WHAT EVERY PHARMACIST SHOULD KNOW ABOUT PATIENTS WITH KIDNEY FAILURE ON DIALYSIS: A PRIMER

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Disclosures

- Advisory board member: Vifor Pharma Inc, Glaxo Smith Kline
- I may reference unlabeled/unapproved uses of drugs or products in the presentation

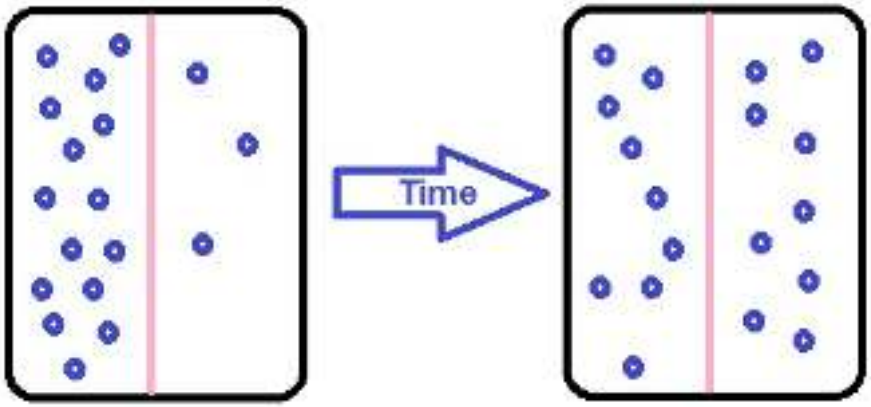
Objectives

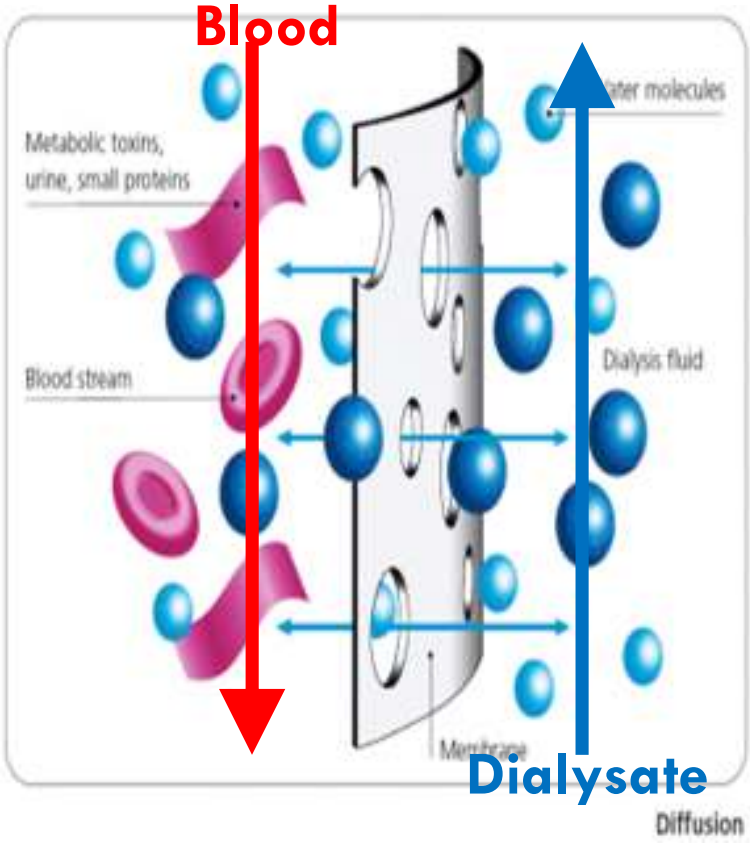
1. Identify updated nomenclature for kidney failure patients.
2. Identify common medications that should be avoided in patients with kidney failure.
3. Describe medication therapy problems that occur in patients on hemodialysis and peritoneal dialysis related to timing of administration, supplemental dosing, and therapeutic drug monitoring.
4. Characterize the appropriate clinical use of medications for common complications of kidney failure: mineral bone disorder and anemia.

What is Dialysis?

Methods of Drug Removal During Dialysis
Diffusion

- Diffusion – random movement of particles in all directions
  - Particles tend to move across concentration gradients
  - Temperature, surface area, flux, diffusion coefficient, and membrane thickness

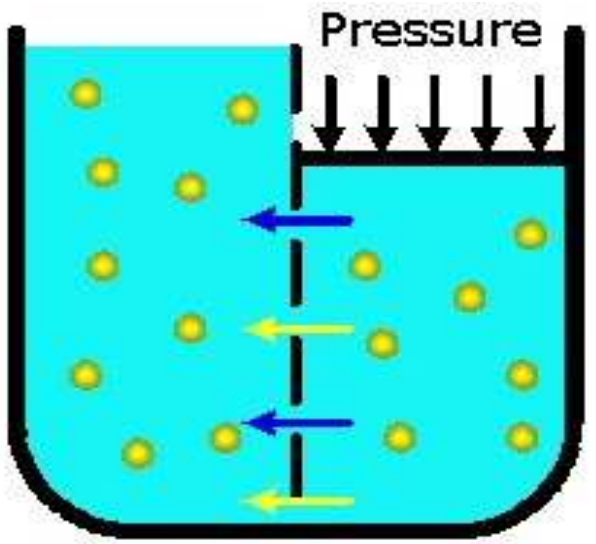




http://www.fmc-ag.com/36.htm

Methods of Drug Removal During Dialysis
Convection

- Convection – fluid movement due to pressure gradient
  - Ultrafiltration=fluid removal
  - "Solvent drag"
  - Independent of concentration gradient or molecular size

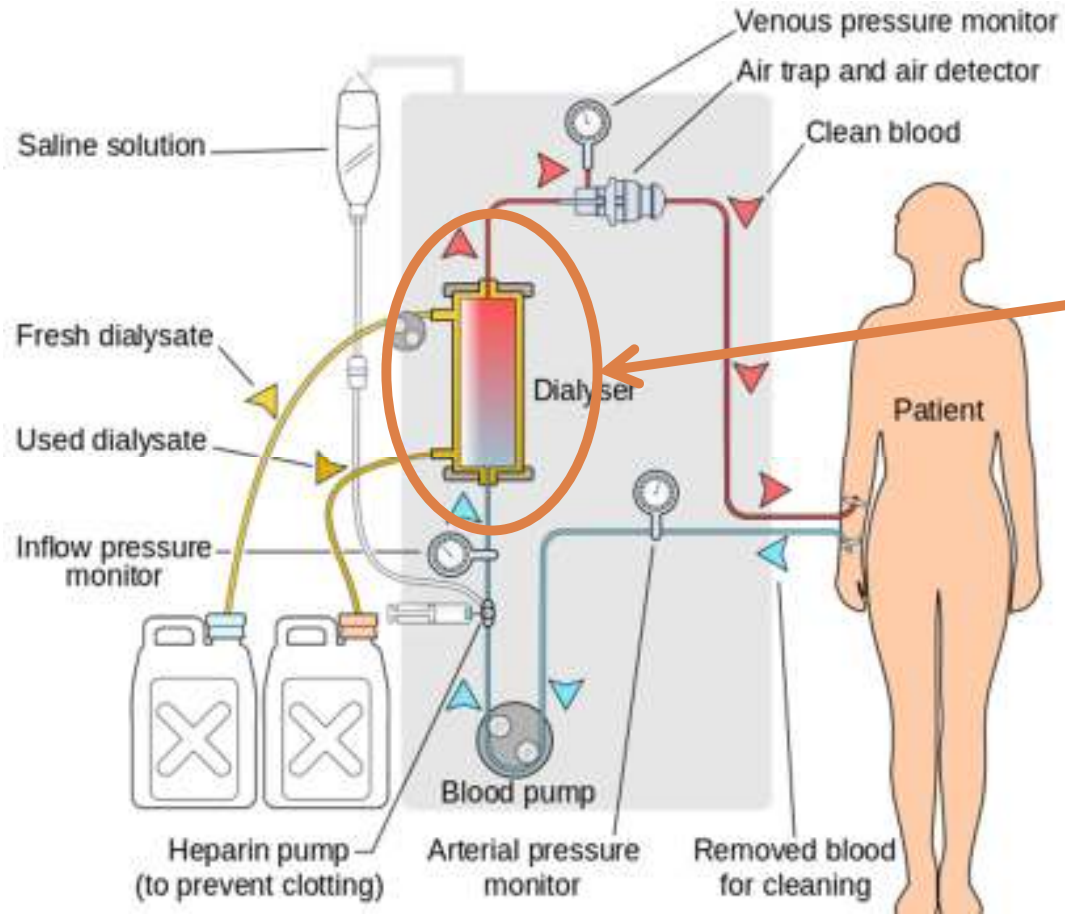


Ultrafiltration

(Solution moves by pressure gradient)

