Go with the Flow: The Development & Implementation of a Continuous Renal Replacement Therapy (CRRT) Program

A presentation for HealthTrust members
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Pharmacist & Nurse Objectives

- Describe the indications for intermittent and continuous renal replacement therapy.
- Identify the key tools and team members necessary for the development and implementation of a continuous renal replacement therapy (CRRT) program.
- Describe the administrative and clinical roles of the Department of Pharmacy and Department of Nursing for a CRRT program.

Pharmacy Technician Objectives

- Recall the indications for intermittent and continuous renal replacement therapy.
- Identify the key tools and team members involved with the implementation of a CRRT program.

Indications for Renal Replacement Therapy (RRT)

Acidosis

- Metabolic acidosis

Electrolytes

- Specifically potassium

Intoxication

- Medications

Overload

- Fluid overload

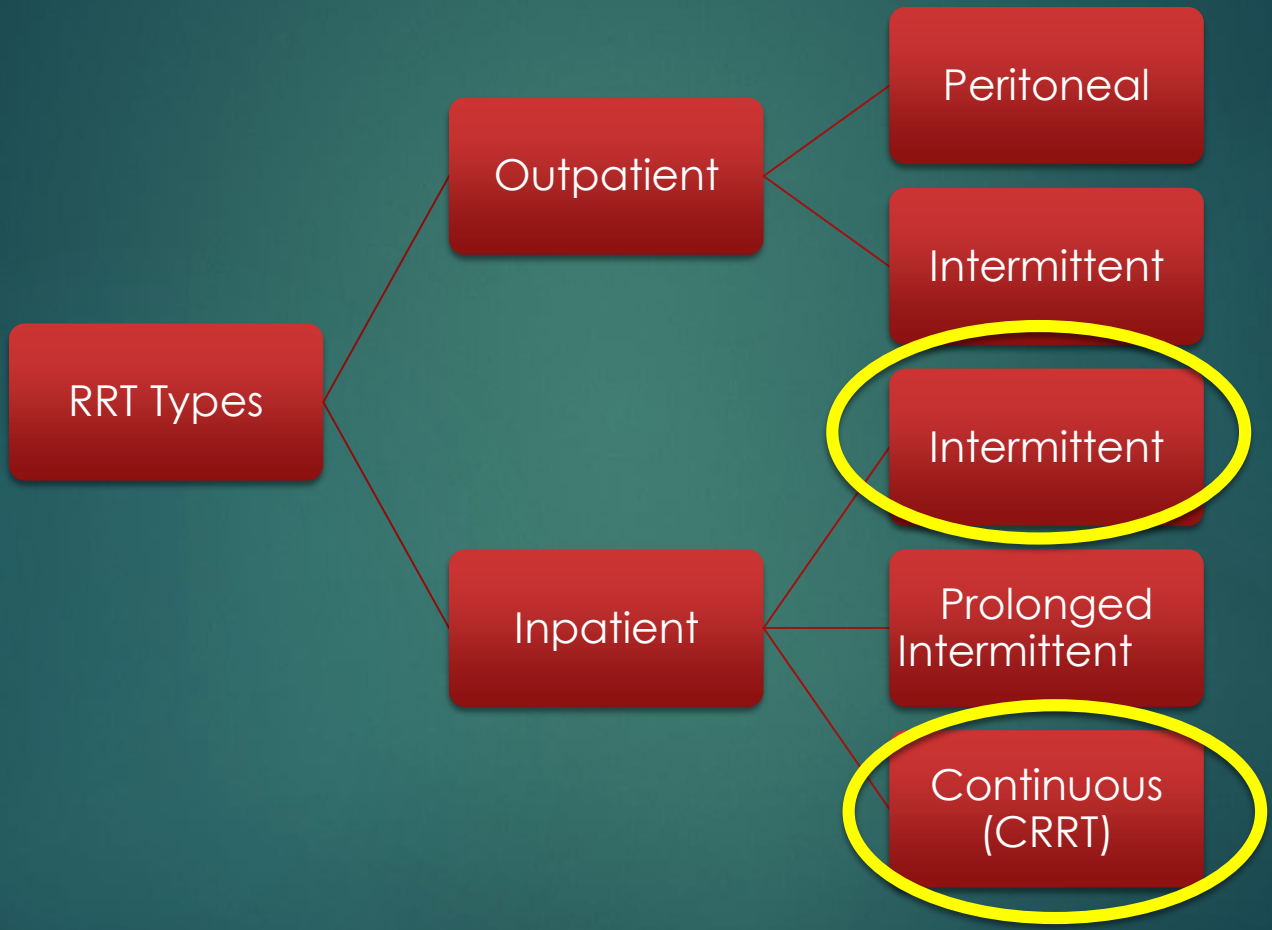
Uremia

- Elevated blood urea nitrogen (BUN) may alter patient status

Contraindications for RRT

- Advanced directives
- Patient or family refusal
- Inability to achieve vascular access

