Dosing for Better Days: Advancing Medication Management in Dialysis

A presentation for HealthTrust Members
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Objectives

- Recall indications for and basic principles of renal replacement therapy.
- Identify barriers that may contribute to missed medication administration during peri-dialysis.
- Recognize the impact of hemodialysis on the pharmacokinetic principles of medications.

Renal Replacement Therapy (RRT) Overview

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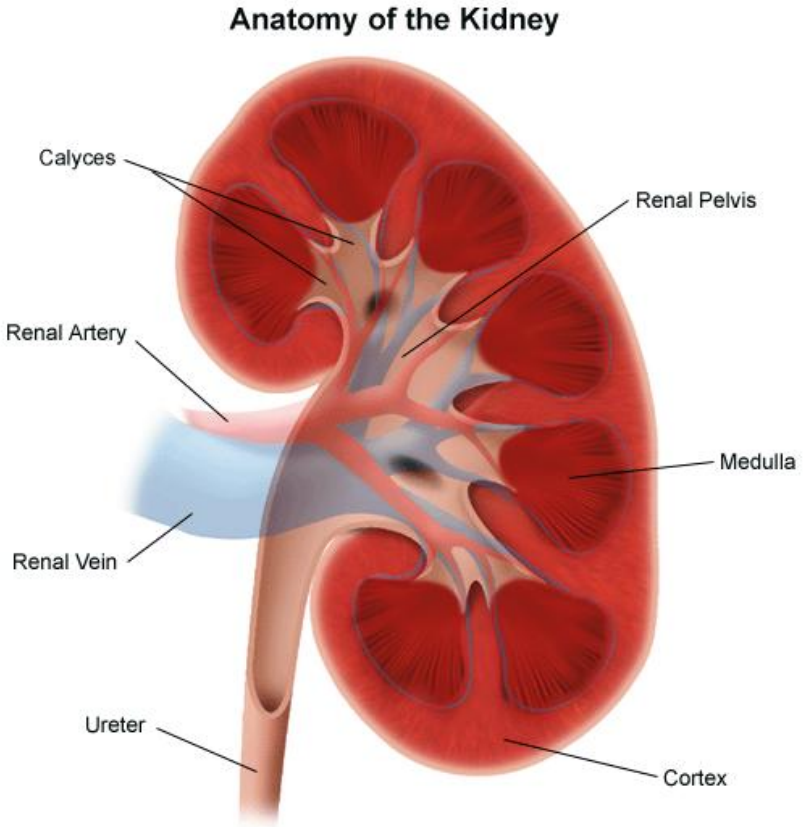
Kidney Function

Functions of the Kidney

- Remove and excrete waste
- Balance bodily fluids
- Regulate blood pressure
- Production of red blood cells



Source: Johns Hopkins Medicine. Anatomy of the urinary system. Johns Hopkins Medicine Health Library. Published 2025. https://www.hopkinsmedicine.org/health/wellness-and-prevention/anatomy-of-the-urinary-system

Indications for Renal Replacement Therapy (RRT)

