

# Stanford Hospital & Clinics Antibiotic Dosing Reference Guide 2011

This document is also located on the SHC Intranet (<http://portal.stanfordmed.org/depts/pharmacy>) P&T Approved April 15, 2011

**Formulas for dosing weights:** Ideal body weight IBW (male) = 50 kg + (2.3 x height in inches > 60 inches) IBW (female) = 45 kg + (2.3 x height inches > 60 inches)  
Adjusted BW (kg) = IBW + 0.4 (TBW – IBW)

Drug	CrCl >50 mL/min	CrCl 10–50 mL/min	CrCl <10 mL/min	Intermittent Hemodialysis (IHD)	CRRT	
<b>Acyclovir (IV)</b> <sup>1,4,5,6,7,8</sup> (Use ideal BW for obese)	HSV: 5 mg/kg q8h HSV encephalitis/zoster: 10 mg/kg q8h	Same dose CrCl 25–50: q12h CrCl 10 – 25: q24h	HSV: 2.5 mg q24h HSV encephalitis/zoster: 5 mg/kg q24h	HSV: 2.5mg/kg q24h HSV encephalitis/zoster: 5mg/kg q24h Dose after HD on HD days	HSV: 5 – 7.5 mg/kg q24h HSV encephalitis/zoster: 7.5–10 mg/kg q12h	
<b>Acyclovir (PO)</b> <sup>1,5</sup>	HSV mucocutaneous: 200 mg q4h (or 5x daily) VZV, HSV zoster: 800 mg q4h (or 5x/day)	Same dose q8h	Same dose q12h	Same dose q12h	n/a	
<b>Ambisome</b> <sup>1</sup> (Ampho BLiposomal)	3 – 6 mg/kg/day	No change (caution: nephrotoxic)	No change	No change	No change	
<b>Amikacin</b> <sup>1,2,3,7</sup> (Use ideal or adjusted BW for obese)  See appendix for complete guidelines	CrCl >60 5 – 7.5 mg/kg q8h Once daily dosing: 15–20 mg/kg q24h	CrCl 40– 60: 5 – 7.5 mg/kg q12h 15–20 mg/kg q36h	CrCl 20–40 5 – 7.5 mg/kg q24h 15–20 mg/kg q48h	CrCl < 20 5 mg/kg load, then by level	5 – 7.5mg/kg post HD only  consult pharmacist	
	<b>Timing of levels:</b> Draw trough 30 min prior to 4 <sup>th</sup> dose. Draw peak 30 min after infusion ends <b>Once daily dosing:</b> goal peak 35–60; goal trough <4. Consult Hartford Nomogram <b>Conventional dosing:</b> goal peak 25–35 for serious infections, 15–20 for UTI goal trough: <5-8				10 mg/kg load, then 7.5mg/kg q24–48h  consult pharmacist	
<b>Ampicillin (IV)</b> <sup>1,3,4,6</sup>	1 – 2 gm q4 – 6h Meningitis/endocarditis: 2 gm q4h	same dose q6 – 12h Meningitis/endocarditis: 2gm q6h	same dose q12h Meningitis/endocarditis: 2gm q12h	1gm q12h Meningitis/endocarditis: 2gm q12h	1gm q6 –8h Meningitis/endocarditis: 2gm q6h	
<b>Ampicillin/sulbactam</b> <sup>1,2,4,6,7</sup> (SHC Restriction)	3 gm q6h	CrCl <50: 3gm q8h CrCl <30: 3gm q12h	CrCl <15 3gm q24h	3 gm q12–24h Dose after HD on HD days	3gm q6 –8h	