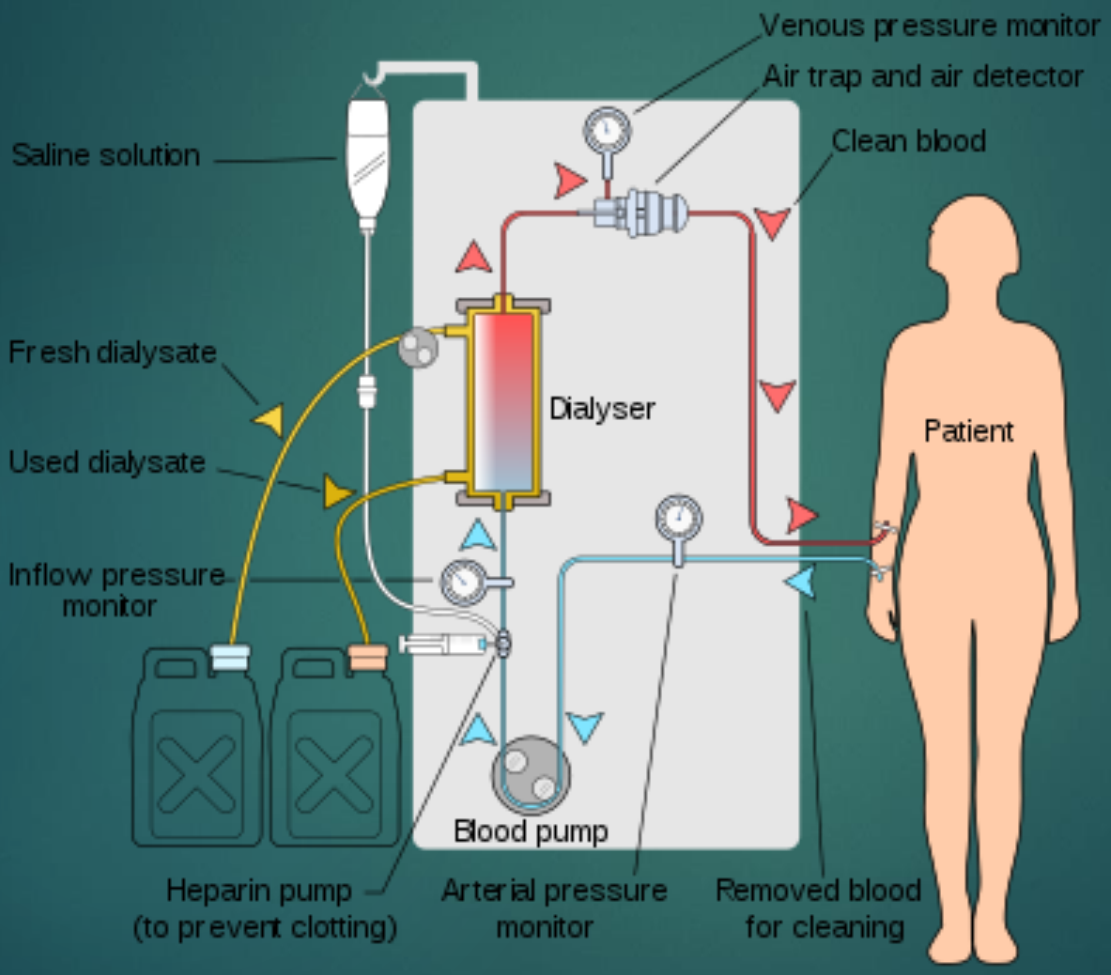
RRT Types


RRT Types
Outpatient
Peritoneal
Intermittent
Inpatient
Intermittent
Prolonged Intermittent
Continuous (CRRT)

CRRT and IHD Comparison

	CRRT	IHD
Continuous	Y	N
Rapid Change in Electrolytes, pH, and fluid balance	N	Y
Need to Reduce Dose of Renally-Eliminated Medications	Depends	Y
Need to Limit Protein, Electrolytes, and Fluid Intake	N	Y
pH and Electrolytes Shift After Therapy	N	Y

Intermittent Hemodialysis



Source: Wikipedia; https://en.wikipedia.org/wiki/Dialysis

Continuous Renal Replacement Therapy

- Types
  - CVVH: Continuous venovenous hemofiltration
  - CVVHD: Continuous venovenous hemodialysis
  - CVVHDF: Continuous venovenous hemodiafiltration

- Indicated for critically ill patients
  - 24 hours/day, 7days/week

CVVH

- Mechanism
  - No dialysate, removes plasma water as it seeps through membrane
  - Removes small and large molecules
    - Drug removal calculated based on sieving coefficient
    - Also depends on ultrafiltrate concentrate/plasma concentration