http://www.toltec.biz/how_hemodialysis_works.htm

Hemodialysis



Drug removal

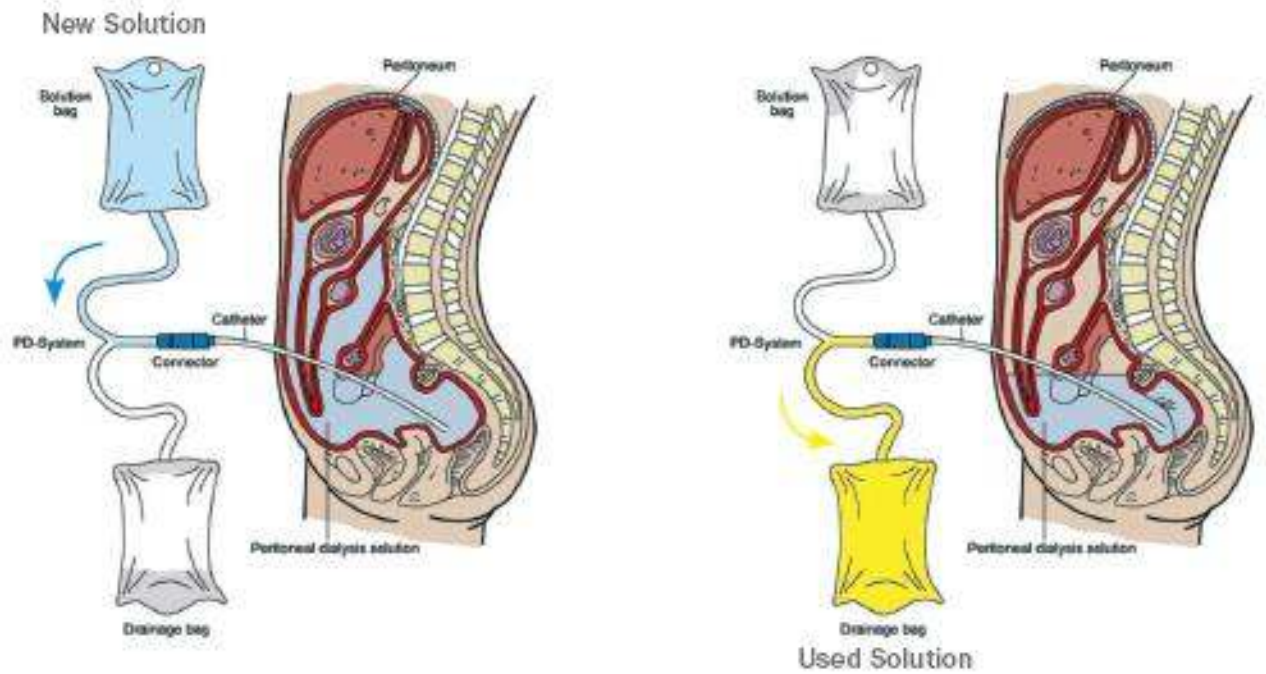
Conventional
- ≤1,000 Da

High-Flux
- ≤20,000 Da

Hemodialysis

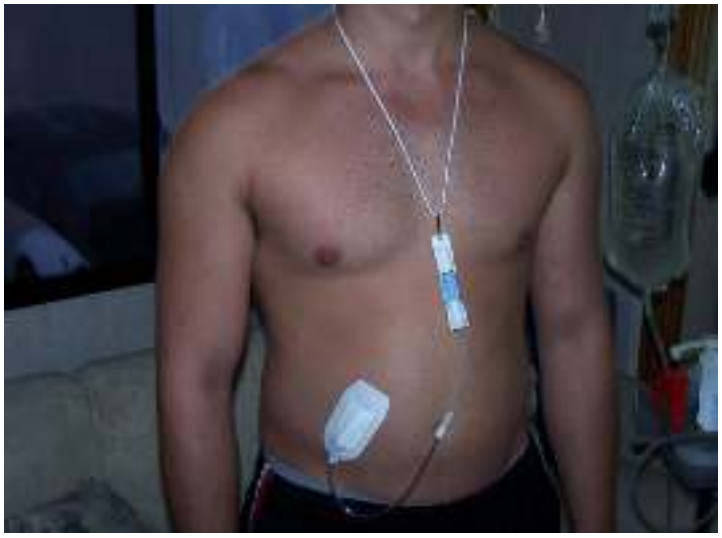
- AV Fistula
- Blood pump
- Dialysis membrane
- Additive ports
- Replacement fluid

Peritoneal Dialysis



- CAPD: Continuous ambulatory peritoneal dialysis
- Automated PD: machine assisted night-time PD with cycler

Peritoneal Dialysis



https://www.nhs.uk/conditions/dialysis/what-happens/

Dialysis Modalities

Hemodialysis	Peritoneal Dialysis
In center three times per week or **at home**	At home
Hemodynamic changes	Stable hemodynamics
Infection-bacteremia	Infection-peritonitis
Loss of residual kidney function	Maintain residual kidney function
Strict dietary requirements	Liberal dietary restrictions
Lower quality of life	Higher quality of life

Nomenclature Updates

Poll Questions – Poll Everywhere

- Go to: **PollEv.com/calvinmeaney221** on an internet browser

-OR-

- Text **CALVINMEANEY221** to **37607** to join
  - Then text A, B, C, or D to answer

Poll Question 1

- Mr. K has an estimated glomerular filtration rate of 10 ml/min per 1.73m^2 and is on hemodialysis three times per week. What BEST describes Mr. K's kidney disease?
  A. End-stage renal disease (ESRD)
  B. End-stage kidney disease (ESKD)
  C. Kidney failure on intermittent hemodialysis
  D. Renal failure with kidney replacement therapy

KDIGO Nomenclature Updates 2020

- **Kidney Failure:** Glomerular Filtrate Rate (GFR) < 15 ml/min per 1.73m^2 or treatment by dialysis
  - End-stage renal disease (ESRD), End-stage kidney disease (ESKD) are terms to AVOID
- **Kidney Replacement Therapy (KRT):** dialysis, and transplantation
  - **Dialysis**
    - Hemodialysis – in-center or home
    - Peritoneal dialysis – ambulatory or automated
    - Continuous kidney replacement therapy (CKRT) vs. Intermittent

AS Levey, et al. *Kidney International* 2020;97:1117-1129

Medications to Consider Avoiding in Dialysis

Principles

Polypharmacy

CNS Adverse Effects

Bleeding Risk

Poll Question 2

- Which is the **safest** analgesic in a dialysis patient?
  - A. Morphine
  - B. Ketorolac
  - C. Duloxetine
  - D. Acetaminophen
  - E. Gabapentin

- Go to: **PollEv.com/calvinmeaney221** on an internet browser

-OR-

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Anticoagulants in Dialysis

Edoxaban
Dabigatran
Betrixaban
Enoxaparin (& other LMWHs)

Rivaroxaban

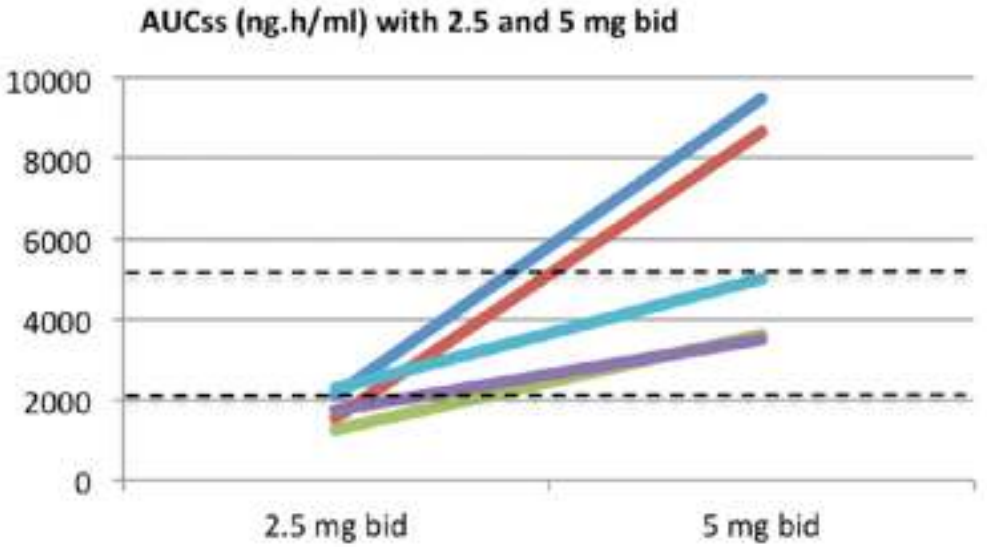
Apixaban

Unfractionated heparin
Wafarin

Apixaban in Dialysis – Pharmacokinetics

- FDA approval for dosing dialysis
  - Single-dose, 16 patient pharmacokinetic study
  - 36% increase in AUC after single dose (90% CI 1.07-1.73)

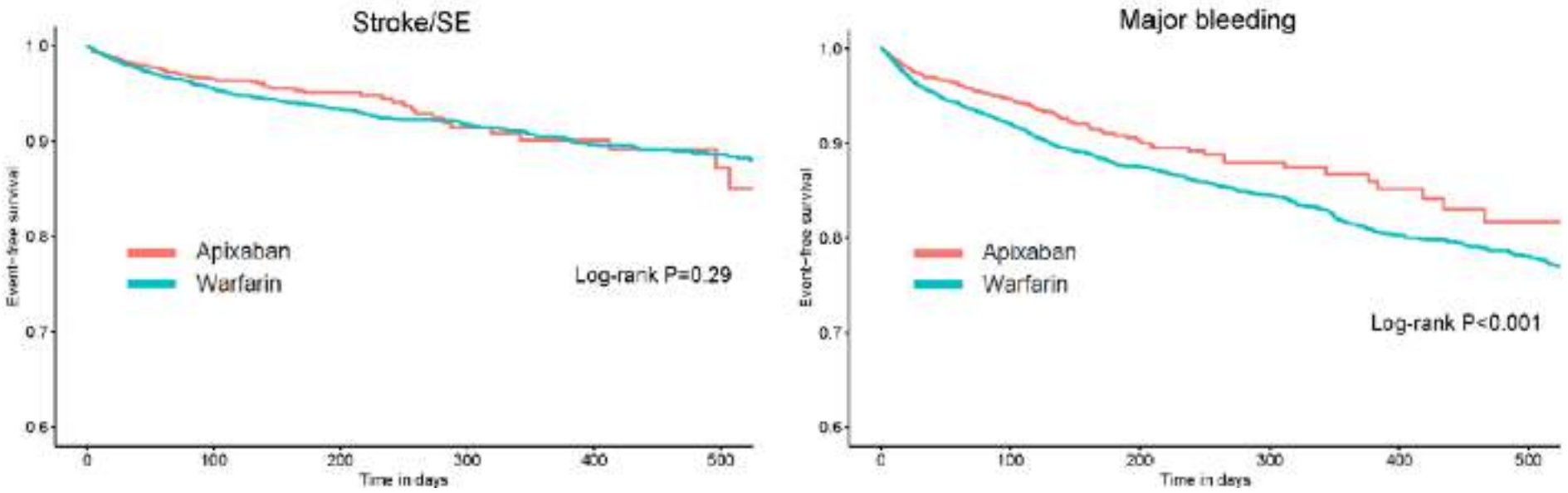
- Steady-state pharmacokinetic study in 7 hemodialysis patients:
  - 2.5mg PO BID dosing for hemodialysis patients had similar pharmacokinetics to 5mg PO BID dosing for patients with preserved kidney function
  - Accumulation index=3.6



X Wang et al. *J Clin Pharmacol* 2016;56(5):628-636
TA Mavrakanas et al. *J Am Soc Nephrol* 2017;28(7):2241-2248.