Acidosis

Electrolyte Abnormality

Intoxication

Overload

Uremia

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024

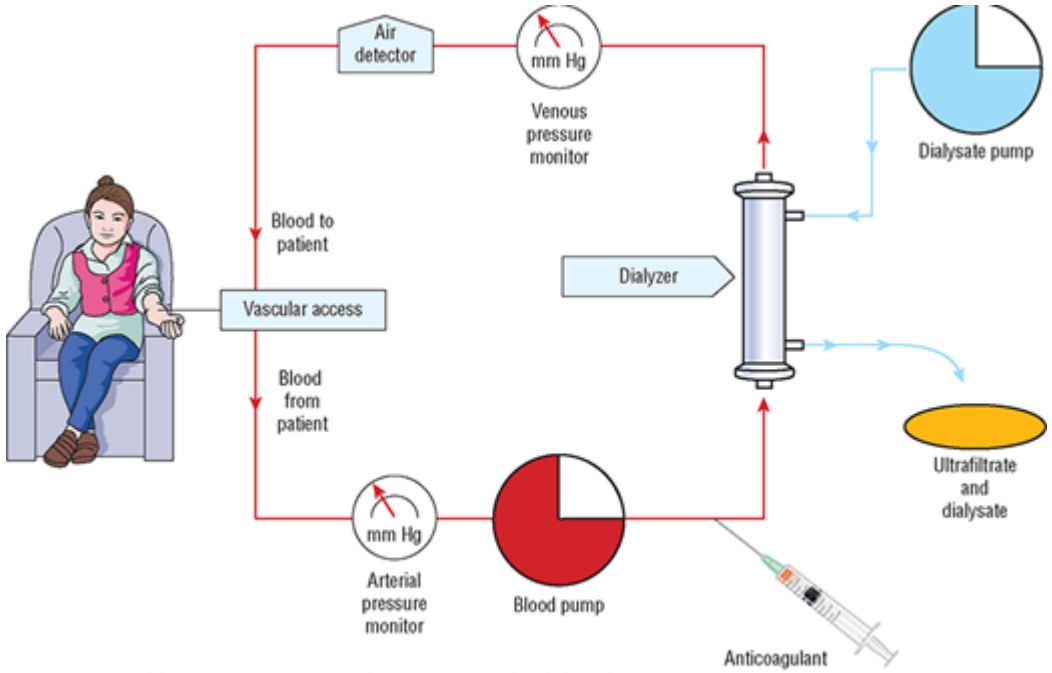
Types of RRT

- Hemodialysis
- Peritoneal Dialysis
- Continuous Renal Replacement Therapy
- Sustained Low Efficiency Dialysis

Source: Sowinski KM, Churchwell MD. Hemodialysis and Peritoneal Dialysis. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

Hemodialysis

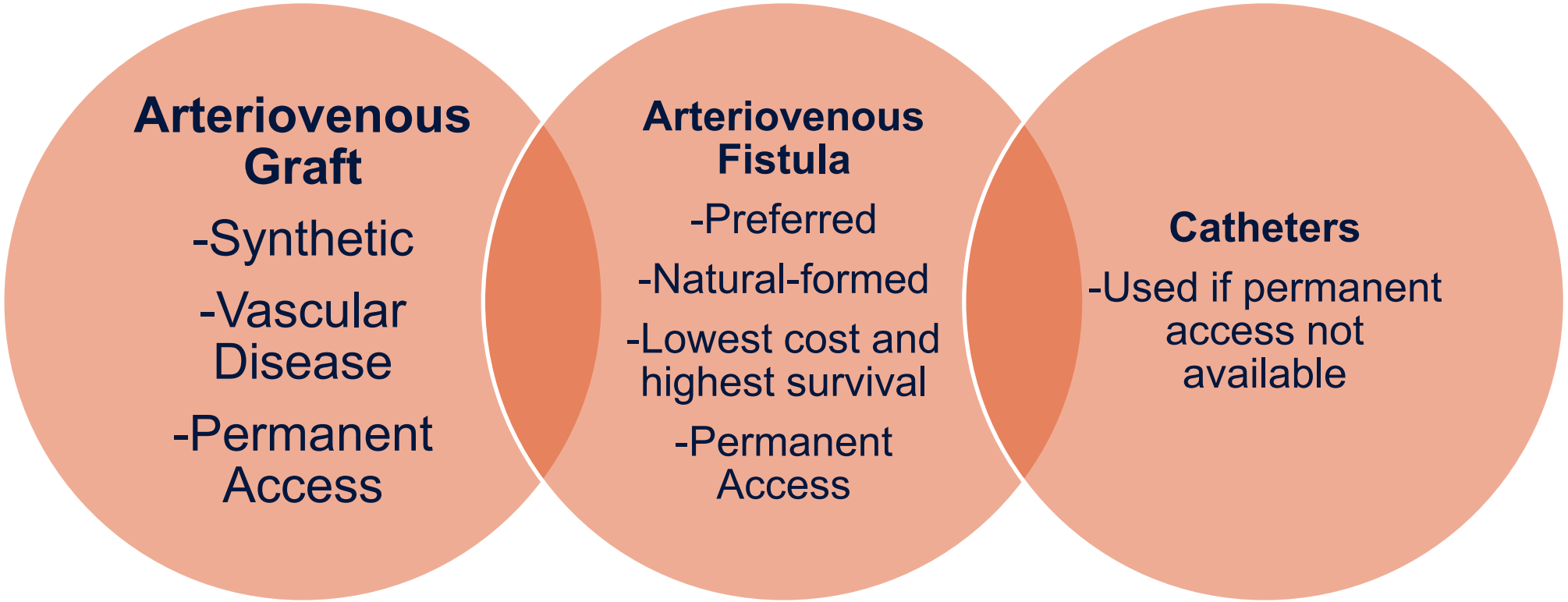
- Removes waste, toxins and excess fluid in the blood
- Performed over 2-4 hours three times weekly
- Vascular Access, Dialyzer (“Artificial Kidney”) and Dialysate



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Source: Sowinski KM, Churchwell MD. Hemodialysis and Peritoneal Dialysis. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