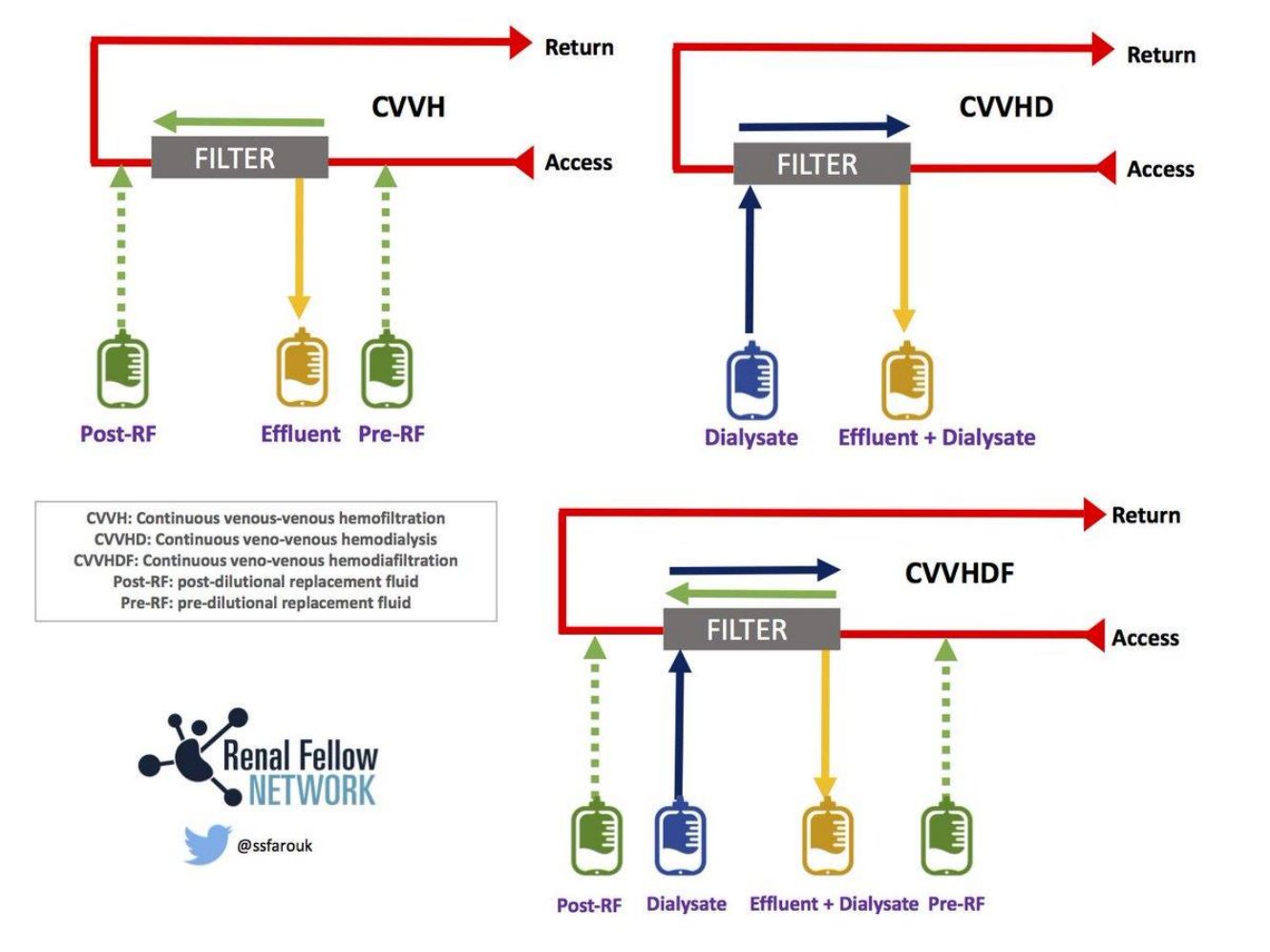
CVVHD

- Mechanism
  - Diffusion-based therapy
  - Blood is pumped through the compartment of the filter and dialysate flows counter currently
- Ideal for small solute removal (<500 Dalton)
- Results in small net volume removal (1-2 ml/hr)

CVVHDF

- Mechanism
  - Remove solutes through diffusion and convection
  - Counter-current flow (diffusion)
  - Plasma fluid infused (convection)
- Effective in removing more volume from patient, especially when fluid overloaded

CRRT Review



Source: https://www.renalfellow.org/2019/05/31/dosing-continuous-renal-replacement-therapies-crrt-what-is-enough/

CRRT Complications

- Bleeding
- Hypothermia
- Electrolyte imbalances
- Acid-base imbalances
- Infection risk
- Clot formation

Multidisciplinary Team

Pharmacist Question 1

- Which renal replacement modality would be best to use for a septic patient?
  A. Intermittent HD
  B. Continuous Renal Replacement Therapy
  C. Peritoneal Dialysis
  D. None

Pharmacist Response 1

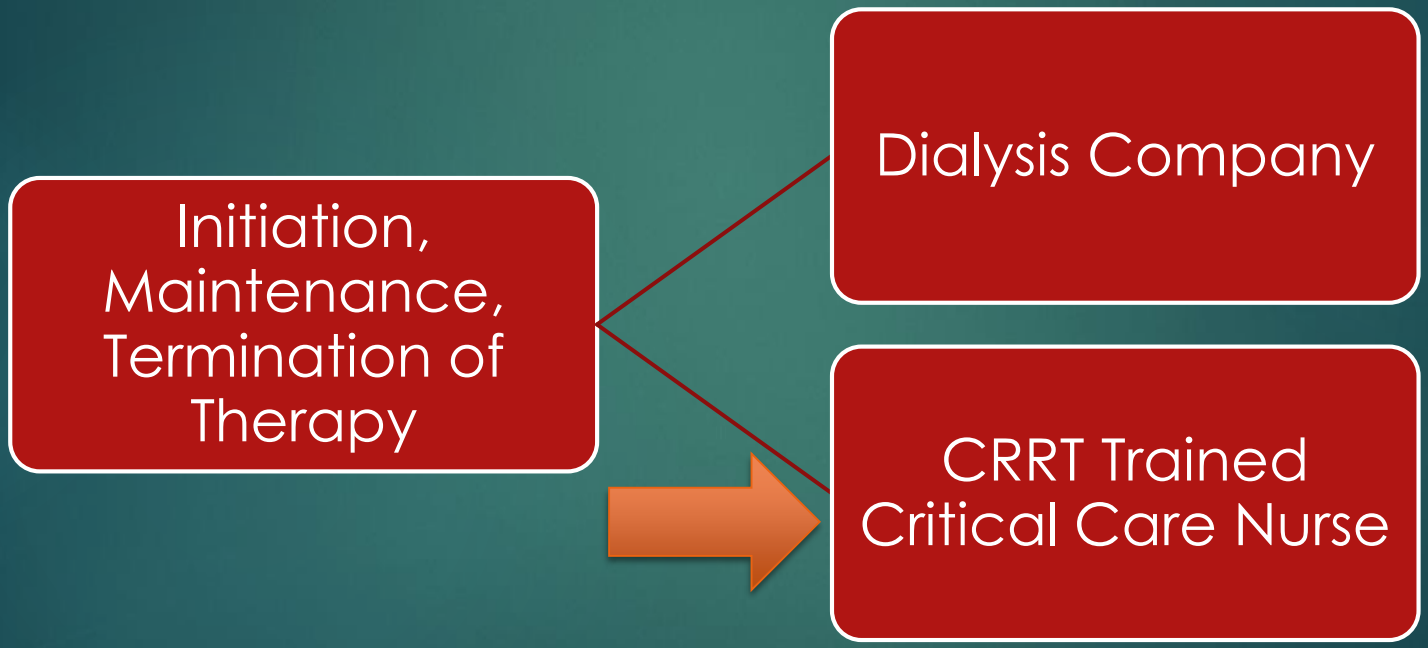
- Which renal replacement modality would be best to use for a septic patient?
  A. Intermittent HD
  B. **Continuous Renal Replacement Therapy**
  C. Peritoneal Dialysis
  D. None