<b>Azithromycin (IV/PO)</b> <sup>1</sup>	500 mg q24h	No change	No change	No change	No change	
<b>Aztreonam</b> <sup>1,2,6</sup> Severe: pseudomonas, meningitis	1 – 2 gm q8h Severe: 2gm q6–8h	CrCl 10 – 30: 1gm q8h Severe: 1gm q6 – 8h	500 mg q8h Severe: 500 mg q6 – 8h	1–2gmLD, then 500 mg q12h Severe: 1–2gm LD, then 500 mg q8h	1gm q8h or 2 gm q12h	
<b>Caspofungin</b> <sup>1</sup> (Hepatic adjustment)	70 mg x1, then 50 mg q24h Consider 70 mg x 1, then 35mg q24h if severe hepatic dysfunction (Child–Pugh score >7); 70 mg q24h if on phenytoin, rifampin, other strong enzyme inducers			No change	No change	
<b>Cefazolin</b> <sup>1,2,5,6,7,8</sup>	UTI/mild: 1 gm q8h General: 2 gm q8h	UTI/mild: 1 gm q12h General: 2 gm q12h	1 gm q24h	1 gm q24h Dose after HD on HD days	2 gm q12h	
<b>Cefepime</b> <sup>1,4,5,6,7</sup> (SHC Interchange) Severe: endocarditis/CF febrile neutropenia/pneumonia/meningitis/pseudomonas	CrCl >60 2 gm q12h or 1gm q6h	CrCl 30 –60: 2 gm q24h or 1 gm q12h	CrCl < 30 1gm q24h	0.5 gm q24h  Severe infections: 1 gm q24h	1gm q8h  Severe infections: 2 gm q12h	
	General Severe	2 gm q12h or 1gm q6h 2 gm q8h	2 gm q24h or 1 gm q12h 2 gm q12h	1 gm q24h 2 gm q24h	0.5 gm q24h Severe: 1 gm q24h Give post HD on HD days	1gm q8h Severe infections: 2 gm q12h
<b>Ceftriaxone</b> <sup>1,5,9</sup>	1 – 2 gm q24h Endocarditis, osteomyelitis: 2 gm q24h Meningitis, E. faecalis endocarditis: 2 gm q12h		No change	No Change Dose after HD on HD days	No Change	
<b>Ciprofloxacin(IV/PO)</b> <sup>1,2,5,6,8</sup>	General infections	CrCl >50 400 mg IV q12h 500 mg PO q12h	CrCl 30 – 50 same	CrCl < 30 400 mg IV q24h 500 mg PO q24h	400 mg IV q24h 500 mg PO q24h Give post HD on HD days	
	Pseudomonas, severe	400 mg IV q8h 750 mg PO q12h	400 mg IV q8 – 12h 500 mg PO q12h	400 mg IV q24h 500 mg PO q24h	400 mg IV q12h 500 mg PO q12h	
<b>Clindamycin</b> <sup>1,2</sup> (caution in severe hepatic disease)	600– 900 mg IV q8h 150 – 450 mg PO q6h	No change	No change	No change	No change	
<b>Colistin</b> <sup>1,5,6</sup> (Use ideal BW in obese)	1.25 – 2.5mg/kg q12h	Cr 1.3 – 1.5: 1.25 – 1.9 mg/kg q12h Cr 1.6 – 2.5: 2.5 mg/kg q24h	Cr 2.6 – 4: 1.5 mg/kg q24h	1.5 mg/kg q24h	2.5mg/kg q12–24h	
<b>Daptomycin</b> <sup>1,10,11,21</sup> (Use adjusted BW in obese) (SHC Restriction)	Skin/Soft tissue: 4 mg/kg q24h Endocarditis/Bacteremia: 6 – 8 mg/kg q24h	(Calculate CrCl using IBW) CrCl < 30: Same dose q48h		Same dose q48h	4 –8mg/kg q48h	
