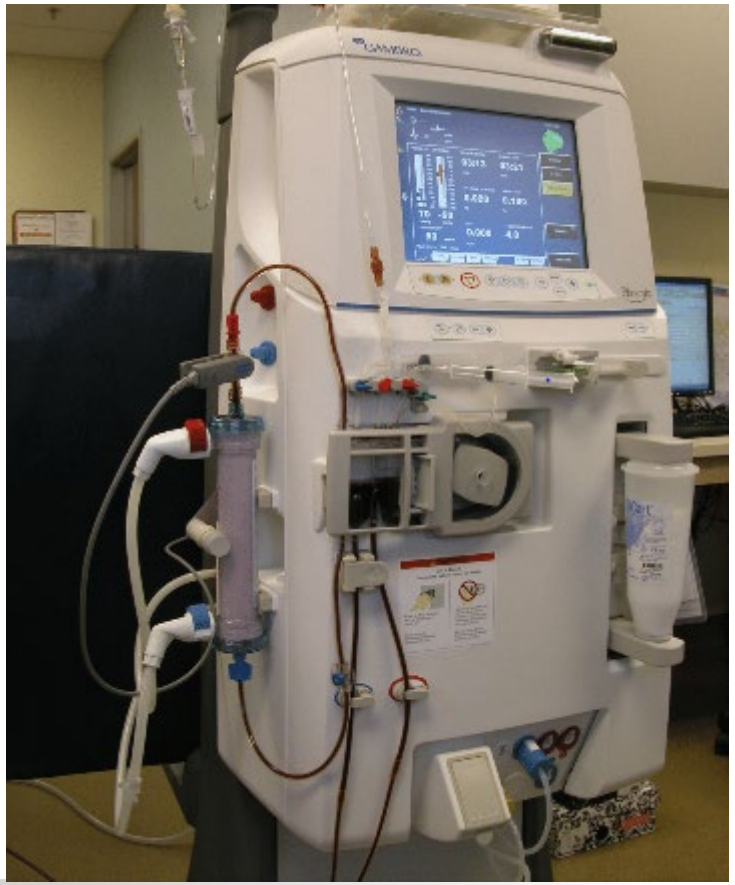
# Intermittent Hemodialysis (IHD)

# Intermittent Hemodialysis (IHD)

- Uses diffusion as its main filtration technic
- High flow rates increase clearance of toxi
- “Countercurrent mechanism”
- Filters small to medium size molecules