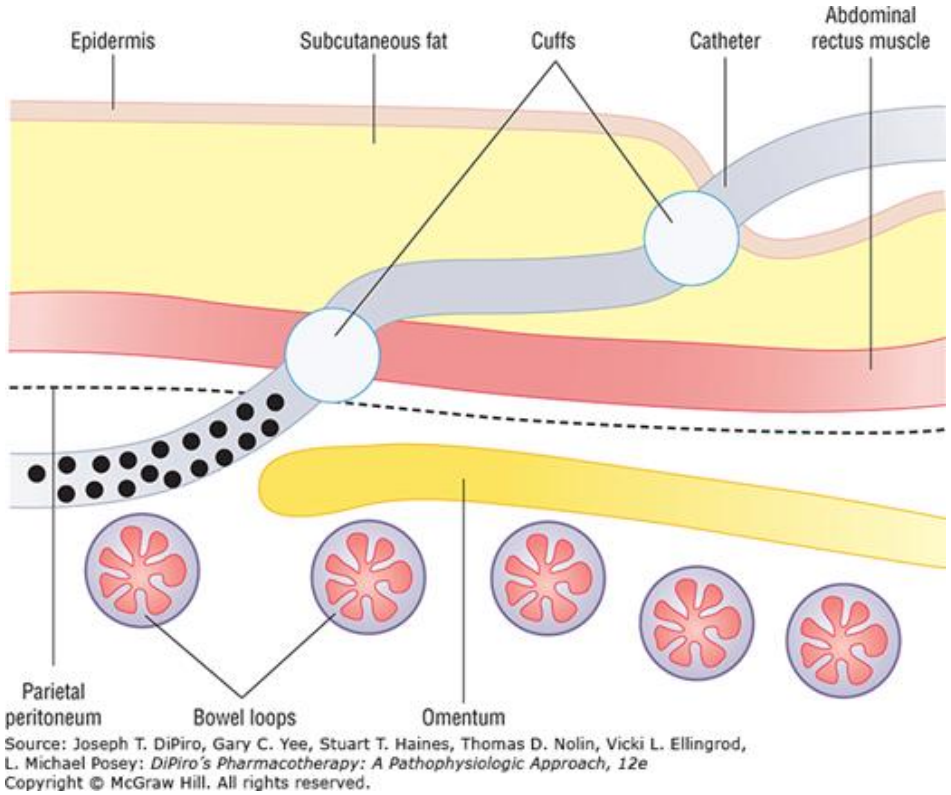
Access Points for Hemodialysis



Source: Lok CE, Huber TS, Lee T, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update.

Peritoneal Dialysis

- Uses the lining of the abdomen
- Instill dialysate to fill the abdomen with the dialysis fluid
  - “Dwell Period”
- The fluid will then drain out through the catheter



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Continuous Renal Replacement Therapy and Sustained Low Efficiency Dialysis

Continuous Renal Replacement Therapy (CRRT)

- ICU patients
- Higher costs
- 24-hour period

Sustained Low Efficiency Dialysis (SLED)

- Hybrid between CRRT and HD
- ICU patients
- Can go up to 24 hours, but usually 8-12 hours

Source: Halilovic J, Dager W. Acute Kidney Injury. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. McGraw-Hill Education; 2017

Hemodialysis vs. Peritoneal Dialysis

Hemodialysis

Advantages

- Higher solute clearance
- Technique failure rate is low
- Close monitoring

Disadvantages

- Multiple visits
- Infections
- Vascular Access

Peritoneal Dialysis

Advantages

- Increased clearance of larger solutes
- Uses a cycler
- Less blood loss

Disadvantages

- Peritonitis
- Patient burnout
- Glucose absorption

Source: Sowinski KM, Churchwell MD. Hemodialysis and Peritoneal Dialysis. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

Knowledge Check #1

Which of the following is the most important indication for initiation of chronic dialysis therapy?

A. Elevated blood urea nitrogen concentrations (greater than 60 mg/dL (21.4 mmol/L)

B. Estimated glomerular filtration rate less than 25 mL/min

C. Persistent symptoms associated with worsening renal function

D. Hyperphosphatemia

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Knowledge Check #2

Which of the following statements is true regarding peritoneal dialysis?

A. In comparison to hemodialysis, peritoneal dialysis is more efficient at removing solutes and water

B. During peritoneal dialysis, there is countercurrent flow of blood and dialysate which increases diffusion and convection

C. Blood flow to the peritoneal membrane is more regulated than blood flow through a vascular access point in hemodialysis

D. The peritoneal membrane helps to filter waste products and excess fluid from the blood

Knowledge Check #2

Which of the following statements is true regarding peritoneal dialysis?