<b>Doxycycline (IV/PO)</b> <sup>1</sup>	100 mg q12h	No change	No change	No change	No change	
<b>Ertapenem</b> <sup>1</sup>	1 gm q24h	CrCl <30: 500 mg q24h	500 mg q24h	500 mg q24h Give post HD on HD days	1 gm q24h	
<b>Ethambutol (PO)</b> <sup>1,7</sup>	15 – 25 mg/kg q24h	15 – 25 mg/kg q24 – 36h	15 – 25 mg/kg q48h	15 – 25 mg/kg post HD only	15 – 25 mg/kg q24 – 36h	
<b>Fluconazole(IV/PO)</b> <sup>1,5,6,8</sup> Load 800 mg for candidemia	200 –400 mg q24h Severe/CNS infections: up to 800 mg q24h	100 – 200 mg (50% of normal dose) q24h	50–100 mg (25% of normal dose) q24h	200 - 400 mg post HD only	400mg q24h (800 mg q24h for less susceptible organisms)	
<b>Foscarnet</b> <sup>1</sup>	<b>Please see Lexi-comp or Micromedex for renal dosing table. Note that dosing is by CrCl per kg (ml/min/kg)</b> CrCl/kg > 1.4: CMV Induction treatment: 60 mg/kg q8h or 90 mg/kg q12h x 14-21 days					
<b>Ganciclovir</b> <sup>1,6</sup> Consider loading dose of 5mg/kg for all patients	CMV	CrCl >70*	CrCl >50	CrCl >25	CrCl >10	CrCl <10
	Induction (I)	5 mg/kg q12h	2.5 mg/kg q12h	2.5 mg/kg q24h	1.25 mg/kg q24h	1.25 mg/kg 3x/wk
Maintenance (M)	5 mg/kg q24h	2.5 mg/kg q24h	1.25 mg/kg q24h	0.625 mg/kg q24h	0.625 mg/kg 3x/wk	0.625 mg/kg 3x/wk
*Manufacturer's CrCl cutoffs. Please refer to BMT protocols if applicable						
<b>Gentamicin</b> <sup>6</sup> (SHC interchange to tobramycin. Exception: gram positive synergy) See appendix for complete guidelines	CrCl >60	CrCl 40–59	CrCl 20–39	CrCl <20	HD	CRRT
	Gram positive synergy	1mg/kg q8h*	1mg/kg q12h	1mg/kg q24h	1mg/kg load, then by level	1mg/kg load, then 1mg/kg post HD only
<b>Timing of levels:</b> Draw trough 30 min prior to 4 <sup>th</sup> dose. Draw peak 30 min after infusion ends (4 <sup>th</sup> dose). (For CrCl <60, check levels sooner than 4 <sup>th</sup> dose) In HD, check trough before each HD session, and peak 30 minutes after each dose. <b>Goal levels:</b> For synergy, goal peak 3–5mg/L (3–4 if using IDSA endocarditis guidelines). Goal trough <1 mg/L * Streptococci, Streptococcus bovis, Strep. viridans endocarditis: optional dosing 3mg/kg q24h for CrCl > 60						
<b>Imipenem/Cilastatin</b> <sup>1,2,6</sup> (Nonformulary)	500 mg q6h	500 mg q8h	250– 500 mg q12h	250 – 500 mg q12h Dose after HD on HD days	500 mg q8h Severe: 500 mg q6h	
<b>Isoniazid</b> <sup>1</sup>	300 mg q24h	No change	No change	No change Dose after HD on HD days	No change	