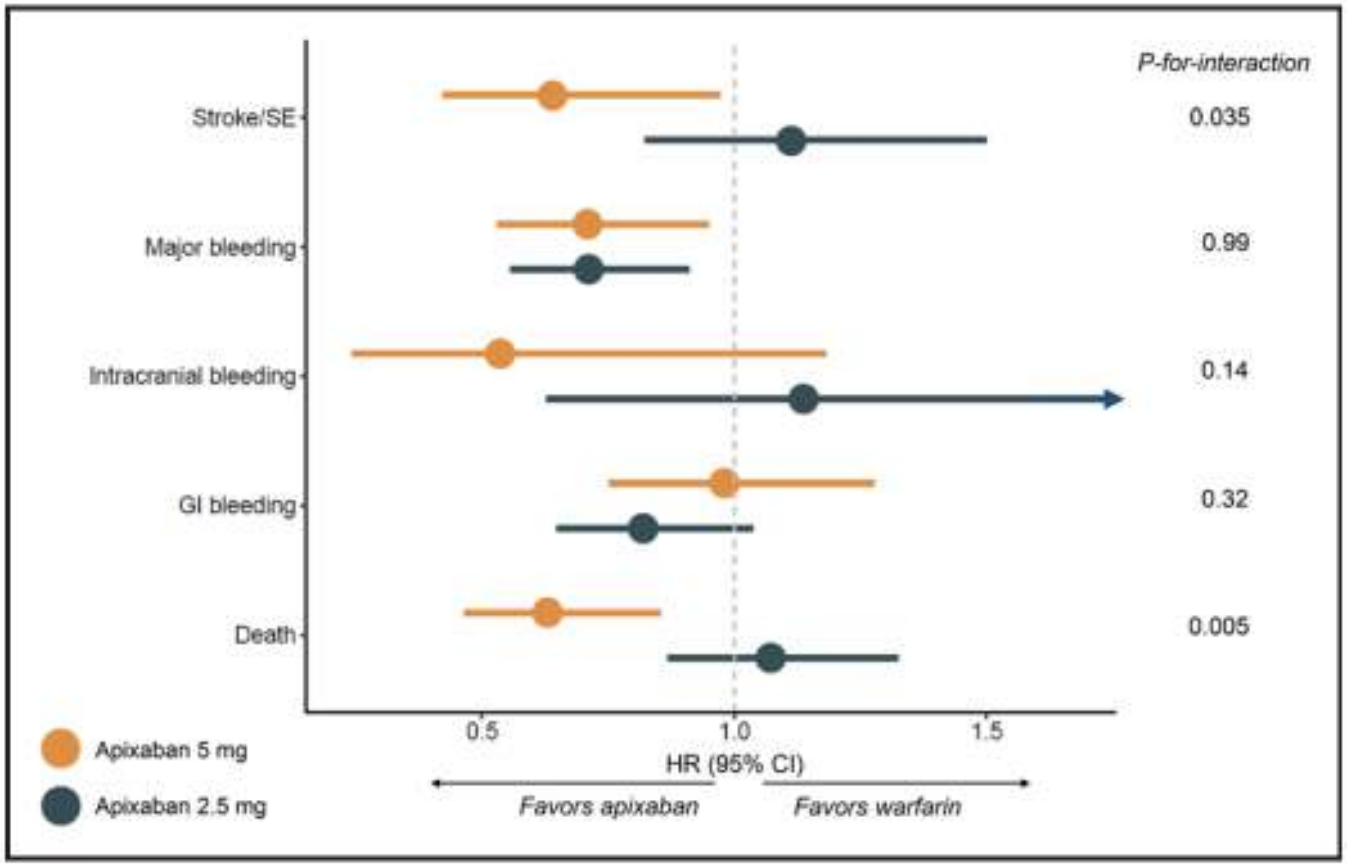
Apixaban in Dialysis – Clinical Outcomes

- Large, retrospective cohort study (n=25,523) compared apixaban to warfarin in kidney failure patients with atrial fibrillation



KC Siontis et al. *Circulation* 2018;138:1519-1529.

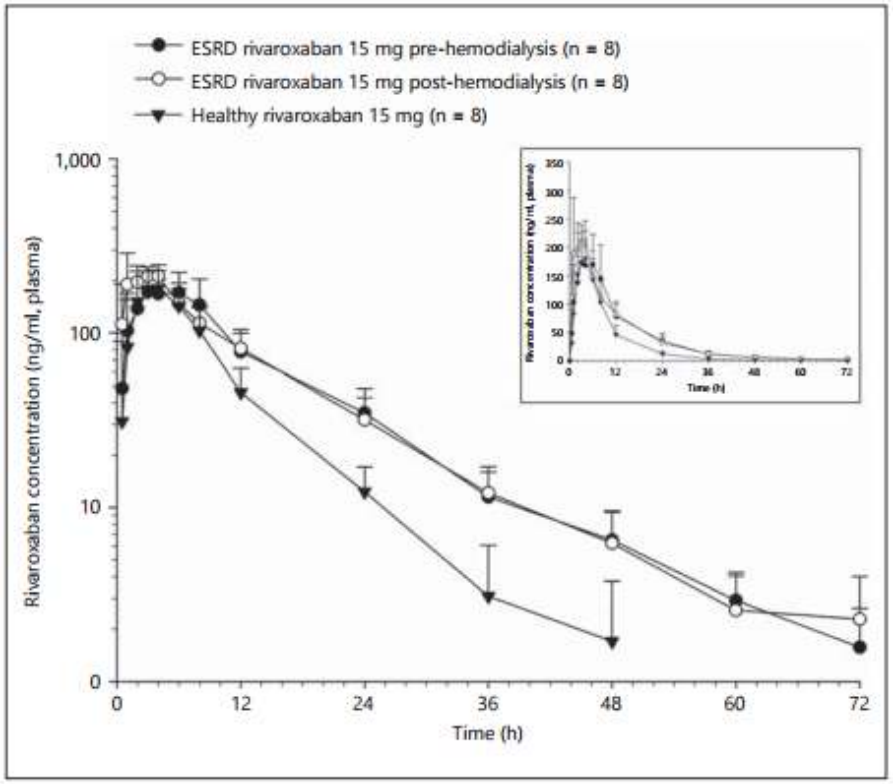
Apixaban in Dialysis – Dose Selection



KC Siontis et al. *Circulation* 2018;138:1519-1529.

Rivaroxaban in Dialysis

Dias et al *Am J Nephrol* 2016;43:229-236.



56% increase in AUC in Kidney failure

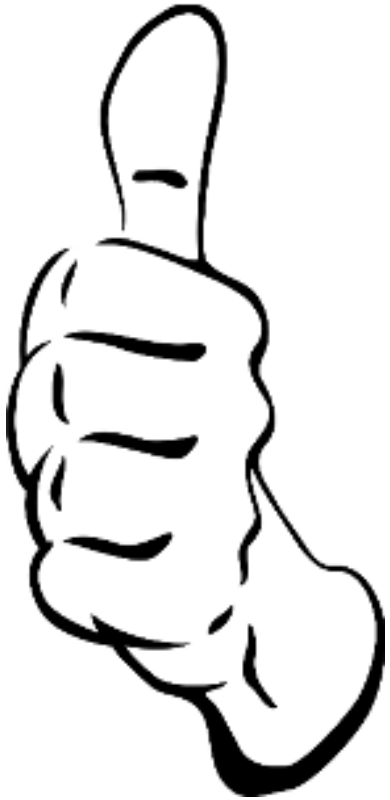
- Single dose, pharma study, n=8 hemodialysis patients
- Authors suggest using 15mg once daily dose in hemodialysis patients
  - "Similar" exposure to CrCl 15-49ml/min group
- Product labeling for dialysis: "15mg once daily will result in concentrations of rivaroxaban and pharmacodynamic activity similar to those observed in the ROCKET AF study"

Anticoagulant Selection in Dialysis Patients with Atrial Fibrillation

- Meta-analysis of 16 observational studies (n=71,877)
- Use of any anticoagulant was NOT associated with a lower risk of ischemic stroke
- Warfarin, Dabigatran & Rivaroxaban: ↑Risk of major bleeding
- Apixaban 5mg BID: ↓mortality

T Kuno et al. *J Am Coll Cardiol* 2020;75(3)273-285.