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Barriers to Medication Administration During RRT

Complications of Hemodialysis

- Hypotension
- Nausea/Vomiting
- Hypertension
- Infection
- Thrombosis
- Cramps
- Headache

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Barriers to Medication Compliance

Non-adherence, medication beliefs and symptom burden among patients receiving hemodialysis -a cross-sectional study

- **Aim:** To investigate non-adherence, beliefs about medications, symptom burden and severity and the association between all the three listed above
- **Methods**: Cross-sectional study
- **Data Collection:**
  - Medication Adherence Report Scale (MARS)
  - Beliefs about Medication Questionnaire (BMQ)
  - Dialysis Symptom Index (DSI)

Source: Non-adherence, medication beliefs and symptom burden among patients receiving hemodialysis -a cross-sectional study. BMC Nephrol. 2023;24(1):321. Published 2023

Non-adherence, medication beliefs and symptom burden among patients receiving hemodialysis -a cross-sectional study

- **Results:** 32% reported nonadherence to dialysis-related medications

Reasons patients believed they were non-adherent:

Non-Adherence Reason	OR, CI	P-Value
Harm	1.10, 1.01 to 1.21	0.140
Overuse	1.18, 1.09 to 1.27	< **0.001**
Symptom Severity	1.02, 1.01 to 1.03	< **0.001**
Symptom Burden	1.09, 1.05 to 1.13	< **0.001**

- The study implies it is important to explain when patients are on multiple different medications the utility of each medication

Source: Non-adherence, medication beliefs and symptom burden among patients receiving hemodialysis -a cross-sectional study. BMC Nephrol. 2023;24(1):321. Published 2023

Human Performance

Diffusion of Responsibility

- Assuming someone else will act
  - Ex: It is the end of your shift, and you have forgotten to give the supplemental dose of medication B. You go home thinking the next person will administer the dose

Normalization of Deviance

- Unacceptable practices become the “norm”
  - Ex: “We never give a supplemental dose of vancomycin during hemodialysis”

Gaps in Knowledge

- Lack of awareness or training
  - Ex: A colleague not knowing to administer vancomycin during the last hour of CRRT

Source: Institute for Safe Medication Practices. *Targeted Medication Safety Best Practices for Hospitals*. Plymouth Meeting, PA: ISMP; 2022-2023. https://www.ismp.org/system/files/resources/2022-02/2022-2023%20TMSBP%20final.pdf

Knowledge Check #3

PK was admitted for sepsis and is currently receiving IV antibiotics every 8 hours. Later that evening the patients blood pressure dropped to 85/72. Nurse A recently started her shift and assumed someone had already alerted the provider. Which type of issue in human performance is present?

A. Plan Continuation

B. Gaps in Knowledge

C. Normalization of Deviance

D. Diffusion of Responsibility

Knowledge Check #3

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C. Normalization of Deviance

D. Diffusion of Responsibility

Pharmacokinetics

ADME

Drug at Site of Administration

- Absorption

Drug in Plasma

- Distribution
- Metabolism
- Excretion

Factors Affecting How Much of a Drug is Dialyzed

- Molecular Weight
- Protein Binding
- Clearance
- Volume of Distribution
- Water Solubility

Molecular Weight

- Smaller molecules (<300 Daltons) are easier to be removed through diffusion
- Medium to higher molecules (>300 Daltons) are harder to remove

Small	Large
• Lisinopril • Sevelamer	• EPO • Vancomycin

Source: Liabeuf S, Pesic V, Goce Spasovski, et al. Drugs with a negative impact on cognitive function (Part 1): chronic kidney disease as a risk factor. Clinical kidney journal. 2023;16(12):2365-2377. doi:https://doi.org/10.1093/ckj/sfad241

Volume of Distribution (Vd)

- The amount of drug dispersed throughout the tissues
- Medications can have higher Vd in patients who have reduced renal function
- High Vd will be more concentrated in the tissues
  - May affect therapeutic efficacy of hydrophilic medications
  - High lipid solubility contributes

Source: Liabeuf S, Pesic V, Goce Spasovski, et al. Drugs with a negative impact on cognitive function (Part 1): chronic kidney disease as a risk factor. Clinical kidney journal. 2023;16(12):2365-2377.doi:https://doi.org/10.1093/ckj/sfad241