Drug	CrCl >50 mL/min	CrCl 10–50 mL/min	CrCl <10 mL/min	Intermittent Hemodialysis (IHD)	CRRT																	
Levofloxacin (IV/PO) <sup>1,2,5,6,8</sup>	General	CrCl >50 250 – 500 mg q24h	CrCl 20–50: 250 – 500 mg q48h	CrCl < 20 500 mg x1, then 250 mg q48h	See CrCl < 20 ml/min Dose after HD on HD days	500 mg q48h Pseudomonas/CAP: 750 mg LD, then 500 mg q24h or 750 mg q48h																
	Pseudomonas/CAP:	750 mg q24h	750 mg q48h	750 mg x1, then 500 mg q48h																		
Linezolid (IV/PO) <sup>1,4</sup> (SHC Restriction)	600 mg q12h	No change	No change	No change. Dose after HD on HD days	No change																	
Meropenem (SHC Restriction) Consider extended infusion (3 hours) or more frequent dosing intervals for pseudomonas or resistant pathogens	General:	CrCl >50 1 gm q8h or extended infusion 3 hr	CrCl 26–50: 1 gm q12h or 0.5gm q6h	CrCl 10–25 0.5gm q8 – 12h	500 mg q24h Give post HD on HD days Severe/CF/CNS: 1gm q24h Give post HD on HD days	1 gm q12h or 500 mg q6h Severe/CF/CNS: 2g q12h																
	Severe/CF/CNS:	2 gm q8h	2 gm q12h	1 gm q12h or 0.5gm q8h			0.5gm q12 – 24h															
Moxifloxacin <sup>1</sup>	400 mg IV/PO q24h	No change	No change	No change (Can consider 500 mg q12h in long term use or severe hepatic disease)	No change																	
Metronidazole (IV/PO) <sup>1</sup>	500 mg q6 – 8h	No change	No change	500 mg q8h	500 mg q6 – 8h																	
Nafcillin <sup>1</sup>	2 gm q4h Mild infections: 1gm q4h	No change	No change	No change	No change																	
Oseltamivir (PO) <sup>1,2,15,16,17</sup>	Prophylaxis	Treatment	Treatment (severe/ICU)	Treatment/prophylaxis: 30 mg Severe/ICU: 60 mg Give after every other HD session	Prophylaxis: 75mg q24h Treatment: 75mg BID Severe/ICU: 150 mg BID																	
	CrCl ≥ 30	CrCl < 30	CrCl ≥ 30			CrCl < 30																
Penicillin G (IV) <sup>1,5,6</sup>	2 – 4 mu q4h	2– 3mu (75% of dose) q4h	1– 2 mu (25–50% of dose) q6h	4mu x1, then 1 – 2 mu q6h	4mu x1, then 2 – 3 mu q6h																	
Piperacillin/tazobactam <sup>1,2,4,5,6,8</sup>	General	CrCl >40 3.375gm q6h	CrCl 20–40 2.25gm q6h	CrCl <20: 2.25 gm q8h	2.25gm q12h Pseudomonas/PNA/ severe infections: 2.25gm q8h	3.375 gm q6h or Extended infusion 3.375 gm q8h (infused over 4 h)																
	Pseudomonas/nosocomial PNA/severe:	4.5 gm q6h Extended infusion for CrCl > 20: 3.375 gm q8h over 4h	3.375gm q6h	2.25 gm q6h																		
Posaconazole (PO) <sup>1,2,22</sup> (SHC Restriction)	Treatment: 200 mg q6h or 400 mg q12h	No change.	Posaconazole levels shown to have great degree of interpatient variability. Many clinicians would recommend blood levels to assess efficacy. Consider drawing a trough 4 - 7 days after initiating dose																			
Pyrazinamide (PO) <sup>1,5,12</sup> (Use ideal BW) Round to nearest tablet size	20 – 25mg/kg IBW q24h (max 2000 mg/day)	CrCl < 30: 25 – 35 mg/kg IBW 3 times per week		25 – 30 mg/kg IBW after HD only	No data																	
Rifampin (IV/PO) <sup>1,13,14</sup>	TB: 600 mg q24h Endocarditis: 300 mg q8h	No change	No change	No change	No change																	
Tobramycin <sup>20</sup> (Use ideal or adjusted BW for obese)  See appendix for complete guidelines	CrCl >60 1.7 mg/kg q8h or 7mg/kg q24h (once-daily dosing*)	CrCl 40–59 1.7 mg/kg q12h	CrCl 20–39 1.7 mg/kg q24h	CrCl <20 2 mg/kg loading dose, then per level	HD 2 mg/kg loading dose, then 1.5 – 2 mg/kg post HD	CRRT 1.5 - 2 mg/kg q24 - 48h, consult pharmacist																