Take Home Message – Anticoagulants



- Unfractionated heparin remains the parenteral anticoagulant of choice for dialysis patients
- Apixaban (*Eliquis*) or Warfarin are the oral anticoagulants of choice for dialysis patients
  - Apixaban data are for Atrial Fibrillation indication ONLY
  - Apixaban dosing 5mg vs 2.5mg BID decision should be individualized

Opioid Metabolites and Activity

Opioid	Pathway	Metabolite(s)	Metabolite Activity
Morphine	Phase II	3-glucuronide (M3G) 6-glucuronide (M6G)	Neurotoxic
Codeine	Phase I (2D6) → Morphine	Norcodeine M3G, M6G	Neurotoxic
Meperidine	Phase 1	Normeperidine	Neurotoxic
Hydromorphone	Phase II	3-glucuronide (H3G)	Neuroexcitatory + Opioid activity
Oxycodone	Phase I (3A4, 2D6)	Oxymorphone* Noroxycodone Norexymorphone	Opioid activity Downstream glucuronide metabolites
Hydrocodone	Phase 1 (3A4, 2D6)	Hydromorphone Norhydrocodone Dihydrocodeine	Opioid activity
Fentanyl	Phase I (3A4)	Norfentanyl Hydroxyfentanyl	Inactive Non/toxic
Methadone	Phase 1 (many)	Many	Inactive

Green=safest to use in kidney dysfunction; Yellow=use with caution in kidney dysfunction; Red=avoid with kidney dysfunction

General Analgesics

- ***All NSAIDs should be avoided in CKD****
  - Use cautiously in dialysis (↑risk of GI bleed, ?↑risk of CV events)
    - E.g. short course for acute pain
- Acetaminophen preferred in kidney disease patients
  - Adult dosing: 1000mg PO TID-QID
  - May take 7-10 days for full therapeutic effect

Adjunctive Analgesics

- Duloxetine: avoid if CrCl<30ml/min (exposure ~2-fold higher)
- Tricyclic antidepressants (amitriptyline, nortriptyline): no kidney dosing, may cause altered mental status
- Anticonvulsants: no kidney dosing but drug-interactions and side effect potential
  - Gabapentin / Pregabalin …

Gabapentin Exposure Across the Spectrum of Kidney Dysfunction

- Mayo clinic case series of n=729 with serum gabapentin concentrations

	Normal Renal Function (n=126)	CKD (n=594)	Dialysis (n=9)
Gabapentin concentration	5.52±0.32mcg/mL	8.39±0.32mcg/mL	58.8±10.2mcg/mL
Gabapentin toxicity	0%	5.6%	77.8%

L Zand et al. *Am J Med* 2010;123(4):367-373.

Adverse Drug Outcomes of Gabapentin and Pregabalin Use in Hemodialysis

METHODS

National cohort study of US hemodialysis patients n=140,899

USRDS
UNITED STATES RENAL DATA SYSTEM

19% and 4% used gabapentin and pregabalin, respectively, in 2011

OUTCOME: Adjusted Hazard Ratio (95% CI)

Dose*	Altered mental status	Fall	Fracture
Gabapentin			
>0-100 mg	1.10 (0.97-1.24)	1.26 (1.07-1.48)	1.04 (0.82-1.32)
>100-200 mg	1.31 (1.17-1.46)	1.35 (1.15-1.57)	1.20 (0.96-1.49)
>200-300 mg	1.41 (1.30-1.54)	1.30 (1.14-1.48)	1.08 (0.89-1.31)
>300 mg	1.50 (1.39-1.63)	1.55 (1.39-1.72)	1.38 (1.18-1.61)
Pregabalin			
>0-100 mg	1.51 (1.32-1.74)	1.24 (1.00-1.54)	1.20 (0.87-1.66)
>100 mg	1.46 (1.24-1.71)	1.68 (1.36-2.08)	1.38 (1.00-1.92)

*Compared to reference of no use.

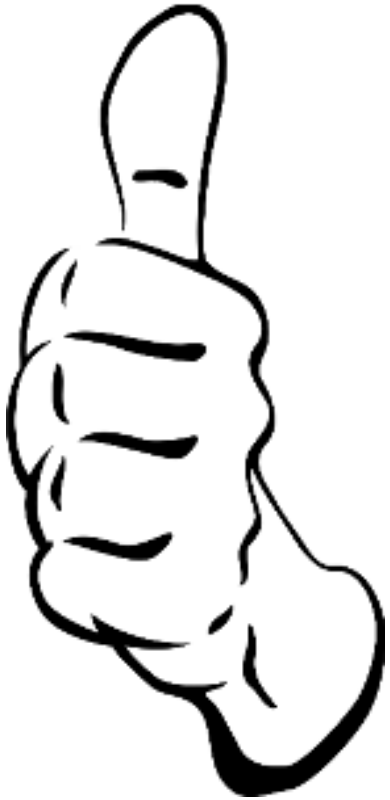
CONCLUSION Gabapentin and pregabalin should be used judiciously in patients on hemodialysis, and research to identify the most optimal dosing is warranted.

doi: 10.1681/ASN.2018010096

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

JH Ishida et al. *J Am Soc Nephrol* 2018;29(7):1970-1978

Take Home Message – Gabapentinoids



- Avoid!
- Use lowest dose (100mg gabapentin, 25mg pregabalin) dosed after dialysis on dialysis days

Muscle Relaxants

Drug	Starting Dose	Adverse Effects	% Kidney Clearance
Methocarbamol (*Robaxin*)	1500mg QID	Less sedation Urine discoloration	Unknown, ≤40%
Cyclobenzaprine (*Flexeril*)	5mg TID	Sedation, dry mouth Serotonin syndrome	Unknown, likely minimal
Carisoprodol (*Soma*)	250-350mg QID	Sedation, dizziness, euphoria Avoid if >65 yrs old Not used >3 weeks Abuse potential	Significant
Metaxalone (*Skelaxin*)	800mg TID-QID	Best AE profile; least sedating $$$	Significant; avoid if CrCl<30ml/min
Tizanidine (*Zanaflex*)	2mg Q6-8hr	Drowsiness, dizziness, dry mouth, QT prolongation Useful for spasticity	60%
Baclofen *(Lioresal)*	5-10mg TID	Drowsiness, sedation, altered mentation, falls Seizure risk Useful for spasticity	>70% Kidney dosing guidelines exist

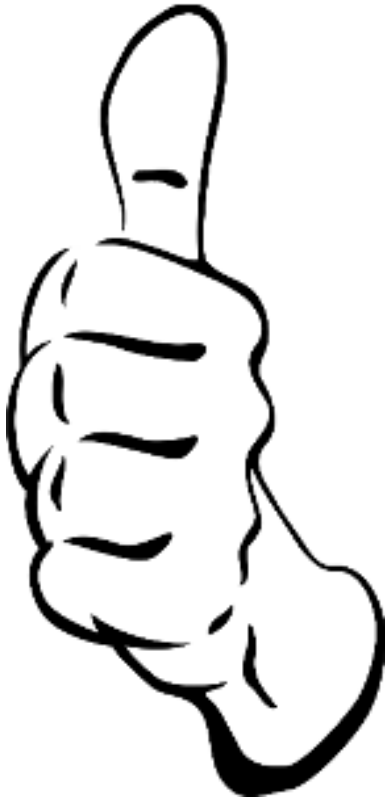
Muscle Relaxants – Outcomes in CKD/Dialysis

- Baclofen doses ≥20mg/day associated with 3.5-fold increased risk of encephalopathy compared to <20mg/day in patients with non-dialysis CKD

- In hemodialysis patients, any muscle relaxant use was associated with a higher risk of: Altered mental status (HR 1.39, 95% CI 1.29-1.51)
  - Fall (HR 1.18, 95% CI 1.05-1.33)

FT Muanda et al. *JAMA* 2019;322(20):1987-1995
D Mina et al *Am J Kid Dis* 2019;73(4):525-532

Take Home Message – Muscle Relaxants



- Cyclobenzaprine or dose-adjusted baclofen appear safest based on limited data
- Use lowest dose for shortest possible duration

Common Medication Therapy Problems in Dialysis

Poll Question 3

- Drug X has the following characteristics:
  - volume of distribution 0.5L/kg
  - 80% eliminated unchanged in the urine
  - <25% protein binding
  - molecular weight 200g/mol
- To what extent will hemodialysis remove drug X?
  A. No removal
  B. Some removal but not clinically significant
  C. Significant removal requiring dose adjustment

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MTPs in Dialysis

Polypharmacy

Pill burden

Drug-drug interactions

Serious ADEs

Dose per kidney function

Dialysis removal

No indication

HJ Manley et al. *Am J Kidney Dis* 2005;46(4):669-680.
AB Pai et al. *Clin J Am Soc Nephrol* 2013;8(11):1988-1999.

Factors Influencing Drug Removal by Dialysis

Drug Factors*	Patient Factors*	Dialysis Factors
Molecular weight (size)	Serum albumin	Conventional vs. High Flux
Protein binding	Fluid status	Membrane type (cellulose vs. synthetic [e.g. polysulfone])
Volume of distribution (Lipophilicity)	Residual renal function	Blood and dialysate flow rates, length of dialysis

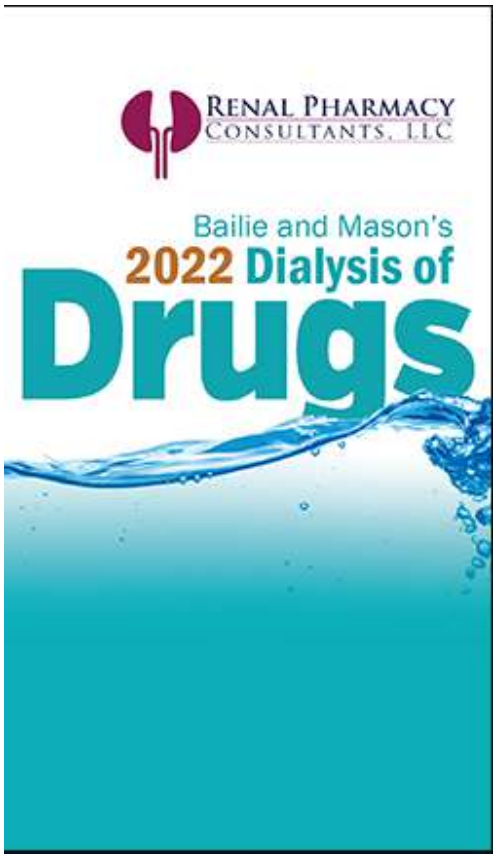
*Drug & Patient Factors are the same for all methods of dialysis: HD, PD, CRRT, etc.