Role of Nursing in CRRT Protocol Development

Nursing Roles

- Staffing Model
- Acquisition & Storage of Materials
- Education & Training
- Critical Care Nurse Responsibility
- Troubleshooting

Staffing Model



Staffing Model

Registered Nurse Responsible for CRRT:

- Hourly interventions
  - Examples:
    - Changing dialysate & effluent bags
    - Recording hourly pressures off machine
- Patient is hemodynamically unstable
- Recommended for these patients, have 1 nurse: 1 patient ratio

Nursing Roles

- Staffing Model
- Acquisition & Storage of Materials
- Education & Training
- Critical Care Nurse Responsibility
- Troubleshooting

Acquisition & Storage of Materials

- Machine
  - Rent or Own
  - NFRMC: 4 Rented through Dialysis Company
- Fluids
  - 5 L bags, all stored in locked cages
    - Dialysate: 4K
    - Replacement Fluid: 2K, 4K
- Filters
  - Different sizes available
  - Filter life is 72 hours

Acquisition and Storage of Materials

- Limited space in hospital
  - Most housed in off-site storage facility
    - Requires courier to bring to hospital
- Therapy initiated, notification required:
  - Supply Chain
  - Pharmacy
  - Administration

Nursing Roles

- Staffing Model
- Acquisition & Storage of Materials
- Education & Training
- Critical Care Nurse Responsibility
- Troubleshooting

Education & Training

- Scope: CVICU & ICU nurses
- NFRMC requires initial & yearly competency
- Dialysis Machine Representative
  - Didactic
  - Technical Skill Assessment

Education & Training

Registered Nurse:

- NFRMC Charting requirements
  - Patient Access Pressures
    - Access Pressure, Return Pressure
  - Dialysis Machine Pressures
    - Transmembrane Pressure, Filter Pressure
  - Hourly Ultrafiltration Rate

- Fluid Status
  - Per 24 hours
    - Net Even, Net Negative 1L, etc.
  - Account for:
    - Continuous medications
    - Intermittent bolus medications

Nursing Role

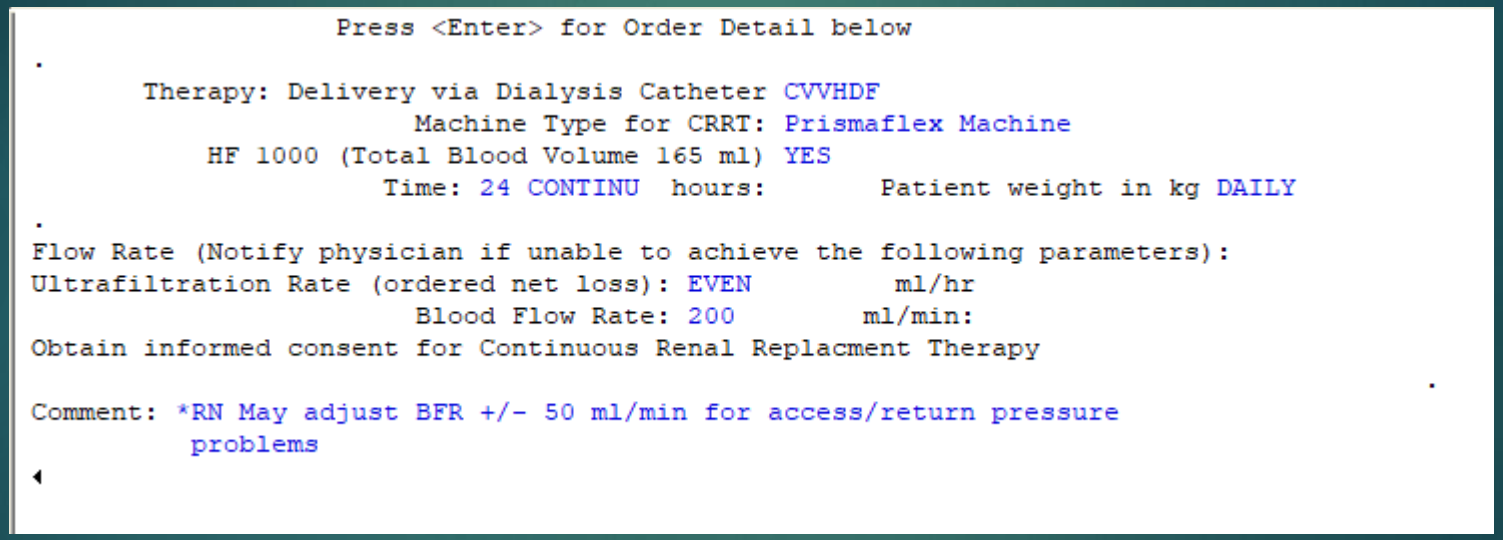
- Staffing Model
- Acquisition & Storage of Materials
- Education & Training
- Critical Care Nurse Responsibility
- Troubleshooting

Critical Care Nurse Responsibility

- Initiation:
  - Receive order
  - Prime the circuit
  - Begin therapy
    - Program per physician order
    - Monitor for hemodynamic changes
- Maintenance/Monitoring:
  - Dialysis machine
  - Patient hemodynamics
- Termination
  - Ending therapy

Critical Care Nurse Responsibility

- Programming Dialysis Machine



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                    Press <Enter> for Order Detail below
.
       Therapy: Delivery via Dialysis Catheter CVVHDF
                        Machine Type for CRRT: Prismaflex Machine
            HF 1000 (Total Blood Volume 165 ml) YES
                       Time: 24 CONTINU  hours:       Patient weight in kg DAILY
.
Flow Rate (Notify physician if unable to achieve the following parameters):
Ultrafiltration Rate (ordered net loss): EVEN          ml/hr
                         Blood Flow Rate: 200        ml/min:
Obtain informed consent for Continuous Renal Replacment Therapy

Comment: *RN May adjust BFR +/- 50 ml/min for access/return pressure
          problems
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Critical Care Nurse Responsibility