	<p><b>Goal levels:</b> Goal peak (4–8mg/L), and trough (&lt;1-2mg/L) for treatment. *certain qualifications for once-daily dosing</p> <p><b>Timing of levels:</b> Draw trough 30 min prior to 4<sup>th</sup> dose. Draw peak 30 minutes after infusion ends (4<sup>th</sup> dose). (For CrCl &lt;20, may check levels sooner than 4<sup>th</sup> dose) For once-daily dosing, draw a single random level 8 to 12 hours after dose given adjustments are made based on a published Hartford nomogram. For HD, draw trough pre-HD, and peak 30 min after end of each infusion.</p>																					
Trimethoprim (TMP)/Sulfamethoxazole <sup>1,5,6</sup> (Dose by ideal or adjusted BW in obese) SS = 80 mg TMP = 10 ml po soln DS = 160 mg TMP = 20ml po soln	5 – 10 mg/kg/day TMP divided q6 – 8h PCP/Stenotrophomonas: 15 – 20 mg/kg/day TMP divided q6-8h	CrCl < 30 2.5 – 5 mg/kg/day TMP divided q8 – 12h PCP/Stenotrophomonas: 7.5 – 10 mg/kg/day TMP divided q8 –12h		2.5 – 5 mg/kg TMP q24h* PCP/ Stenotrophomonas: 7.5 –10 mg/kg TMP q24h* *Give after HD on HD days	5 – 10 mg/kg/day TMP divided q12h PCP/ Stenotrophomonas: 10 –15mg/kg/day TMP divided q12h																	
	<p><b>Valganciclovir (PO)<sup>1</sup></b> Please refer to transplant protocols if applicable</p> <table border="1"> <thead> <tr> <th></th> <th>CrCl &gt; 60</th> <th>CrCl 40 – 59</th> <th>CrCl 25 – 39:</th> <th>CrCl 10 – 24</th> <th>CrCl &lt; 10, IHD, CRRT</th> </tr> </thead> <tbody> <tr> <td>Induction (14-21 days)</td> <td>900 mg q12h</td> <td>450 mg q12h</td> <td>450 mg q24h</td> <td>450 mg q48h</td> <td rowspan="2">Not recommended, use ganciclovir</td> </tr> <tr> <td>Maintenance/ ppx</td> <td>900 mg q24h</td> <td>450 mg q24h</td> <td>450 mg q48h</td> <td>450 mg twice/week</td> </tr> </tbody> </table>							CrCl > 60	CrCl 40 – 59	CrCl 25 – 39:	CrCl 10 – 24	CrCl < 10, IHD, CRRT	Induction (14-21 days)	900 mg q12h	450 mg q12h	450 mg q24h	450 mg q48h	Not recommended, use ganciclovir	Maintenance/ ppx	900 mg q24h	450 mg q24h	450 mg q48h
	CrCl > 60	CrCl 40 – 59	CrCl 25 – 39:	CrCl 10 – 24	CrCl < 10, IHD, CRRT																	
Induction (14-21 days)	900 mg q12h	450 mg q12h	450 mg q24h	450 mg q48h	Not recommended, use ganciclovir																	
Maintenance/ ppx	900 mg q24h	450 mg q24h	450 mg q48h	450 mg twice/week																		
Vancomycin <sup>6,19,21</sup> (Use actual body weight) Consider loading dose of 20–25mg/kg (max 2gm) for severe infections and ICU	CrCl >50 15 – 20 mg/kg q8 – 12h	CrCl 30–49 15 – 20 mg/kg q24h	CrCl 15–29 10 – 15 mg/kg q24h	CrCl <15 10 – 15 mg/kg q24 – 48h	20 – 25mg/kg LD, then redose with 10 – 15mg/kg post dialysis when level <15 – 20	20 – 25mg/kg LD, then 10 – 15mg/kg q24h  Draw level prior to 3 <sup>rd</sup> dose. Adjust to levels																
	<p><b>Goal levels:</b> Goal trough 10–15 mcg/ml (cellulitis, skin/soft tissue infections) Goal trough 15–20 mcg/ml (pneumonia, bacteremia, endocarditis, osteomyelitis)</p> <p><b>Timing of levels:</b> Draw trough &lt; 30 minutes before 4<sup>th</sup> dose of new regimen. When SCr acutely rises, hold dose, restart when level &lt;15 - 20</p> <p>See appendix for complete guidelines</p>																					
Voriconazole (IV/PO) <sup>1,22</sup> (SHC Restriction)	6 mg/kg IV q12h x 2, then 4 mg/kg IV q12h 400 mg PO q12h x 2, then 200 mg PO q12h	Caution with IV: accumulation of IV vehicle cyclodextran occurs. Consider PO unless benefits justify risks of IV use. Levels shown to have great degree of interpatient variability. Many clinicians would recommend blood levels to assess efficacy. Consider drawing a trough 4 - 7 days after new dose																				