Amount of drug removal by mode of dialysis: CKRT > HD > PD

Factors Influencing Drug Removal by Dialysis

- **Drug removal is increased by:**
  - Hemodialysis has greater clearance than peritoneal dialysis
  - Small molecular weight
  - Low protein binding
  - Small volume of distribution (low lipophilicity)
  - High-flux hemodialysis (AKA: High permeability)
  - Semi-synthetic and synthetic dialysis membranes

Resources for Drug Dosing in Dialysis



Drug	HEMODIALYSIS		Peritoneal Dialysis
	Conventional	High Permeability	
Cefadroxil	Yes (NS)	L	No
Cefalotin	Yes (NS)	L	No
Cefamandole	Yes (NS)	L	No
Cefazolin	Yes (6, 8)	Yes (8.1-60)	No
Cefdinir	ND	Yes (NS)	ND
Cefditoren	No (NS)	ND	ND
Cefepime	Yes (NS)	Yes (40, 60)	Yes
Cefixime	No (NS)	ND	No
Cefmenoxime	Yes (NS)	L	ND
Cefmetazole	Yes (NS)	L	No
Cefodizime	No (NS)	ND	No
Cefonicid	No (NS)	ND	No
Cefoperazone	No (NS)	ND	No
Ceforanide	Yes (NS)	L	No
Cefotaxime	Yes (NS)	L	No
Cefoxitin	Yes (NS)	L	No

Key

Yes Indicates that dialysis enhances plasma clearance by 30% or more. Supplemental dosing may be required or dosing after dialysis should be considered.

No Indicates that dialysis does not have a clinically important effect on plasma clearance. Supplemental dosing is usually not required.

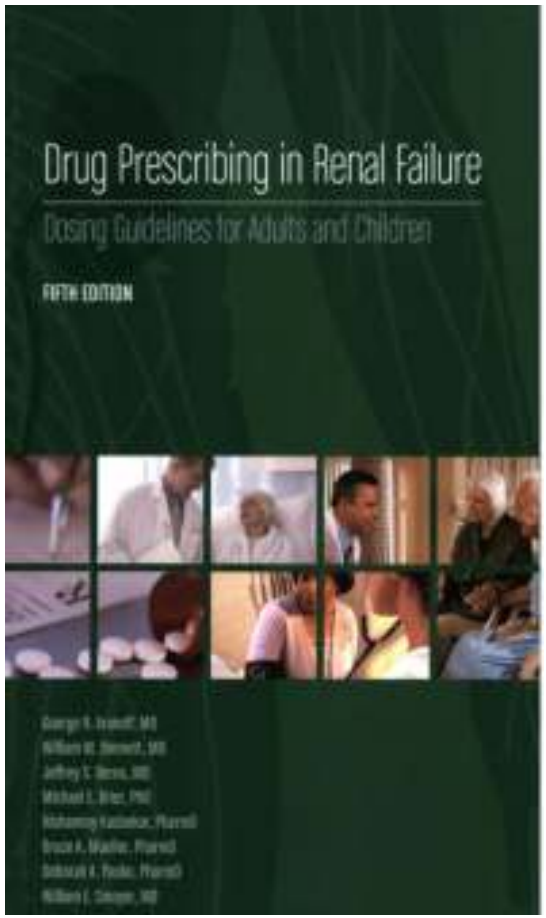
U Indicates that no published data exist but physicochemical characteristics of the drug suggest that significant drug removal is **unlikely** during dialysis.

L Indicates that no published data exist but physicochemical characteristics of the drug suggest that significant drug removal is **likely** during dialysis.

ND Indicates no data exist on drug dialyzability with this type of dialysis.

NS Indicates the type of membrane was not specified.

Resources for Drug Dosing in Dialysis



Adult **Antimicrobial Agents (continued)**

Drug/ Toxicity Notes	Excreted Unchanged	Half-Life (Normal/ ESRD)	Plasma Protein Binding	Volume of Distribution	Dose for Normal Renal Function	Adjustment for Renal Failure: Method	GFR, *mL/min*: >50 [Recommendation Level]	GFR, *mL/min*: 10-50 [Recommendation Level]	GFR, *mL/min*: <10 [Recommendation Level]	Supplement for Dialysis [Recommendation Level]
	%	*hours*	%	*L/kg*						
Antibacterial Antibiotics (continued)										
Cefepime	85	2.2/18	16	0.3	250-2000 mg q8-12h	D, I	100% [A]	50-100% q24h [A]	25-50% q24h [A]	IHD: Dose for GFR <10 PD: Dose for GFR <10 CRRT: 1-2 g q12h, [A]
Cefoperazone	20	1.6-2.5/2.9	90	0.14-0.20	1-2 g q12h	D	100% [A]	100% [A]	100% [A]	IHD: 1 g after dialysis PD: None CRRT: Dose for GFR 10-50, [C]
Cefotaxime	60	1/15	37	0.15-0.55	1-2 g q6-12h	I	q6h [A]	q6-12h [A]	q24h or ½ dose [A]	IHD: 0.5-2 g after dialysis PD: 1 g/d CRRT: 1 g q12h, [B]
Cefotetan	75	3.5/13-25	85	0.15	1-2 g q12h	I	100% [A]	1-2 g q24h [A]	1-2 g q48h [A]	IHD: 1 g after dialysis PD: 1 g/d CRRT: 1-2 g q24h, [D]
Cefoxitin	80	1/13-23	41-75	0.2	1-2 g q6-8h	I	q6-8h [A]	q8-12h [A]	q24-48h [A]	IHD: 1 g after dialysis PD: 1 g/d CRRT: Dose for GFR 10-50, [B]
Cefpodoxime	30	2.5/6-10	22-33	0.6-1.2	100-400 mg q12h	I	q12h [A]	q24h [A]	q24h [A]	IHD: Dose after dialysis, [D] PD: Dose for GFR <10 CRRT: Not applicable

Cefepime (Lexi-Drugs)

Hemodialysis, intermittent (thrice weekly): **Note:** Achievement of cefepime pharmacodynamic targets is dependent on organism MIC, the absence or presence of residual kidney function, and interval between dialysis sessions (ie, 2- or 3-day interdialytic interval) (Descombes 2016; Perez 2012; Schmaldienst 2000). Factors such as severity of illness, location of infection, and patient weight should be considered when selecting between the higher and lower dosing regimens as well.

IV: Dialyzable (70% to 85% reduction in serum concentration from a 3.5- to 4-hour hemodialysis treatment with high flux filters [Descombes 2016; Schmaldienst 2000]).

Daily dosing (administer after hemodialysis on dialysis days): IV: Initial: 1 g (single dose) on day 1. Maintenance: 500 mg to 1 g every 24 hours (Heintz 2009; manufacturer's labeling). **Note:** If the usual recommended dose for normal renal function is 2 g every 8 hours or 1 g every 6 hours, utilize 1 g every 24 hours; use 500 mg every 24 hours for all other doses (Lodise 2006; manufacturer's labeling).

Thrice-Weekly (postdialysis) Dosing[1]

Residual kidney function and organism susceptibility	Cefepime dose for a 2-day interdialytic interval (ie, next dialysis expected in 48 hours)	Cefepime dose for a 3-day interdialytic interval (ie, next dialysis expected in 72 hours)
Patient is anuric **AND** the organism MIC <4 mg/L	1 g after hemodialysis	2 g after hemodialysis
Any of the following: Empiric therapy **OR** Patient has residual kidney function **OR** Organism MIC ≥4 mg/L	2 g after hemodialysis	3 g after hemodialysis

[1] Expert opinion derived from Descombes 2016; Perez 2012; Schmaldienst 2000

Peritoneal dialysis:

IV: 1 g every 24 hours (Lodise 2006; expert opinion).

CRRT: Drug clearance is dependent on the effluent flow rate, filter type, and method of renal replacement. Recommendations are based on high-flux dialyzers and effluent flow rates of 20 to 25 mL/kg/hour (or approximately 1,500 to 3,000 mL/hour) unless otherwise noted. Appropriate dosing requires consideration of adequate drug concentrations (eg, site of infection), organism MIC, residual kidney function, and consideration of initial loading doses. Close monitoring of response and adverse reactions (eg, neurotoxicity) due to drug accumulation is important.

CVVH/CVVHD/CVVHDF: IV: 2 g every 8 to 12 hours (Baumier 2014; Carlier 2015; Chaijamorn 2018; Privitpot 2019; Shaw 2016).

Note: For severe infections or sepsis, the risks/benefits favor dosing on the higher side of the recommended frequency (Shaw 2016). For CRRT with other effluent rates: If effluent rate is <20 mL/kg/hour, 2 g every 12 hours is preferred (Allaouchiche 1997; Malone 2001). If effluent rate is ≥35 mL/kg/hour, 2 g every 8 hours is preferred (Chaijamorn 2018; Droege 2013).

PIRRT (eg, sustained, low-efficiency diafiltration): Drug clearance is dependent on the effluent flow rate, filter type, and method of renal replacement. Appropriate dosing requires consideration of adequate drug concentrations (eg, site of infection), organism MIC, residual kidney function, and consideration of initial loading doses. Close monitoring of response and adverse reactions (eg, neurotoxicity) due to drug accumulation is important.

Note: Regimens developed through Monte Carlo simulation only and based on daily treatments with 4 to 5 L/hour of dialysate/ultrafiltrate flow rate for each 8- to 10-hour session (Jang 2018).