- Patient hemodynamics
  - Is the patient tolerating the fluid removal?
  - Blood pressure goal
- Labs
  - Monitor labs every 4 hours
    - Potassium, Magnesium, Phosphorus
      - Sodium Phosphate & Potassium Chloride replacements
  - Replacement fluid/Dialysate prescription

Critical Care Nurse Responsibility

- Effluent Bag
  - Emptying when full, usually every 2 hours
- Replacement Fluid/Dialysate Bag
  - 5L bags
  - Require changing every 3–4 hours depending on therapy prescription

Critical Care Nurse Responsibility

- Charting requirements
  - Dialysis machine
    - Transmembrane Pressure
    - Filter Pressure
  - Patient
    - Access Pressure
    - Return Pressure
  - Hourly ultrafiltration rate

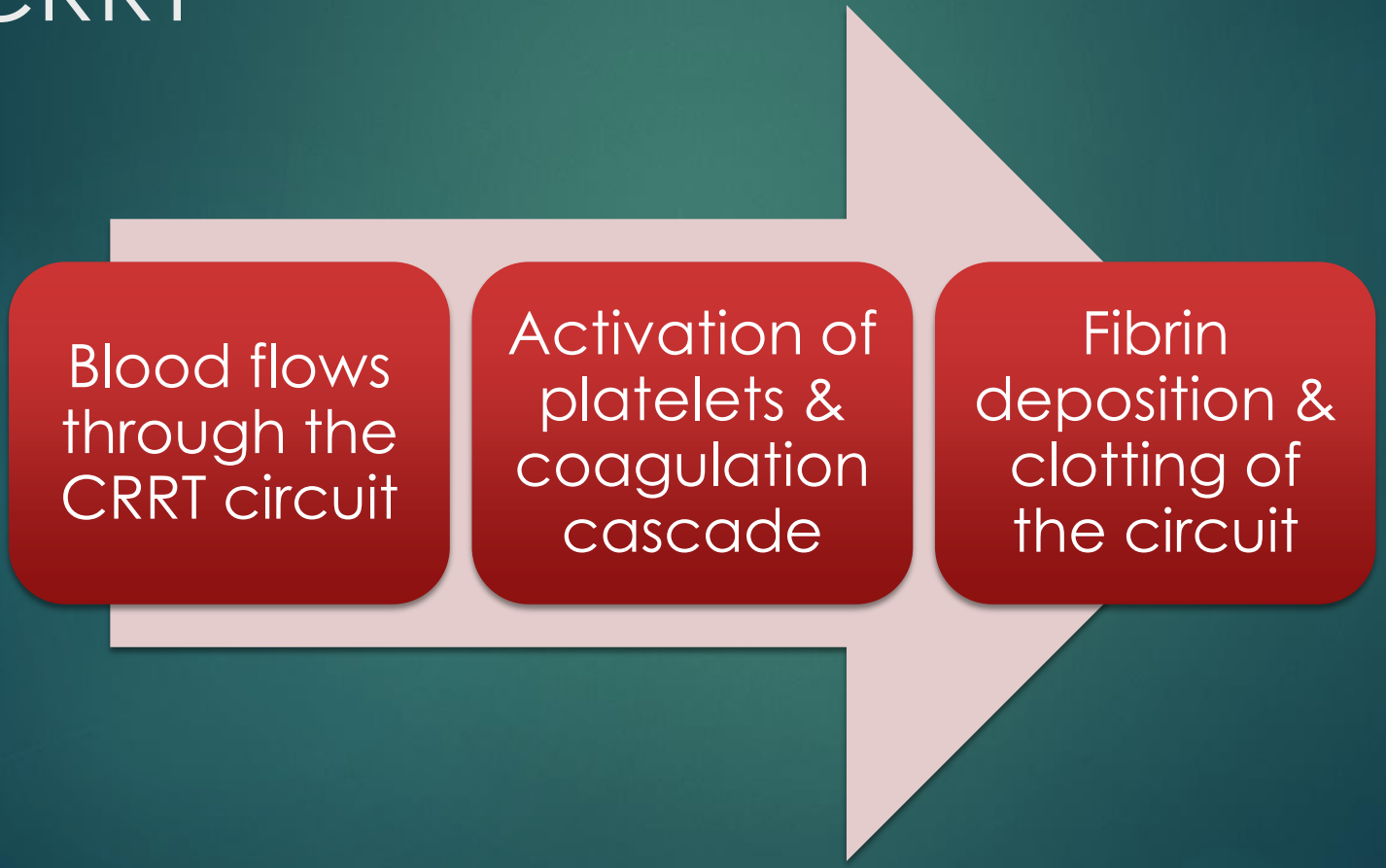
Nursing Role

- Staffing Model
- Acquisition & Storage of Materials
- Education & Training
- Critical Care Nurse Responsibility
- Troubleshooting

Troubleshooting

- Clotting
  - Increase the Pre Blood Pump Rate to thin blood prior to filter
  - Add Systemic Anticoagulation
  - Add Citrate + CaCl
- Clogging
  - Increase the Pre Blood Pump Rate

Troubleshooting: Anticoagulation Pathway in CRRT



Troubleshooting: Clotting Complications

- Reduced RRT treatment & time
- Increased expense, time & nursing workload
- Potential blood loss
- Affects solute and drug clearance with time off CRRT
- Increased infection risk

Troubleshooting: Clotting Management

Anticoagulation:
None: increase flow, change membrane
Heparin- Circuit
Citrate
Heparin- Systemic
Direct Thrombin Inhibitor

Troubleshooting: Clotting Management

Ultimately, the goal is to be able to return the blood to the patient, not lose in the filter.

Monitoring filter pressures can help identify when the blood return should take place.