**Abbreviations:** SCr = serum creatinine LD = loading dose; MU= million units; PNA = pneumonia; HD = hemodialysis; CAP = community acquired pneumonia; CRRT = continuous renal replacement therapy; TMP = trimethoprim; PCP: pneumocystis jiroveci pneumonia TB = tuberculosis; UF = ultrafiltration

**CRRT dosing:** doses listed are for CVVHDF and CVVHD modalities, which are the most common modes at SHC. Note that these are generally higher than doses used in CVVH.

All SHC formulary Restrictions/Interchange program descriptions can be accessed using Lexi-Comp and the intranet under pharmacy policies (intranet > Departments > Pharmacy)

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## Stanford Hospital & Clinics Vancomycin Dosing Guidelines

Vancomycin is a tricyclic Glycopeptide antibiotic that exhibits bactericidal activity by preventing the synthesis and assembly of a growing bacterial cell wall, altering the permeability of the bacterial cytoplasmic membrane, and selectively inhibiting bacterial RNA synthesis. Vancomycin is considered to be a concentration-independent or time-dependent killer of bacteria.

### A. Determine creatinine clearance and dose

- a) Determine the dose with total body weight (TBW)
- b) Calculate creatinine clearance with the Cockcroft-Gault equation using an ideal body weight (IBW) or an adjusted body weight (ABW) if the patient is obese (TBW >20% over IBW)

$$\text{CrCL (mL/min)} = \frac{(140 - \text{age}) \times \text{IBW}}{\text{SCr} \times 72} \quad (\times 0.85 \text{ for females})$$

IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)

IBW (female) = 45 kg + (2.3 x height inches > 60 inches)

ABW (kg) = IBW + 0.4 (TBW – IBW)

### B. Initial Empiric Dosing

**Loading Dose:** Consider a loading dose of 20-25mg/kg (max 2gm) for severe infections and ICU patients

Creatinine Clearance (mL/min)	Dose		Interval
	Total body weight (TBW)		
> 50	15-20 mg/kg		Q8-12H
30-49	15-20 mg/kg		Q12-24H
15-29	10-15 mg/kg		Q24H
<15	10-15 mg/kg		Q24 – 48H
Hemodialysis	Load: 20-25 mg/kg x 1	Maintenance: 10-15 mg/kg	Post-dialysis when levels <15mg/L or <20 mg/L in severe infections (i.e. meningitis, pneumonia)
CRRT	Load: 20-25 mg/kg x 1	Maintenance: 10-15 mg/kg	Q24H

### C. Administration

Vancomycin Dose	Infusion Rate
500 mg	60 minutes
1000 mg	60 minutes
1250 mg	90 minutes
1500 mg	90 minutes

Central line only: Up to 1gm in 100 mL  
Peripheral line: Dilute drug in 250 ml

Red man syndrome may occur if the infusion is too rapid. It is not an allergic reaction, but may be characterized by hypotension and/or a maculopapular rash appearing on the face, neck, trunk, and/or upper extremities. If this should occur, slow the infusion rate to over 1½ to 2 hours and increase the dilution volume. Reactions are often treated with antihistamines and steroids.