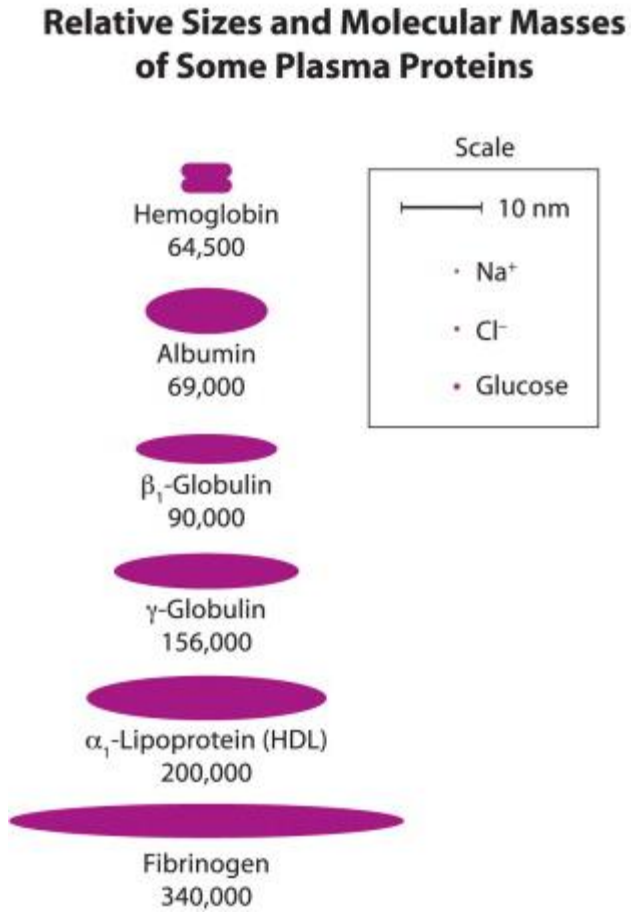
Protein Binding

- Medications can be protein bound or free
  - Only free forms are pharmacologically active
- Medications that are highly protein bound are unlikely to cross the dialysis membrane
  - There is a small amount of medication that can be dialyzed
- >94% likely not dialyzable
- Uremia and inflammation can alter protein binding

Source: Liabeuf S, Pesic V, Goce Spasovski, et al. Drugs with a negative impact on cognitive function (Part 1): chronic kidney disease as a risk factor. Clinical kidney journal. 2023;16(12):2365-2377. doi:https://doi.org/10.1093/ckj/sfad241

Plasma Proteins

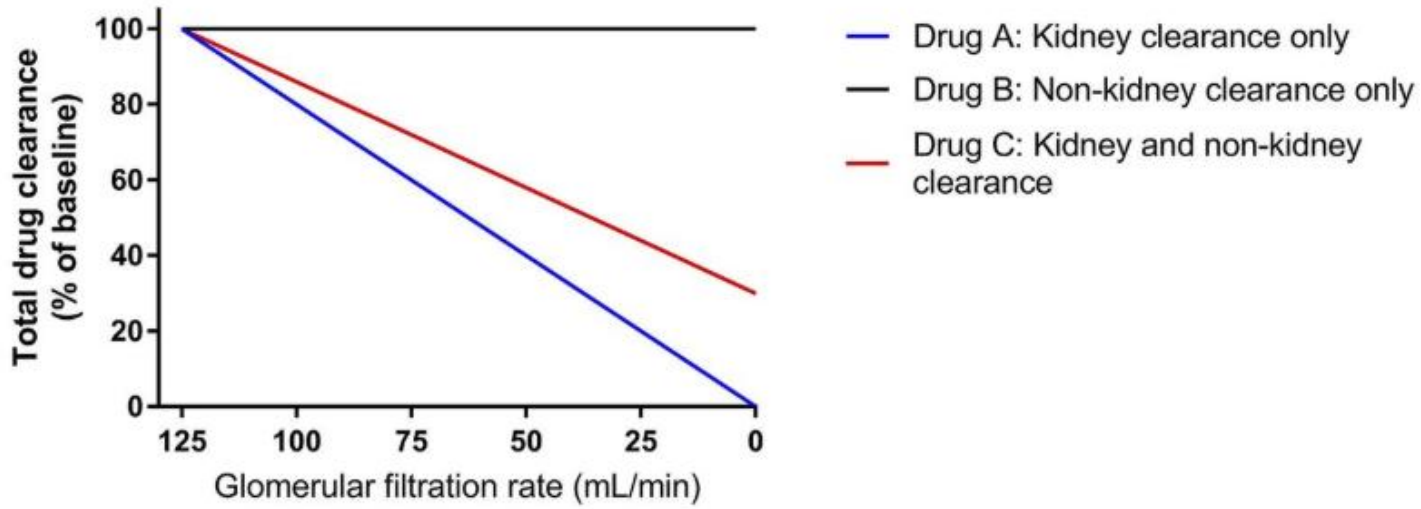
- **Albumin**
  - Most common
- **A1-Acid Glycoprotein (AAG)**
- **Lipoproteins**
- **Globulins**
  - Steroids, Vitamins



Source: Plasma Protein - an overview | ScienceDirect Topics. Sciencedirect.com. Published 2012. https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/plasma-protein

Clearance

- Useful term when describing excretion
  - Dependent on blood flow and organ status mainly the kidney
- High renal clearance → high dialyzability



Source: Lea-Henry TN, Carland JE, Stocker SL, Sevastos J, Roberts DM. Clinical Pharmacokinetics in Kidney Disease. Clinical Journal of the American Society of Nephrology. 2018;13(7):1085-1095. doi:https://doi.org/10.2215/cjn.00340118