Troubleshooting

- Hypotension
  - Decrease the Blood Flow Rate
  - Decrease Ultrafiltration Rate
  - Adjust Vasopressor Support

Nursing Question 1

- What do you do when your patient's blood pressure drops?
  A. Give a fluid bolus
  B. Return blood and terminate treatment
  C. Reduce the ultrafiltration rate
  D. Stop blood pump

Nursing Response 1

- What do you do when your patient's blood pressure drops?
  A. Give a fluid bolus
  B. Return blood and terminate treatment
  C. **Reduce the ultrafiltration rate**
  D. Stop blood pump

Nursing Question 2

- Which of the following is NOT an intervention for filter clotting?
  A. Initiate systemic anticoagulation
  B. Decrease pre-blood pump rate
  C. Increase blood pump rate
  D. Initiate Citrate

Nursing Response 2

- Which of the following is NOT an intervention for filter clotting?
  A. Initiate systemic anticoagulation
  B. Decrease pre-blood pump rate
  C. Increase blood pump rate
  D. Initiate Citrate

Role of a Pharmacist in CRRT Protocol Development

Pharmacist Roles

- Medication Dosing
- Anticoagulation
- Purchasing & distribution of certain products
- Education

Considerations for Medication Dosing

Utilize Higher Doses	Decreased Dosing
Retained non-renal clearance in AKI	Concern for toxicity
Ensure adequate concentration in infected site	Decreased renal clearance
Extracorporeal drug clearance	Reduced drug costs
Increased antimicrobial resistance	
Increased volume of distribution and decreased protein binding	

Dosing of Medications

- CRRT therapies clear mostly renally excreted medications
- Drug removal dependent on
  - Small volume of distribution
  - Not protein bound
  - Molecular weight
  - Sieving coefficient

Medication Changes in a Critically Ill Patient

Pharmacokinetic Changes	Ability to Reach Pharmacodynamic Target
Fluid overload	Reduced ability
Decreased serum albumin/decreased protein binding	Mixed effects
Retained non-renal clearance	Reduced ability
CRRT initiation	Reduced ability
Augmented renal function	Reduced ability

CRRT and Pharmacodynamics

Objective

- Determine optimal dosing of antibiotic during CRRT

Method

- Obtain serum concentration and must be maintained 4x minimum inhibitory concentration (MIC)

Results

- 53 patients enrolled
  - 81% meropenem 1000 mg IV q12h
  - 71% piperacillin/tazobactam 4.5 g IV q6h
  - 53% ceftazidime 2 g IV q12h
  - O% cefepime 2 g IV q12h

SOURCE: Seyer L, et al. Critical Care 2011;15:R137

Pharmacist Roles

- Medication Dosing
- Anticoagulation
- Purchasing & distribution of certain products
- Education

Troubleshooting: Clotting Management

Anticoagulation:
None: increase flow, change membrane
Heparin- Circuit
Citrate
Heparin- Systemic
Direct Thrombin Inhibitor

Heparin

ORDERS **NOT CHECKED** ARE NOT TO BE FOLLOWED

ALLERGIES:

ORDERS WITH CHECK BOXES MUST BE SELECTED. ALL OTHER ORDERS WILL BE AUTOMATICALLY INITIATED

1. **Patient's measured weight: _____ kg**

2. **Obtain baseline CBC, aPTT, INR, Anti-Xa unfractionated heparin (UFH) prior to starting heparin infusion**

3. Indication: ☐ Acute MI ☐ Unstable Angina ☐ Acute Coronary Syndrome ☐ Atrial Fibrillation ☐ Pulmonary Embolism ☐ Venous Thromboembolism ☐ Other: _____

4.

☐ **Standard Dose Protocol** (Recommended for use in DVT, Pulmonary Embolism, Atrial Fibrillation, Valvular Heart Disease, Valve Replacement, Arterial Thrombus, Left ventricular thrombus) Goal anti-Xa UFH 0.3-0.7 units/mL	☐ **Low Dose Protocol** (Recommended for use in Acute Coronary Syndrome and Neuroscience Patients) ☐ **No Boluses to be administered** (Recommended for Neuroscience Patients) Goal anti-Xa UFH 0.3-0.5 units/mL
Initial heparin IV bolus (Rounded to the nearest 500 units) Heparin 80 units/kg = _____ units **(Maximum INITIAL loading dose 10,000 units)**	Initial heparin IV bolus (Rounded to the nearest 500 units) Heparin 60 units/kg = _____ units **(Maximum INITIAL loading dose 4000 units)**
Heparin IV infusion 25,000 units/250 mL 0.45% sodium chloride at **18** units/kg/hour = _____ units/hour = _____ mL/hour Heparin infusion concentration: 100 units/mL	Heparin IV infusion 25,000 units/250 mL 0.45% sodium chloride at **12** units/kg/hour = _____ units/hour = _____ mL/hour **(Maximum INITIAL infusion 1000 units/hour)** Heparin infusion concentration: 100 units/mL
RN to adjust heparin based upon the following:	RN to adjust heparin based upon the following:

Anti-Xa UFH value	IVP Bolus Dose	Infusion Rate Change	Anti-Xa UFH value	IVP Bolus Dose	Infusion Rate Change
Less than 0.1 Units/mL	80 units/kg and (Max 10,000 units)	Increase 4 units/kg/hr	Less than 0.1 Units/mL	60 units/kg and (Max 4000 units)	Increase 4 units/kg/hr
0.1 - 0.29 Units/mL	40 units/kg and (Max 10,000 units)	Increase 2 units/kg/hr	0.1 - 0.29 Units/mL	30 units/kg and (Max 4000 units)	Increase 2 units/kg/hr
0.3 - 0.7 Units/mL	NONE and	NO CHANGE	0.3 - 0.5 Units/mL	NONE and	NO CHANGE
0.71 - 1 Units/mL	NONE and	Decrease 2 units/kg/hr	0.51 - 1 Units/mL	NONE and	Decrease 2 units/kg/hr
Greater than 1 Unit/mL	Hold heparin infusion for 1 hour and	Decrease 3 units/kg/hr	Greater than 1 Unit/mL	Hold heparin infusion for 1 hour and	Decrease 3 units/kg/hr

☐ **Prescriber Defined Heparin Infusion** 25,000 units/250 mL 0.45% Sodium Chloride (100 units/mL)

Initial heparin IV bolus (Rounded to the nearest 500 units): _____ units = _____ units/kg

Heparin IV infusion (Rounded to the nearest 100 units per hour) at _____ units/hour = _____ mL/hour OR _____ units/kg/hour = _____ mL/hour

Dose Adjustment: Prescriber is to order subsequent rate adjustments, additional boluses and appropriate labs using standard provider order processes.