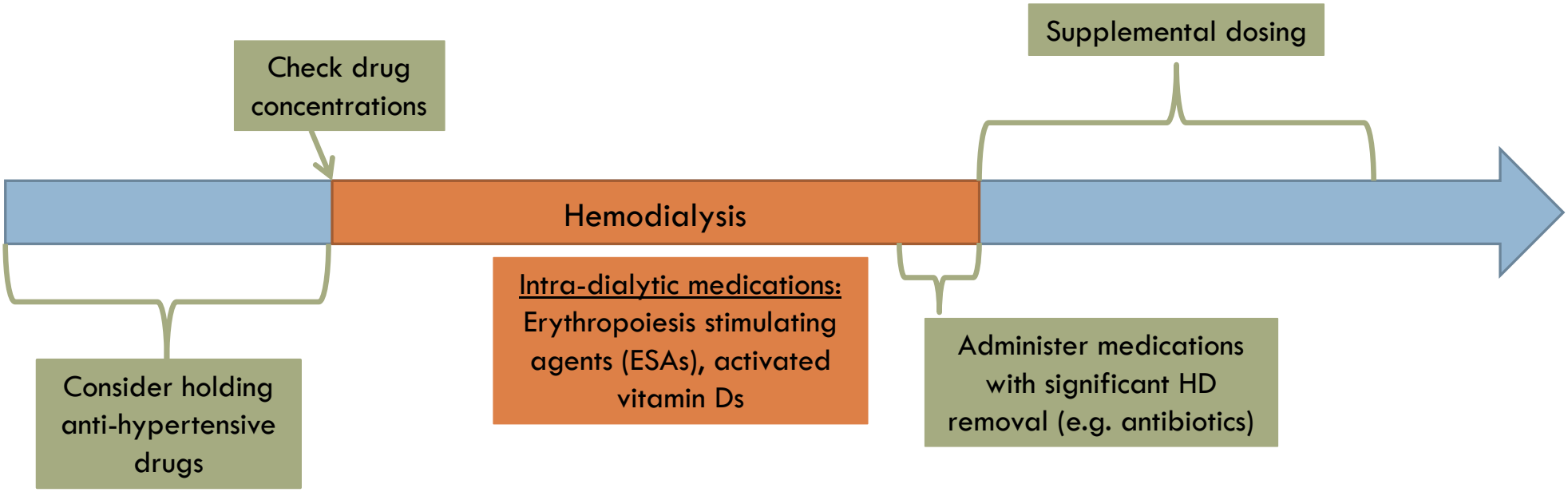
Option 1: IV: 2 g loading dose, followed by 1 g every 6 hours regardless of when prolonged intermittent renal replacement therapy (PIRRT) treatments occur relative to cefepime infusions (Jang 2018).

Option 2 (if every 6 hours not desired [eg, patient self-administering]): IV: 2 g at beginning of PIRRT session, then 3 g after PIRRT session ends. Repeat regimen with every PIRRT session (Jang 2018).

Non-PIRRT days: IV: Select dose based on assessment of nondialysis kidney function (eg, CrCl <11, then 1 g every 24 hours).

Hemodialysis Dosing Considerations

Timeline



Hemodialysis Dosing Considerations

General Rules

- **Dose drugs with significant (~>30%) removal after hemodialysis**

- **Supplemental Dosing:** replace the amount of drug that was removed by hemodialysis
  - Determine need for supplemental dose:
    - >30-40% removal by HD? → yes
    - **<u>Supplemental dose = normal dose X fraction removed by hemodialysis</u>**
    - E.g. Levetiracetam undergoes 50% hemodialysis removal
      - Levetiracetam 1000mg PO once daily
      - Supplemental dose=1000mg x 50% = 500mg post-hemodialysis

Poll Question 4

- An outpatient on hemodialysis is started on vancomycin with a 1500mg loading dose today (Friday) after their routine dialysis session. When should a vancomycin concentration be measured?
  A. Sunday morning
  B. Immediately before dialysis on Monday
  C. Any time during dialysis on Monday
  D. Immediately after dialysis on Monday
  E. At steady state in 21 days

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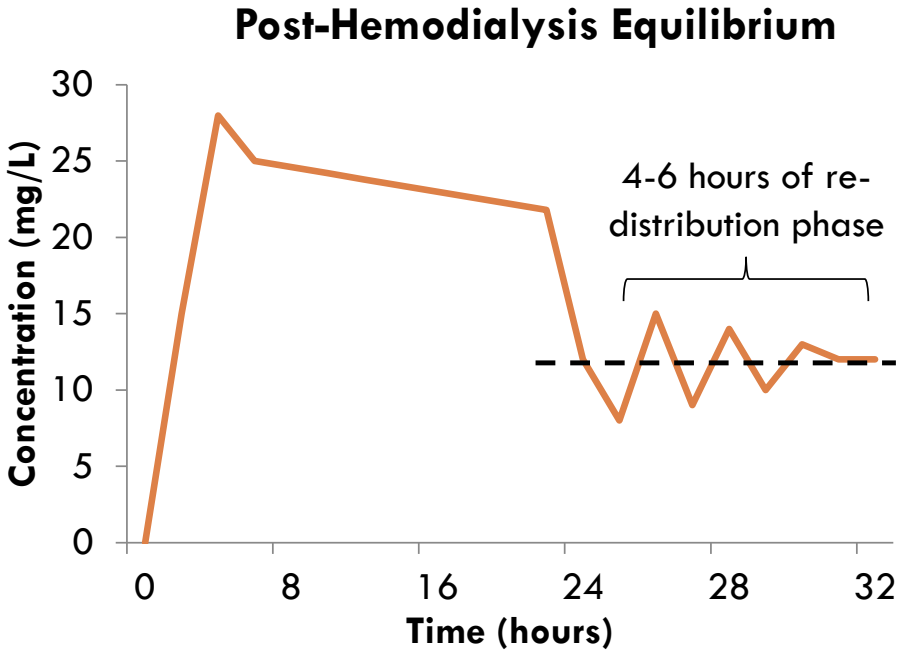
TDM Considerations in Dialysis

- Timing of drug concentration monitoring:
  - Hemodialysis: Prior to HD session
  - Peritoneal dialysis: Random

Post-Dialysis Equilibrium



Dotted line reflects "true" post-HD concentration
Example Conc vs. Time curve for vancomycin

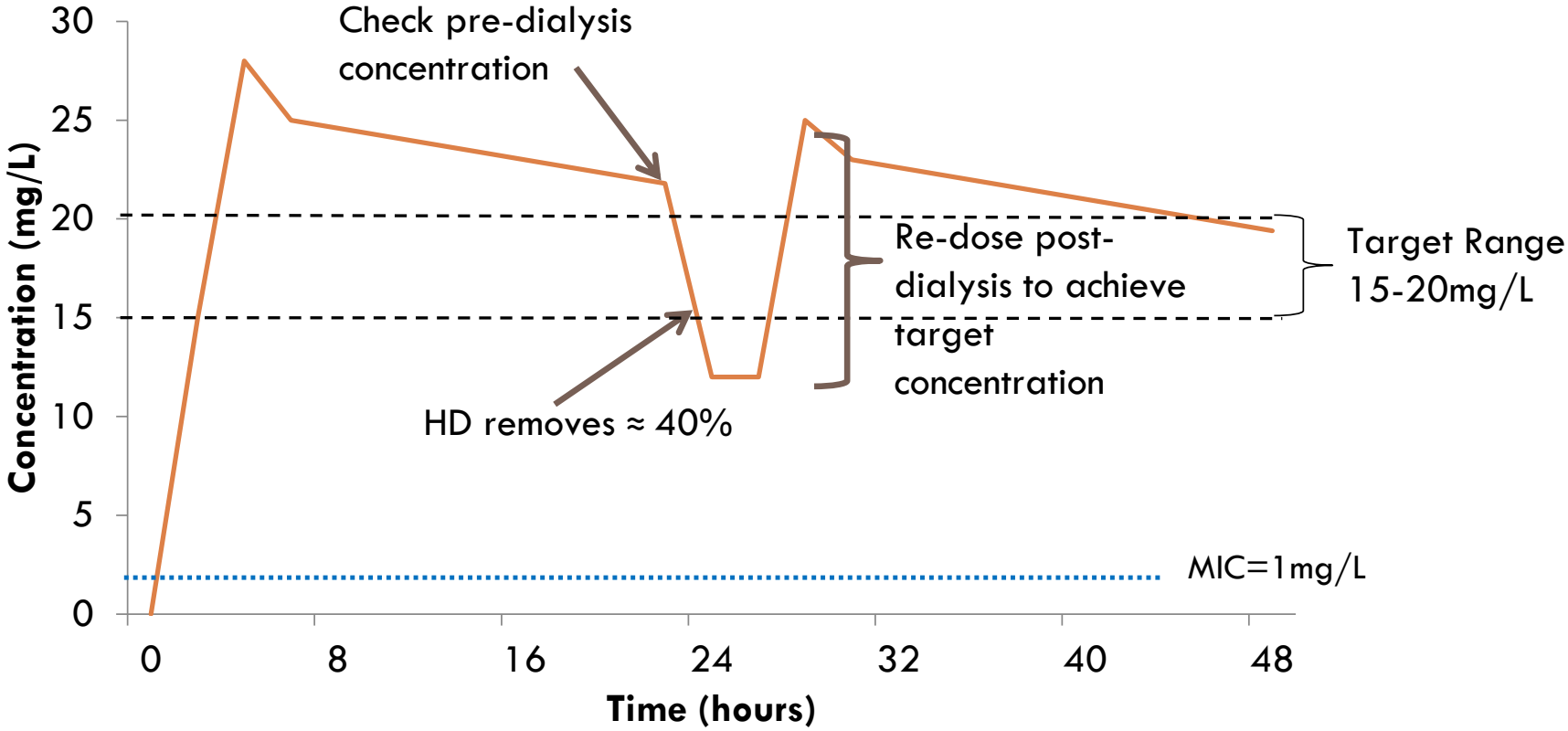
- Re-distribution of drug from tissue stores and/or protein binding sites; fluid shifts
- Fluctuating drug concentrations post-HD
- Unreliable for TDM

TDM Considerations in Dialysis

- Hemodialysis procedure:
  1. Obtain drug concentrations prior to hemodialysis
  2. Estimate intra-dialytic drug removal
  3. Base additional doses on estimated post-hemodialysis concentration and target concentration

TDM Example: Vancomycin in Hemodialysis

Crew et al. *Am J Health-System Pharm* 2015;72:1856-1864.