# Intermittent Hemodialysis (IHD)

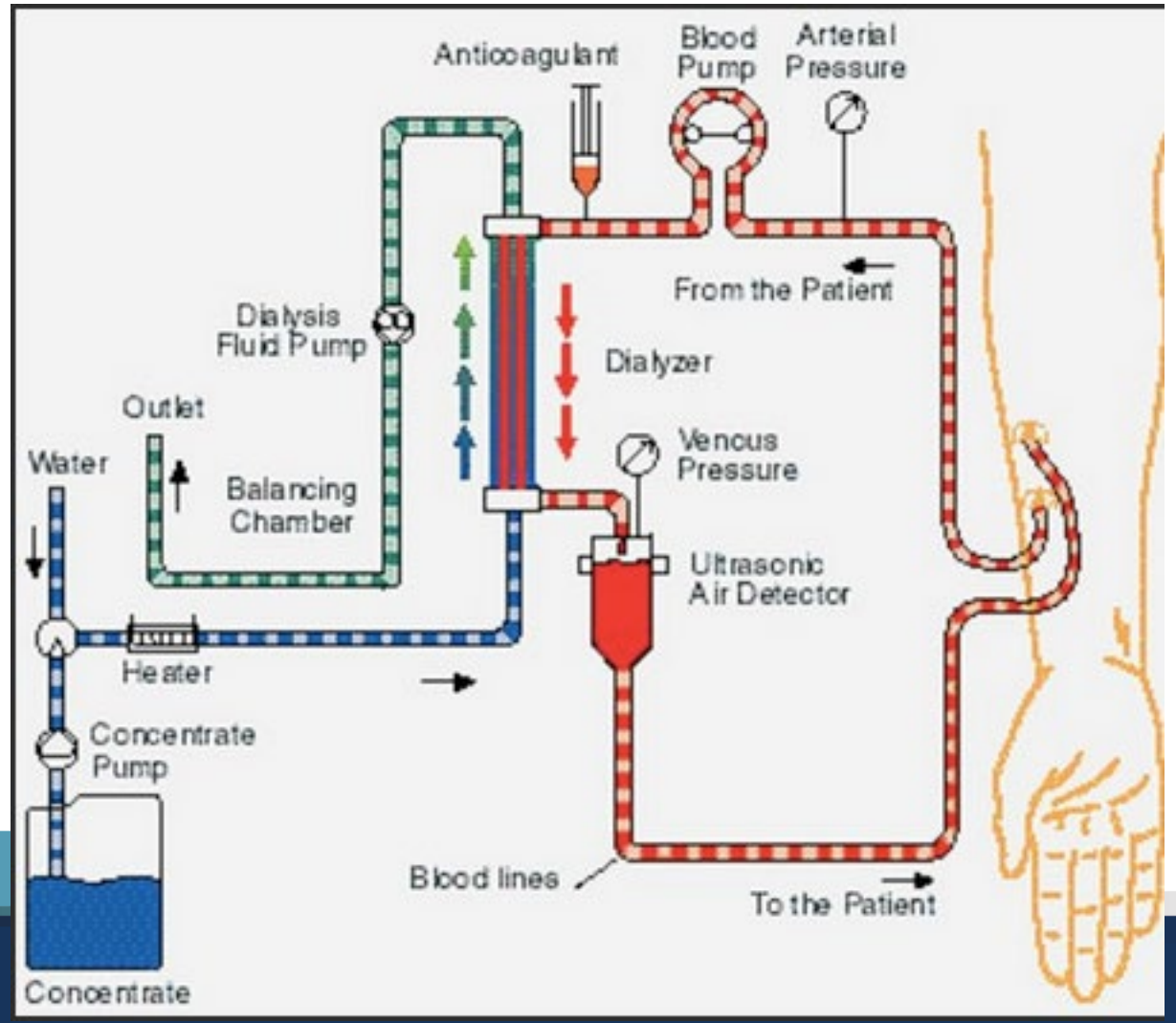
- Intermittent (3-5 hour treatments)
- Can cause hemodynamic instability
- Better for intoxications
- Standard for AKI and CKD in humans



# Intermittent Hemodialysis (IHD)

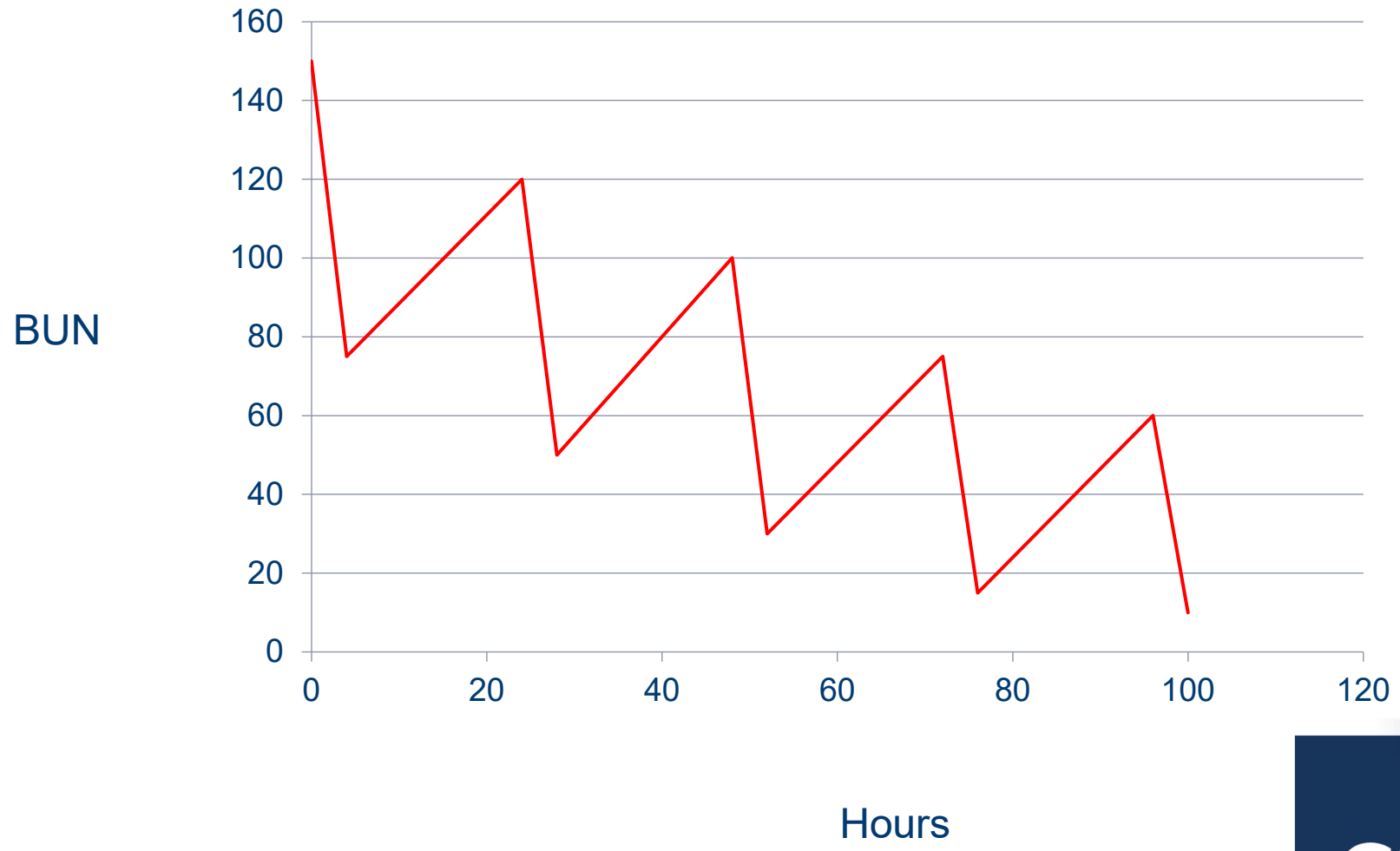
- Equipment
  - Water filtration/purification system
  - Venous access
  - Dialysis machine
  - Dialysis filter
  - Dialysate