5. Additional orders:
   - ☑ NO IM INJECTIONS
   - ☑ CBC every 3 days
   - ☑ Anti-Xa UFH 6 hours after initiation and after every infusion rate change. **Continue every 6 hours Anti-Xa UFH until 2 consecutive values are in therapeutic range.** Then, take Anti-Xa UFH every morning.

6. Notify the physician for any of the following:
   (1) Abnormal baseline PT, INR, aPTT, Anti-Xa UFH, or platelets
   (2) Acute bleeding or persistent oozing from IV sites
   (3) Changes in neurological status

7. Do not give enoxaparin, or any other low molecular weight heparin, while on heparin.

DTI

Weight-Based Argatroban Protocol

Instructions: Prescriber to check dose based on level of hepatic impairment for both initial dose and dose adjustments

Discontinue heparin and low molecular weight heparins (LMWH) including flushes

Obtain patient's actual body weight: _____ kg (1 kg = 2.2 lbs)

Obtain Baseline Laboratory Values: CBC, PTT, INR, Platelet Count, Hepatic Profile

Obtain all Argatroban infusion rates from the standardized chart on the reverse side of this form. See the Child-Pugh Grading of Hepatic Function to determine initial rate and dosage adjustments

Begin Argatroban 250 mg/250 mL by intravenous infusion

Initial Argatroban Rate: _____ mL/hour

☐ For patients **WITHOUT** hepatic impairment or **MILD** hepatic impairment (Child-Pugh Score below 7) begin Argatroban infusion at 2 mcg/kg/minute

☐ For patients **WITH** moderate to severe hepatic impairment (Child-Pugh Score equal to or above 7), begin Argatroban infusion at 0.5 mcg/kg/minute

Dosage Adjustment - Nursing to adjust infusion rate based on the PTT and the following chart
(Do not exceed 10 mcg/kg/minute total)

PTT (secs)	☐ Action for patients without hepatic impairment or mild hepatic impairment	☐ Action for patients with moderate or severe hepatic impairment
Below 30	Increase rate by 0.5 mcg/kg/minute	Increase rate by 0.25 mcg/kg/minute
30-39	Increase rate by 0.25 mcg/kg/minute	Increase rate by 0.125 mcg/kg/minute
40-75	No change	No change
76-90	Decrease rate by 0.25 mcg/kg/minute	Decrease rate by 0.125 mcg/kg/minute
Above 90	Hold Infusion 30 minutes, then decrease rate by 0.5 mcg/kg/minute	Hold Infusion 30 minutes, then decrease rate by 0.25 mcg/kg/minute

Standing Orders:

- PTT 3 hours after initiation, and after any infusion rate change
- PTT every morning
- Platelet Count every morning

Nursing to document all dosage changes and PTT results on physician order form

No IM injections

Call prescriber for any signs or symptoms of active bleeding

NOTE: Co-administration of Argatroban and Warfarin produces a combined effect on the laboratory measurement of INR values. See package insert for procedure to convert patient from Argatroban to Warfarin. For patients on Argatroban 2 mcg/kg/minute, an INR of 4 on cotherapy is usually used as the cut off for stopping Argatroban infusion.

Pharmacist Roles

- Medication Dosing
- Anticoagulation
- Purchasing & distribution of certain products
- Education

Electrolyte Protocol: Potassium

- **Potassium Chloride 40 meq in 100 mL**

- Begin infusion at 2 mEq/hr once serum potassium is less than/equal to 5 mmol/L
- Administer via blood return line

- CRRT Sliding Scale Adjustment:
- Serum [K] (mmol/L) less than 3.1—Call nephrologist
- Serum [K] (mmol/L) 3.1 – 3.3—Increase by 2 mEq/hr
- Serum [K] (mmol/L) 3.4 – 3.6—Increase by 1 mEq/hr
- Serum [K] (mmol/L) 3.7 – 3.9—Increase by 0.5 mEq/hr
- Serum [K] (mmol/L) 4 – 4.5—NO CHANGE (GOAL)
- Serum [K] (mmol/L) 4.6 – 4.8—decrease by 0.5 mEq/hr
- Serum [K] (mmol/L) 4.9 – 5.1—decrease by 1 mEq/hr
- Serum [K] (mmol/L) 5.2 – 5.3—decrease by 2 mEq/hr
- Serum [K] (mmol/L) greater than 5.3—Call nephrologist

- Stop infusion if CRRT has been paused or discontinued. Re-initiate infusion at previous rate if downtime is less than 4 hours. If downtime is 4 hours or greater, restart infusion at 2 mEq/hr once serum potassium is less than/equal to 5 mmol/L and follow sliding scale adjustments.