Clearance, *Continued*

- When you increase the CL (RRT), it can decrease half life
- Ultimately lead to steady state levels quicker
  - Could lead to toxicity quicker
- In hemodialysis, diffusion is the main driver
- In CCRT, there is diffusion + hemofiltration which ultimately increases the clearance

$$t_{1/2} = \frac{0.693 \times V_d}{CL}$$

Source: Lea-Henry TN, Carland JE, Stocker SL, Sevastos J, Roberts DM. Clinical Pharmacokinetics in Kidney Disease. Clinical Journal of the American Society of Nephrology. 2018;13(7):1085-1095. doi:https://doi.org/10.2215/cjn.00340118

Water Solubility

- Dialysate in hemodialysis is aqueous based
- Lipophilic medications during CRRT are more easily removed than with hemodialysis
- Lipid soluble medications are not easily removed
  - Medications are concentrated in the tissues

Source: Liabeuf S, Pesic V, Goce Spasovski, et al. Drugs with a negative impact on cognitive function (Part 1): chronic kidney disease as a risk factor. Clinical kidney journal. 2023;16(12):2365-2377. doi:https://doi.org/10.1093/ckj/sfad241

Knowledge Check #4

Which pharmacokinetic property most influences how much of a drug is removed during hemodialysis?

A. Volume of Distribution

B. Oral Bioavailability

C. Half Life

D. Hepatic Metabolism

Knowledge Check #4

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Medications Administered During RRT

Select Medications that Need Supplemental Dosing During Hemodialysis

- Acyclovir
- B-Lactams
- Ertapenem
- Phenobarbital, Levetiracetam, Pregabalin, Lacosamide
- Metronidazole
- Tranexamic Acid
- Vancomycin

Source: Lexicomp. 2025

Supplemental Dosing for Vancomycin

Properties	
Molecular Weight	1485 Daltons
Protein Binding	~55%
Volume of Distribution	0.4-1 L/kg
Elimination Route	Urine (Kidney) -1.6-6.2L/hr
Water Solubility	Yes
Dialyzability	~25-40%

Vancomycin is **dialyzable** based on the factors above and increased with the use of high-flux machines

