Renal Dose Adjustment Guidelines for Antimicrobials
CRRT Dosing Recommendations

CRRT Background:

- When a patient is initiated on CRRT, antimicrobial therapy often requires adjustment to ensure adequate drug concentrations are achieved.
- ***CVVHD*** removes solutes (including drugs) via diffusion. An electrolyte solution (dialysate) runs countercurrent to the patient's blood flow which creates a concentration gradient, driving the removal of solutes.
    - Drug removal is impacted by protein binding (e.g. highly protein bound drugs will be minimally removed) and rate of dialysate flow (increased removal with higher flow rates).
    - Drugs that are renally cleared or removed by hemodialysis are likely to be impacted by CVVHD.
- ***CVVH*** removes solutes (including drugs) via convection. Convection is a transport mechanism that is accomplished by using a high-permeability membrane to generate a large ultrafiltrate volume. Along with the ultrafiltrate, plasma water and certain solutes are forced across the membrane.

Important Considerations:

- In patients with renal failure, the time to achievement of steady-state is increased for renally-eliminated agents. Additionally, patients on CRRT frequently have an increased volume of distribution. Therefore, ***a loading dose should be utilized if not initiating therapy at the full dose.***
- Patients undergoing CRRT may be predisposed to changes in pharmaceutical agents' volume of distributions (Vd). When agents with relatively large therapeutic windows (e.g. beta-lactams) and low levels of toxicity are utilized in critically ill patients, it may be prudent to err on the side of more aggressive dosing to account for any increases in (Vd).
- While on CRRT, patients' residual renal function may continue to change. Improvements or reductions in residual renal function may warrant a change in dosing strategy. Residual renal function should be evaluated on a daily basis when making CRRT dosing plans.
- Monitor patients for interruption of CRRT (e.g. clotting) or changing filtration rates. When CRRT is off, dose as hemodialysis patients or based on any residual renal function.
- ***The recommendations below should be used as a guide*** to aid in antibiotic dosing while on CRRT. Dosing regimens should be tailored based on presumed source of infection, MIC data (when available), and residual renal function. When a dosing range is indicated in the tables below (e.g., ampicillin/sulbactam 1.5-3 g q6-8h), a more aggressive dose should be selected for severe infections.
- Pharmacists should document final dosing recommendations and any necessary rationale using the preformatted note available in One Chart.

The following anti-infectives do NOT require dose adjustment during CRRT:

- Amphotericin
- Azithromycin
- Ceftriaxone
- Clindamycin
- Doxycycline
- Linezolid
- Metronidazole
- Micafungin
- Oxacillin
- Rifampin
- Tigecycline
- Voriconazole

Table 1. CVVHD Dosing Recommendations

Drug	Loading Dose for CRRT	Standard Anephric Dose	Dose by CVVHD Dialysate Flow Rate			Ref.
			1 L/h	2 L/h	3-4 L/h	
Aminoglycosides		Provide loading dose then dose per TDM	Provide loading dose then dose per TDM; patients may require repeat dosing q24h at flow rates >1 L/h			1, 2
Amikacin	10 mg/kg					
Gentamicin	3 mg/kg					
Tobramycin	3 mg/kg					
Acyclovir[a]	NA	2.5-5 mg/kg q24h	5-7.5 mg/kg q24h	5-10 mg/kg q24h	5-10 mg/kg q12h[b]	1, 2
Ampicillin/sulbactam	3 g	1.5-3 g q24h	1.5-3g q8h	1.5-3g q6-8h[b]	1.5-3g q6h[b]	1, 2
Aztreonam	2 g	1-2 g q24h	1 g q8h or 2 g q12h	1g q8h or 2 g q12h	2 g q8h[b]	1
Cefazolin	2 g	1-2 g q24h	1 g q8h or 2 g q12h	1 g q8h or 2 g q12h	2 g q8h[b]	1
Cefepime (*Standard dose)*	2 g	1 g q24h	1 g q8h	1 g q6h	2 g q8h[b]	1, 2, 3, 4, 18
Cefepime (*High dose for neutropenic fever)*	2g	1 g q24h	2g q12h		2g q8h	
Ceftazidime	2 g	1 g q24h	1 g q8h or 2 g q12h	1 g q8h or 2 g q12h	2 g q8h[b]	1, 2
Ceftolozane/tazobactam[c]	1.5 g	150 mg q8h	375 mg q8h	750 mg q8h	1.5g q8h	16
Colistin	NA	50 mg q12h	2.5 mg/kg q24h	2.5 mg/kg q24h	2-3 mg/kg q12h	1, 2, 13, 22, 23
Daptomycin	NA	6 mg/kg q48h	4-6 mg/kg q24hr	6 mg/kg q24hr	6-8 mg/kg q24h	1, 2, 5, 6, 19
Ertapenem	1g	500mg IV q24h	1g IV q24h			13
Fluconazole[d]	800 mg (12 mg/kg)	400 mg (6 mg/kg) after HD three times weekly	400 mg q24h 800 mg q24h	800 mg q24h	800 mg q24h	1, 2, 7
Ganciclovir	5 mg/kg	1.25 mg/kg after HD three times weekly	2.5 mg/kg q24h	5 mg/kg q24h or 2.5 mg/kg q12h	5 mg/kg q12h	1, 12
Levofloxacin	500 mg	250-500 mg q48h	250-750 mg q24h			1, 2, 17
Meropenem (*Standard dose)*	1-2 g	500-1000 mg q24h	500 mg q8h	500 mg q8h	500 mg q6h	1, 2, 3, 9
Meropenem (*High dose for meningitis, cystic fibrosis, or MIC of 4 mcg/mL)*	2 g	2g IV q24h	2g q12h		2g q8h	
Oseltamivir	NA	If not undergoing HD – Not recommended; *If undergoing HD* – 30 mg after every HD cycle	150 mg q12h			
Piperacillin/tazobactam[f] EI	NA	4.5 g EI q12h	4.5 g EI q8h			10, 15
Trimethoprim/sulfamethoxazole (TMP/SMX)	10 mg/kg	Severe infections/PJP: 7.5-10 mg/kg/day (TMP) divided q12-24h	10 mg/kg/day (TMP) divided q12h			20, 21
Vancomycin	20-25 mg/kg	Provide loading dose then dose accordingly to obtain serum concentrations within desired range	Provide loading dose then dose patients 10-15 mg/kg q24h and adjust accordingly to obtain serum concentrations within desired range			1, 11