Electrolyte Protocol: Phosphate

- **Sodium phosphorous 15 mmol in 250 mL**
- Begin infusion at 2.5 mmol/hr once serum phosphorous is less than or equal to 3.4 mg/dL.
- Administer Via blood return line
- CRRT Sliding Scale Adjustment:
- Serum [PO4] (mg/dL) less than 1.5—Call nephrologist
- Serum [PO4] (mg/dL) 1.5 – 2.0—increase by 1 mmol/hr
- Serum [PO4] (mg/dL) 2.1 – 2.3—increase by 0.5 mmol/hr
- Serum [PO4] (mg/dL) 2.4 – 2.6—increase by 0.25 mmol/hr
- Serum [PO4] (mg/dL) 2.7 – 3.3—NO CHANGE (GOAL); continue monitoring
- Serum [PO4] (mg/dL) 3.4 – 3.6—decrease by 0.25 mmol/hr
- Serum [PO4] (mg/dL) 3.7 – 3.9—decrease by 0.5 mmol/hr
- Serum [PO4] (mg/dL) 4.0 – 4.5 —hold infusion for 3 hours; restart at 1 mmol/hr less than rate prior to hold
- Serum [PO4] (mg/dL) greater than 4.5—hold infusion for 6 hours; restart at 1.5 mmol/hr less than rate prior to hold
- Stop infusion if CRRT has been paused or discontinued. Re-initiate infusion at previous rate if downtime is less than 4 hours. If downtime is 4 hours or greater, restart infusion at 2.5 mmol/hr once serum phosphorous is less than or equal to 3.4 mg/dL and follow sliding scale adjustments.

Pharmacist Roles

- Medication Dosing
- Anticoagulation
- Purchasing & distribution of certain products
- Education

Education

- Provided education to pharmacy department
  - Mechanism of CRRT
  - Different types of CRRT
  - Medication dosing
  - Monitoring
- Provided education to nursing
  - Pharmacist must be informed for dose adjustments if CRRT is stopped for >4 hours

Pharmacy Question 2

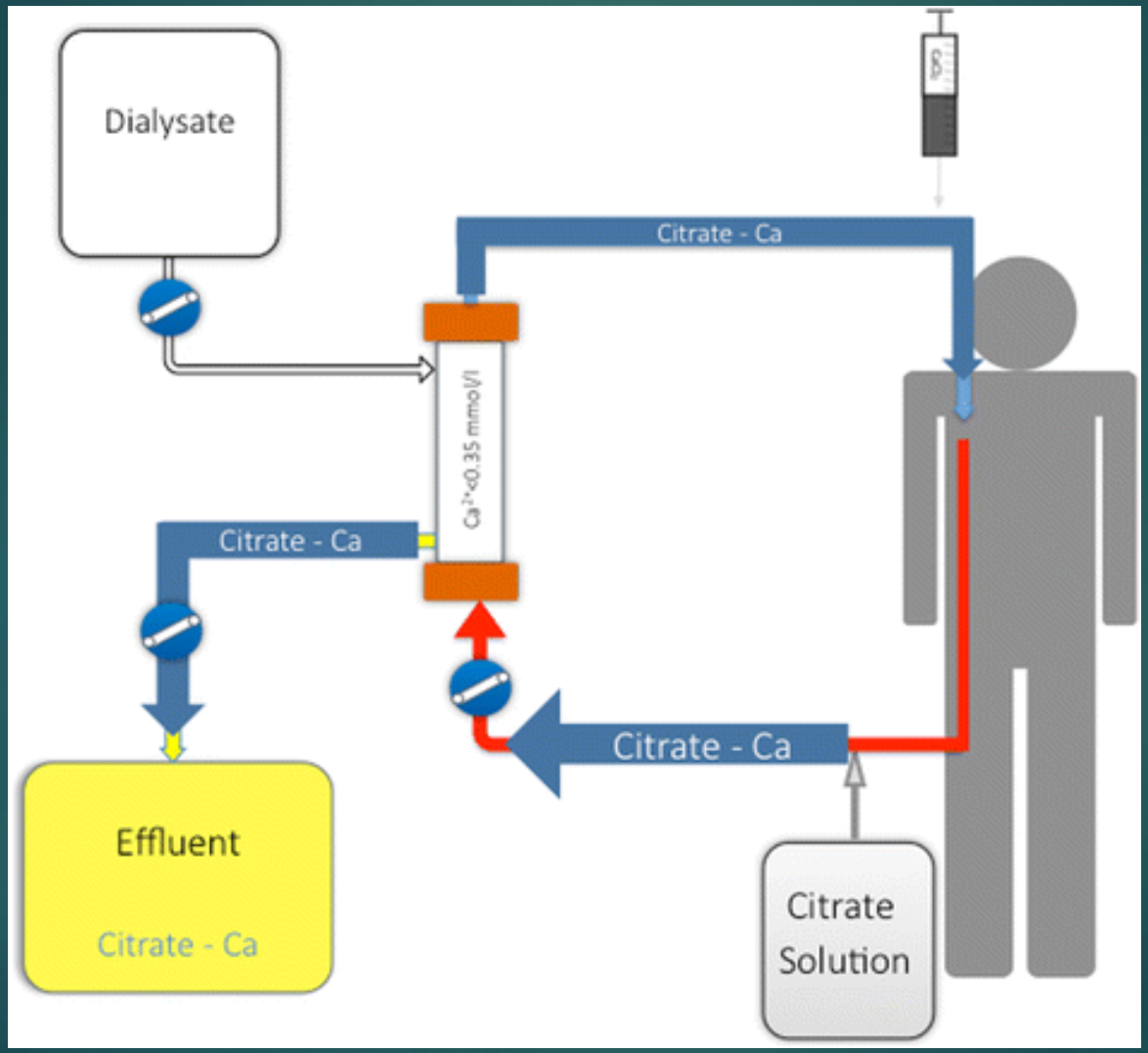
- Which of the following drug properties must be considered for renal replacement therapy?
  A. Drug Weight
  B. Drug Size
  C. Protein Binding
  D. All of the above

Pharmacy Response 2

- Which of the following drug properties must be considered for renal replacement therapy?
  A. Drug Weight
  B. Drug Size
  C. Protein Binding
  D. **All of the above**

Future Direction

Citrate Use in CRRT



Source: https://link.springer.com/article/10.1186/s13054-017-1880-1

Conclusion

- Initiation of a CRRT protocol requires key stakeholders in the institution
  - Provider and/or nurse champion necessary to take the lead
- Multidisciplinary team necessary for a successful program
- Management of CRRT needs to be outlined in a protocol

Thank you!

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