Source: Vancomycin. Lexicomp. 2025

Supplemental Dosing for Other Select Medications

B-Lactams

- Time dependent antibiotics
- Highly dialyzable
- Renal Clearance

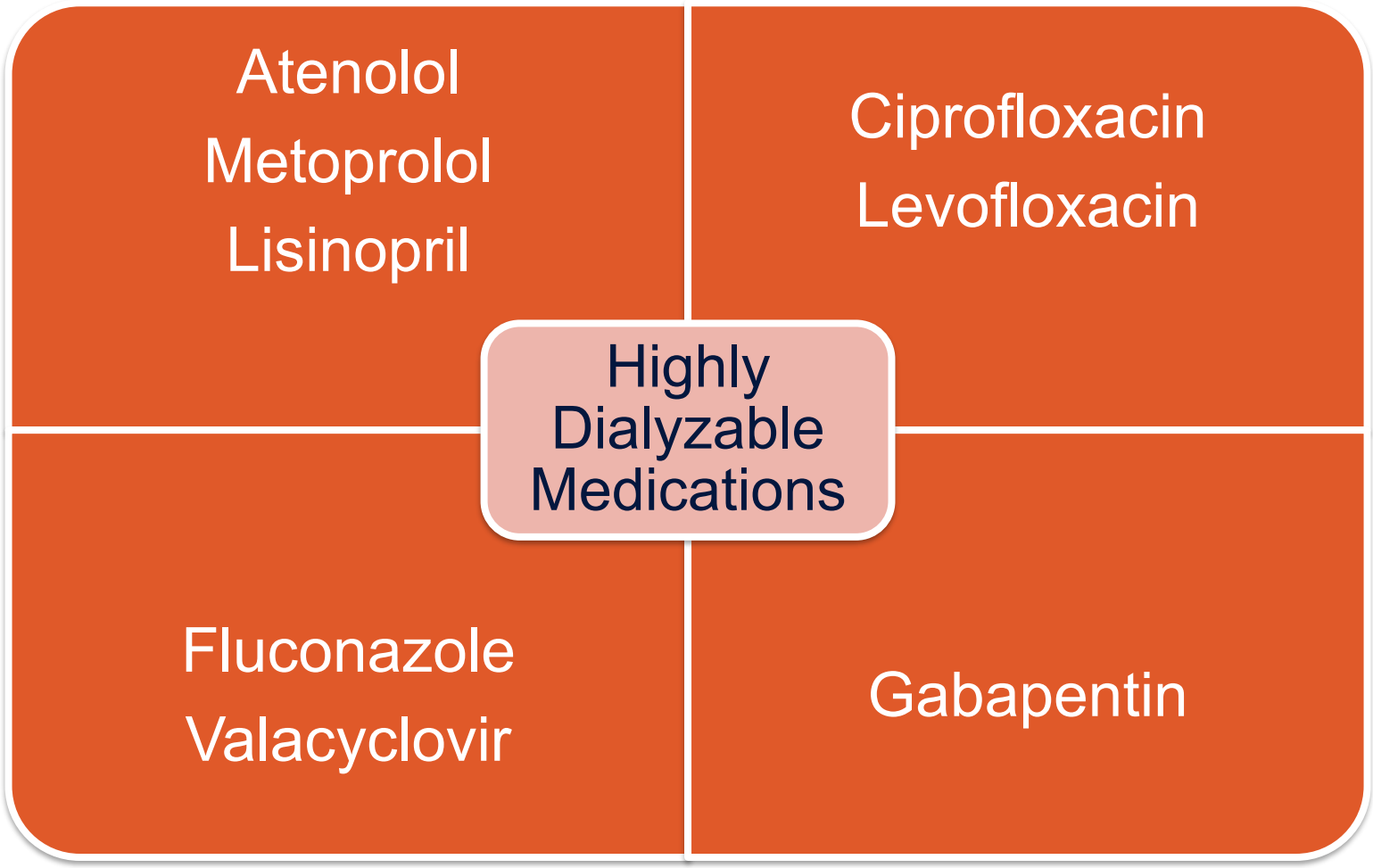
Antiseizure Medications

- Therapeutic monitored medications
- Renally cleared
- High dialyzable

Antivirals

- Highly dialyzable
- Renally cleared

Select Medications for Post-Dialysis Dosing



Medications Administered through RRT

Timing of Antihypertensive Medications on Key Outcomes in Hemodialysis: A Cluster Randomized Trial

- **Aim:** Examine the effect of taking versus holding antihypertensives before hemodialysis on intradialytic hemodialysis
- **Methods:** Cluster Randomized Control Trial
  - TAKE vs HOLD groups
    - 65 in TAKE
    - 66 in HOLD
  - 10 dialysis units in a 1:1 ration

Source: Chang TI, Tatoian ET, Montez-Rath ME, Chertow GM. Timing of Antihypertensive Medications on Key Outcomes in Hemodialysis: A Cluster Randomized Trial. *Kidney360*. 2021;2(11):1752-1760. doi:https://doi.org/10.34067/kid.0001922021

Timing of Antihypertensive Medications on Key Outcomes in Hemodialysis: A Cluster Randomized Trial

- **Results:**

Outcome	Take	Hold	Mean Difference
Intradialytic Hypotension	18.6%	10.6%	5.9% (-1.7% -13.5%)
Uncontrolled Hypertension	38.5%	53%	-9.9% (-17.9% -1.9%)

Did not show that “Take” was noninferior, but does show that the use of blood pressure medications in hemodialysis is dependent specifically on the patient

Source: Chang TI, Tatoian ET, Montez-Rath ME, Chertow GM. Timing of Antihypertensive Medications on Key Outcomes in Hemodialysis: A Cluster Randomized Trial. *Kidney360*. 2021;2(11):1752-1760. doi:https://doi.org/10.34067/kid.0001922021

Knowledge Check #5

JT is 60 y/o M presenting to the hemodialysis clinic for the first time. You as the pharmacist review his medication list and notice that she is taking medication X that has a narrow therapeutic range. When obtaining more research on this medication, you notice it is 75% dialyzable. What would you as the pharmacist recommend to the team?

A. Continue current dosing

B. Discontinue the medication

C. Supplement with another dose

Knowledge Check #5

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Nephrotoxic Medications

- **C** Calcineurin Inhibitors
- **A** Aminoglycosides
- **R** Radiocontrast Media
- **N** Non-Steroidal Anti-Inflammatory Drugs
- **I** Ifosfamide
- **V** Vancomycin
- **A** Angiotensin Converting Enzyme Inhibitors
  Angiotensin II Receptor Blockers
- **L** Lithium

- **C** Cisplatin
- **A** Amphotericin B
- **M** Methotrexate
- **P** Penicillins

Source: Common Nephrotoxic Medications | PharmacyLibrary. Default Digital Object Series. Published 2021.

Select Medications with Rebound Levels after RRT

- **Rebound Effect**
  - Gradient that causes quick reduction in plasma blood levels
  - Some medications can be left in the tissues after RRT
  - Caused by high-flux membranes
  - Important to obtain levels in certain medications
- **Select Medications**
  - Vancomycin
  - Aminoglycosides
  - Methotrexate