Post-Dialysis Dose = $\Delta Conc_{desired}$ x V_D

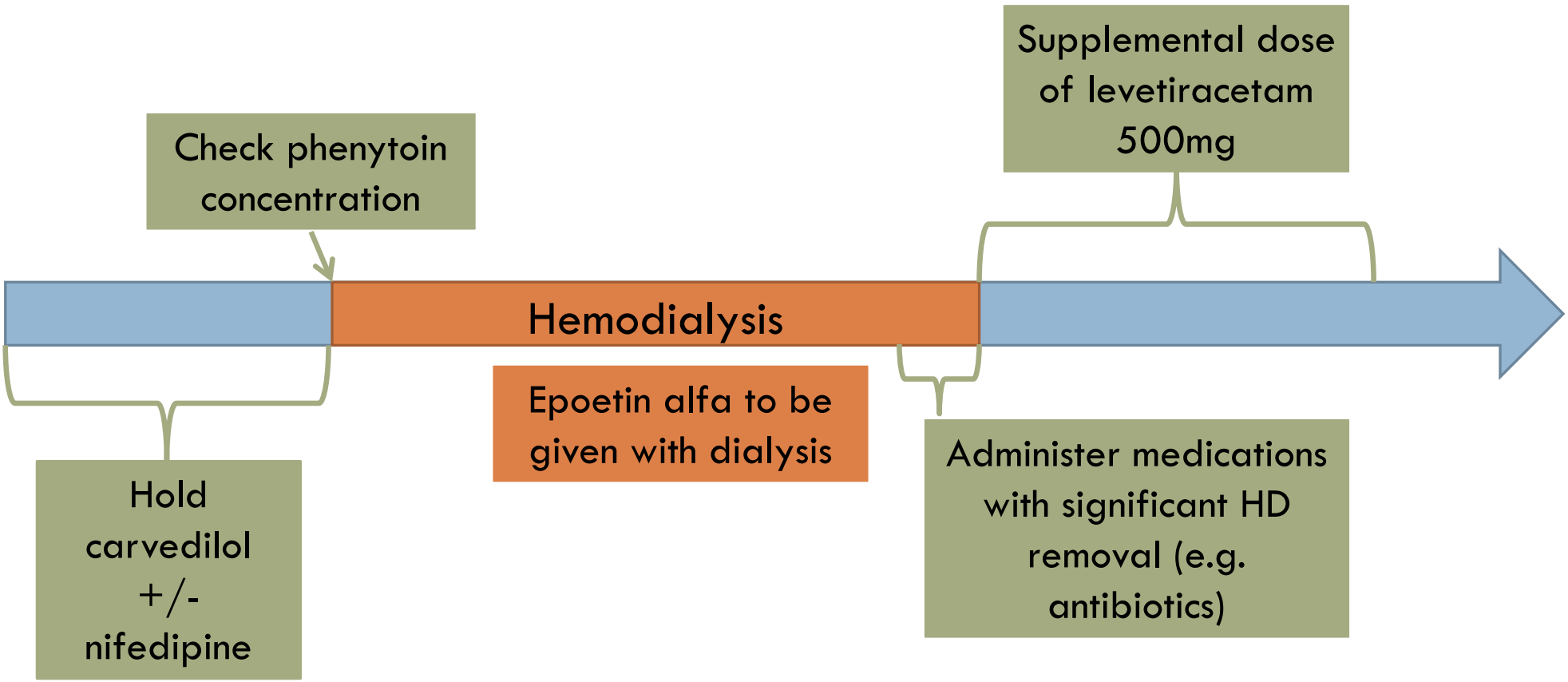
Hemodialysis Dosing Considerations

Case Application

- TM is a 62yo male with kidney failure on intermittent hemodialysis, HTN, seizure disorder, Afib, CAD, HF with EF 30-35%.
- Medications:
  - Nifedipine ER 60mg PO BID
  - Carvedilol 12.5mg PO BID
  - Lisinopril 20mg PO daily
  - Levetiracetam 1000mg PO QAM
  - Phenytoin 100mg PO TID
  - Atorvastatin 20mg PO QHS
  - Sevelamer carbonate 1600mg PO TID
  - Calcitriol 0.5mcg PO daily
  - Epoetin alfa 5,000 units IV MWF with dialysis
- How would you counsel TM to take his medications surrounding dialysis?

Hemodialysis Dosing Considerations

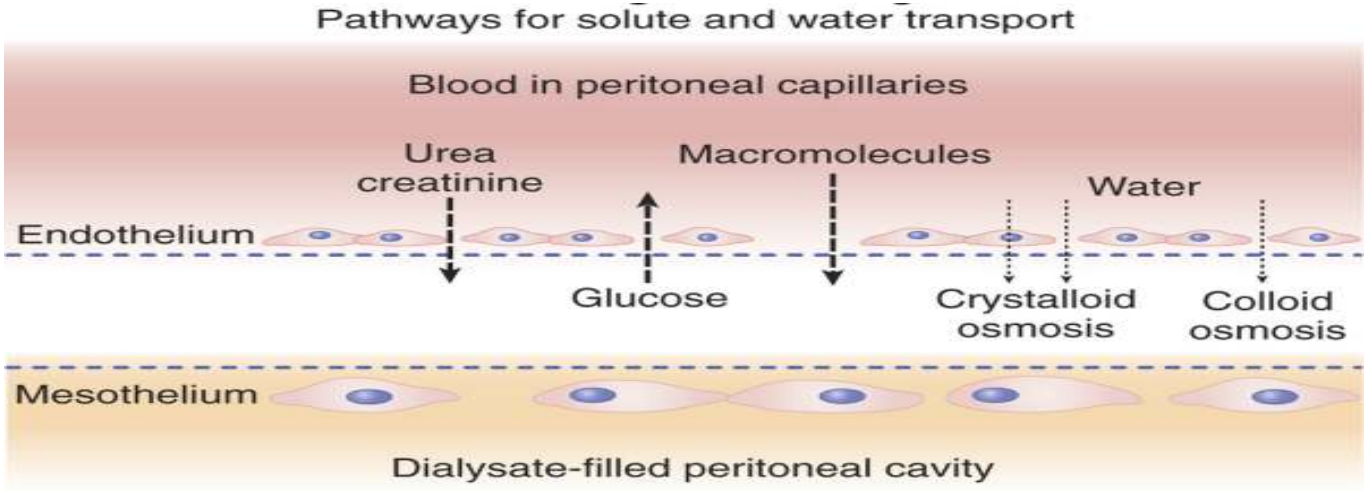
Timeline



Peritoneal Dialysis

Systemic Drug Removal

- Substantially less drug removal than with hemodialysis
  - 10ml/min maximum clearance
  - Dosing guidelines based on CrCl<15ml/min range
- Majority of pores are small: 40-60 Å, account for 95% of surface area
  - Large pores (100-200Å) account for 3% of surface area



L Goldman and AE Schafer. Goldman's Cecil Medicine Volume 2, 24th Edition, Elsevier. 2012. Figure 133-2.

Peritoneal Dialysis

Practical Dosing Consideration

- Drug removal is not as efficient as with HD
- Significant removal occurs if:
  - Very low V_D
  - Low protein binding
  - Few other routes of elimination
  - Above factors, and rapid exchanges
- If giving drug by peritoneal route (i.e. to treat peritonitis) be aware that can achieve potentially toxic serum levels (eg. aminoglycosides 40-50%)

Complications of Kidney Failure

Medication Management

Poll Question 5

- A hemodialysis patient has the following labs:
  - calcium of 7.8 mg/dL (normal range 8.4-10.2 mg/dL)
  - serum phosphorus of 6.8 mg/dL (normal range 2.4-4.2 mg/dL)
  - iPTH 318 pg/mL (normal range 15-60 pg/mL)
- What is the best option to treat their CKD-mineral bone disorder?

A. Sevelamer carbonate
B. Calcium acetate
C. Lanthanum carbonate
D. Ferric citrate
E. Calcitriol

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Anemia of Kidney Disease

Iron Deficiency

- KDIGO 2012 Guidelines for all CKD patients (including dialysis):
  - Goal transferrin saturation >30% and ferritin >500ng/mL