# Intermittent Hemodialysis (IHD)




Adapted from www.sainternshipsnfs.com

# Elimination of Solutes with IHD

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# Complications of IHD

- Hypotension
- Bleeding due to anti-coagulation
- Clotting the dialyzer
- Dialysis disequilibrium
- Catheter related infection

# Outcome for IHD patients with AKI

- Retrospective case series
- 42 cats, 93 dogs
- Survival to discharge ~50%
- Survivors had a good long-term outcome


Fatroff et al. 2012 JAVMA

# How IHD and CRRT Compare

**Intermittent Hemodialysis**

- 3 – 6 hours per session
- “Saw-tooth”
- Highly purified $H_2O$ system
- Actively programmed/warmed dialysate
- Can cause hypotension

**Continuous Renal Replacement**

- Continuous for up to 3 days
- Smooth curve
- Pre-made dialysate in bags
- No warming of solutions
- More physiologic
- Better for unstable pets
- Removes $H_2O$ better

# Therapeutic Plasma Exchange (TPE)

# Therapeutic Plasma Exchange (TPE)

- Removal of a patient's blood via a dialysis catheter
- Separation of blood and plasma
  - Filter vs. Centrifugation
- Replace plasma with donor plasma
- Reunite with patient's blood and return to patient

# Indications for TPE

- Toxicities
  - NSAIDs
- Neuromuscular disease
  - Myasthenia gravis
  - Polyradiculoneuritis
  - Acute Polymyositis
- Metabolic/Kidney Disease
  - Acute hepatic failure
  - Lyme nephritis
  - Systemic lupus
- Hematologic disease
  - IMHA (refractory)
  - ITP (refractory)
  - Hyperviscoscity Syndrome
- Miscellaneous
  - Drug overdose (drug dependent)
  - Exogenous toxin removal
  - Pemphigus foliaceus

# Outcomes of TPE

- Mostly anecdotal at this time
- Unpublished data (UC Davis) shows increased survival for refractory IMHA cases
- JVIM 2020; TPE safe in ITP and improved Plt counts in 3 of 4 patients
- Toxicity outcomes:
  - Largely based on time to initiation of treatment
  - Dependent on how efficiently toxin can be removed
- Further studies are needed

# What is Available for Your Patients at MV?

- PrismaFlex Machine
  - CRRT available
  - TPE available
- AK98 Intermittent Dialysis Machine
  - Available Q3, 2021
- Please call our Dialysis Team if you have a case that may be a good candidate for extracorporeal therapy!!
  - Max Parkanzky
  - Jordan Scherk
  - Liz Lee
  - Josh Rosenbaum


Questions?

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