Sources: Launay-Vacher V, Izzedine H, Mercadal L, Deray G. Clinical review: use of vancomycin in haemodialysis patients. Crit Care. 2002 Aug;6(4):313-6. doi: 10.1186/cc1516. Epub 2002 Jun 10. PMID: 12225605; PMCID: PMC137311.
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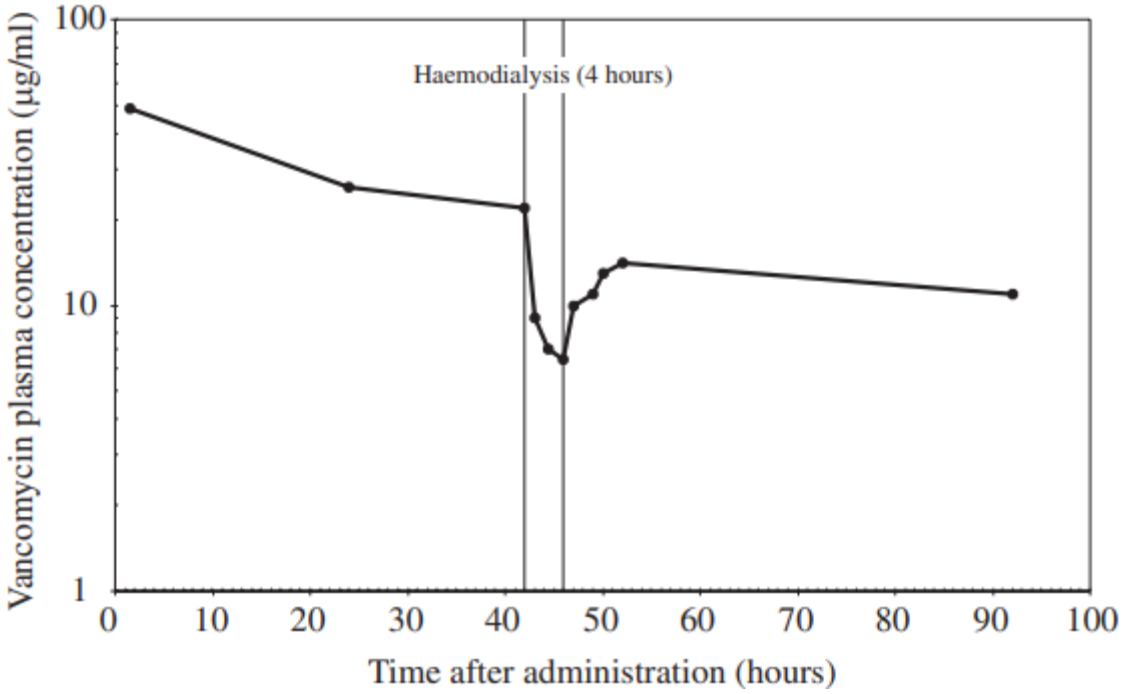
Supplemental Dosing for Vancomycin

- High-Flux Membranes
  - Concentrations of vancomycin can significantly decrease during hemodialysis and then rebound 3-6 hours later
  - Increases dialyzability
- Crucial to obtain trough levels prior to dialysis session



Source: Launay-Vacher V, Izzedine H, Mercadal L, Deray G. Clinical review: use of vancomycin in haemodialysis patients. Crit Care. 2002 Aug;6(4):313-6. doi: 10.1186/cc1516. Epub 2002 Jun 10. PMID: 12225605; PMCID: PMC137311.

Pharmacist Role in RRT

- Medication Adjustments
  - No dose adjustments during RRT <30% dialyzability
  - Less necessary when using low nephrotoxic medications for short periods of time
  - Ensuring medication dosages are appropriate
- Electrolyte Imbalances
  - RRT can eliminate key electrolytes needed
  - Important for us as pharmacists to monitor
- Education of Medications to Patients
  - 12+ medications

Medication of Choice for Patients on RRT

Non-Steroidal Anti-Inflammatories vs. Acetaminophen

- Ibuprofen: Nephrotoxic & eliminated through the kidney
- **Acetaminophen:** Metabolized through the liver

Warfarin vs DOACS

- DOACs: Eliminated through kidneys and could lead to accumulation
- Warfarin: higher risk of bleeding, narrow therapeutic range
- **Heparin:** shorter half life, metabolized through the liver

Sulfonylureas vs SGLTs, GLPs, Insulin

- **Insulin**
  - Kidney helps to produce insulin

Morphine, Hydrocodone vs Hydromorphone

- Morphine, Hydrocodone: Can accumulate throughout the body
- **Hydromorphone:** more cleared through dialysis than others

Sources: Baker, Megan, and Mark A. Perazella. "NSAIDs in CKD: are they safe?." American Journal of Kidney Diseases 76.4 (2020): 546-557.
Dean, Mervyn. "Opioids in renal failure and dialysis patients." Journal of pain and symptom management 28.5 (2004): 497-504.

Takeaways

Types of Renal Replacement Therapy

Barriers Preventing Appropriate Medication Administration

Importance of Pharmacokinetics for RRT patients

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Acknowledgements

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- Kaleb Roemer, PharmD, BCPS – Clinical Pharmacy Services Manager, Clinical Services Group HCA Healthcare
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Thank you!!

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