Abbreviations: EI, extended infusion (4 hours); HD, hemodialysis; NA, not applicable; PJP, *Pneumocystis jiroveci* pneumonia; TDM, therapeutic drug monitoring

[a]Use lower dose for mucocutaneous HSV and higher dose for HSV encephalitis or VZV
[b]Flow rates > 2 L/hr are rarely addressed in literature; decreasing the interval is done empirically to maintain levels above MIC for time-dependent antibiotics, specifically those with limited protein binding
[c]Dose adjustments based on data from CVVH since data is lacking for CVVHD
[d]Dose assuming invasive candidiasis
[e]Decreased interval is based on data from CVVH since data is lacking for CVVHD and some antimicrobials; however, CVVHD solute elimination is in general greater than CVVH
[f]Tazobactam can accumulate as it is not removed as readily; caution in decreasing interval beyond every 8 hours (i.e. q6h) in patients with lack of residual renal function

Table 2. CVVH Dosing Recommendations

Drug	Loading Dose for CRRT	Standard Anephric Dose	Dose by CVVH Dialysate Flow Rate				Ref.
			1 L/h	2 L/h	3 L/h	4 L/h	
Aminoglycosides		Provide loading dose then dose per TDM	Provide loading dose then dose per TDM; patients may require repeat dosing q24h at flow rates >1 L/h				1
Amikacin	10 mg/kg						
Gentamicin	3 mg/kg						
Tobramycin	3 mg/kg						
Acyclovir[a]	NA	2.5-5 mg/kg q24h	5-7.5 mg/kg q24h	5-10 mg/kg q24h			1
Ampicillin/sulbactam	1.5-3 g	1.5-3 g q24h	1.5-3 g q8-12h				1
Aztreonam	2 g	1-2 g q24h	1 g q8h	2g q12h	2 g q8h	2 g q6h	2
Cefazolin	2 g	1-2 g q24h	1 g q12h	1 g q12h	1 g q8h	1 g q8h	2
Cefepime (*Standard dose)*	2 g	1 g q24h	1 g q8h	1 g q6h	2g q8h	2g q8h	1, 3
Cefepime (*High dose for neutropenic fever)*	2g	1 g q24h	2g q12h		2g q8h		
Ceftazidime	2 g	1 g q24h	1 g q12h	2g q12h	2 g q8h	2 g q8h	2
Ceftolozane/tazobactam[b]	1.5 g	150 mg q8h	375 mg q8h	750 mg q8h	1.5g q8h		4
Colistin		50 mg q12h	2.5 mg/kg q48h				1, 8
Daptomycin	NA	6 mg/kg q48h	No adjustment necessary; dose as anephric				1
Fluconazole[c]	800 mg (12 mg/kg)	400 mg (6 mg/kg) after HD three times weekly	200 mg q24h	400 mg q24h	400 mg q12h	400 mg q12h	1, 5
Levofloxacin	500-750 mg	250-500 mg q48h	250 mg q24h				1
Meropenem (*Standard dose)*	1-2 g	500-1000 mg q24h	500 mg q12h	500 mg q8h	500 mg q6h	500 mg q6h	1, 6
Meropenem (*High dose for meningitis, cystic fibrosis, or MIC of 4 mcg/mL)*	2 g	2g q24h	2g q12h		2g q8h		
Piperacillin/tazobactam EI	NA	4.5 g EI q12h	4.5 g EI q8h				7
Trimethoprim/sulfamethoxazole (TMP/SMX)	NA	Severe infections/PJP: 7.5-10 mg/kg/day (TMP) divided q12-24h	2.5-7.5mg/kg (TMP) q12h				1
Vancomycin	20-25 mg/kg	Provide loading dose then dose accordingly to obtain serum concentrations within desired range	Provide loading dose then dose patients approximately 500 mg q12h when dialysate flow rates >1 L/h and adjust accordingly to obtain serum concentrations within desired range				6

Abbreviations: EI, extended infusion (4 hours); HD, hemodialysis; NA, not applicable; PJP, *Pneumocystis jiroveci* pneumonia; TDM, therapeutic drug monitoring

[a]Use lower dose for mucocutaneous HSV and higher dose for HSV encephalitis or VZV
[b] Data limited to dialysate flow rates of 2 L/hr
[c] Dose assuming invasive candidiasis

CVVHD References:

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