- Correct iron deficiency first before using erythropoiesis stimulating agents

Iron Therapy

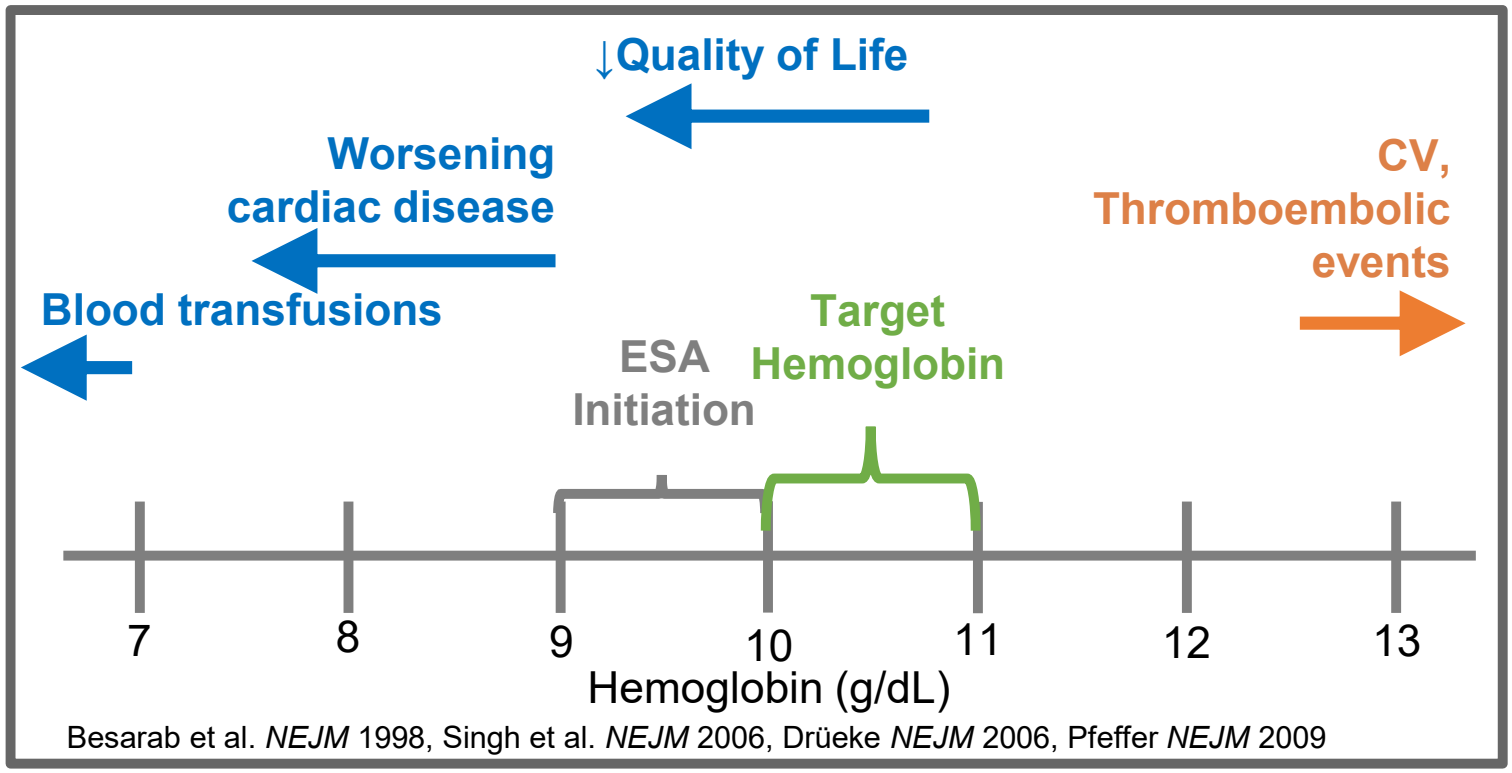
Oral

- Poor absorption
- GI complications: nausea, constipation
- Poor adherence
- Inexpensive
- Slow replenishment of iron stores

Parenteral

- Preferred in hemodialysis patients
- Expensive
- Rapid replenishment of iron stores
- Risk of iron overload
- Infusion / Anaphylactic reactions
- Avoid with active infection

Clinical Complications of Anemia in Kidney Failure over a Range of Hemoglobin Concentrations



Besarab et al. *NEJM* 1998, Singh et al. *NEJM* 2006, Drüeke *NEJM* 2006, Pfeffer *NEJM* 2009

ESA: Erythropoiesis stimulating agent

Erythropoiesis Stimulating Agents

Brand Name	Generic Name	Initial Dosing	Notes
Epogen	Epoetin alfa	50-100 units/kg IV or SubQ three times per week	May be given once per week
Retacrit	Epoetin alfa epbx	50-100 units/kg IV or SubQ three times per week	Biosimilar of *Epogen*
Aranesp	Darbepoetin alfa	0.45mcg/kg IV or SubQ once weekly -OR- 0.75mcg/kg IV or SubQ every 2 weeks	May be given once per month
Mircera	Methoxy Polyethylene Glycol Epoetin beta	0.6mcg/kg IV or SubQ every 2 weeks	May be given once per month

Erythropoiesis Stimulating Agents

Goals of Therapy

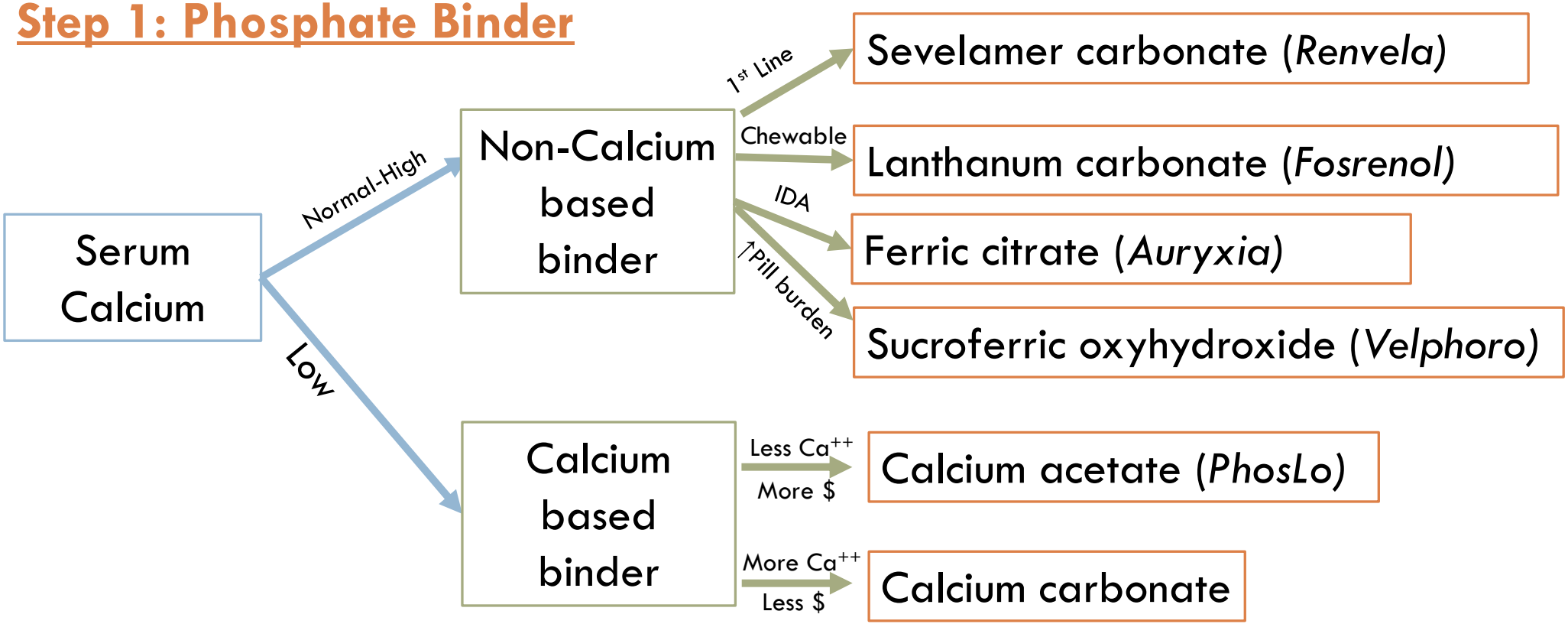
1. Prevent the need for blood transfusions
2. Improve quality of life

Guideline		CKD (Non-Dialysis)	ESRD (Dialysis)
HGB	KDOQI 2007	11-12g/dL	11-12g/dL
	KDIGO 2012	10-11.5g/dL	10-11.5g/dL
	FDA & KDOQI 2013	10g/dL	10-11g/dL

- KDIGO:
  - Do not use ESA to maintain HGB>11.5g/dL
  - Initiate ESA if: HGB 9-10g/dL or to avoid a drop in HGB<9g/dL
- FDA:
  - Use lowest effective dose to reduce risk of blood transfusions
  - An optimal target hemoglobin level, dose or dosing strategy to reduce these risks has not been identified in clinical trials

CKD-Mineral Bone Disease

Step 1: Phosphate Binder

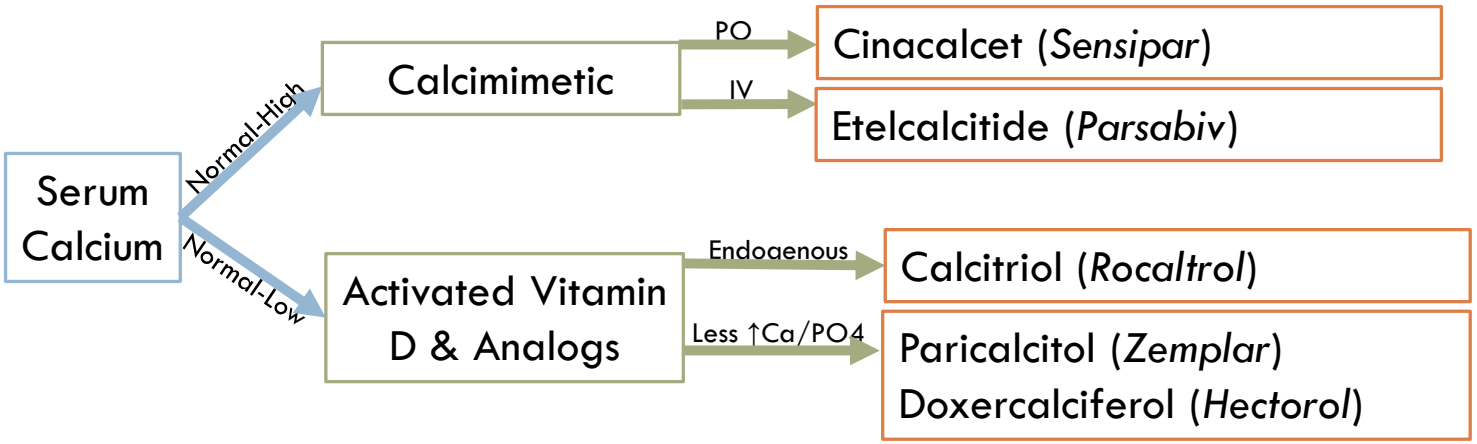


IDA: Iron deficiency anemia

KDIGO Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements* 2017

CKD-Mineral Bone Disease

Step 2: Lower Parathyroid Hormone



KDIGO 2017 Guidelines:

Goal Serum Calcium: Avoid hypercalcemia; asymptomatic hypocalcemia is acceptable

Goal Serum Phosphate: Towards the normal range (or 3.5-5.5mg/dL)

Goal iPTH: 2-9x ULN (~150-600pg/ml)

KDIGO Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements* 2017

Questions

"The kidney is the most important organ in the body"
@DGlaucomflecken