### D. Therapeutic Drug Monitoring

1. Clinical situations to obtain serum trough concentrations
  - Serious or life-threatening infections
  - Patients with rapidly changing renal function
  - Concomitant administration of nephrotoxic medication (i.e. aminoglycosides, amphotericin B)
  - Patients on intermittent or continuous dialysis
  - Patients requiring higher than usual doses of vancomycin (>20 mg/kg/dose)
  - Altered volume of distribution (i.e. Morbidly obese patients)
  - Treating organisms with higher MICs
  - Patients receiving prolonged course of therapy
2. Timing of serum trough levels
  - Trough levels should be obtained within 30 minutes before the 4<sup>th</sup> dose of a new regimen
  - For q24h and q48h regimens, consider drawing levels prior to 3<sup>rd</sup> or 2<sup>nd</sup> dose respectively
  - Recommend trough levels >10 mcg/mL to avoid microbial resistance
  - When SCr acutely rises, hold dose and draw level. Restart therapy when level <15 - 20
3. Dialysis
  - CRRT: obtain level within 30 minutes prior to 3<sup>rd</sup> or 4<sup>th</sup> dose
  - Intermittent hemodialysis (IHD): obtain levels daily before dialysis or consider waiting >4 hours after dialysis to avoid rebound effect
  - Dosing assumes that HD is high flux and removes ~20% of vancomycin per 3 hour session
4. Goal trough levels
  - 10–15 mcg/ml (cellulitis, skin/soft tissue infections)
  - 15–20 mcg/ml (pneumonia, bacteremia, endocarditis, osteomyelitis)

## Stanford Hospital & Clinics Aminoglycoside Dosing Guidelines

Aminoglycosides are concentration dependent antibiotics, meaning that as aminoglycoside concentration increases, the rate and extent of bacterial killing increases. Optimum bactericidal activity for the aminoglycosides is achieved when the exposure concentration is approximately 8 to 10 times the MIC.

### Determining dose and creatinine clearance

- a) Use of ideal body weight (IBW) for determining the mg/kg/dose appears to be more accurate than dosing on the basis of total body weight (TBW). In morbid obesity, dosage requirement may best be estimated using an adjusted body weight (ABW) of:  $IBW + 0.4 (TBW - IBW)$

Obese patients:

Obese is defined as a Total body weight (TBW) > 20% over Ideal body weight (IBW)

$$IBW \text{ (male)} = 50 \text{ kg} + (2.3 \times \text{height in inches} > 60 \text{ inches})$$

$$IBW \text{ (female)} = 45 \text{ kg} + (2.3 \times \text{height inches} > 60 \text{ inches})$$

- b) Calculate creatinine clearance with the Cockcroft-Gault equation using an ideal body weight (IBW) or an adjusted body weight (ABW) if the patient is obese

$$CrCL \text{ (mL/min)} = \frac{(140 - \text{age}) \times IBW}{SCr \times 72} \text{ (} \times 0.85 \text{ for females )}$$

### Extended-Interval Therapy (Once daily dosing)

#### Hartford Nomogram

The method of once-daily dosing intends to optimize the peak/MIC ratio in the majority of clinical situations by administering a dose of 7mg/kg of either gentamicin or tobramycin. Similar to that of conventional regimens, once-daily protocols also require modification for patients with renal dysfunction in order to minimize drug accumulation. Due to high peak concentrations obtained and the drug-free period at the end of the dosing interval, it is usually not necessary to draw standard peak and trough samples, rather a single random blood sample is obtained between 6 to 14 hours after the start of the aminoglycoside infusion. This concentration is used to determine the dosing interval based on a nomogram for once-daily dosing.

#### Non-Hartford Nomogram

The second method of extended-interval therapy utilizes a 5mg/kg gentamicin or tobramycin dose in patients without renal dysfunction. If dosage adjustment is required to compensate for impaired renal function, the dose and/or dosing interval may be modified to optimize therapy and minimize drug accumulation.

Exclusion Criteria for Extended Interval Therapy:

- Renal insufficiency (CrCL <30 mL/min or rapidly declining renal function)
- Dialysis
- Pregnancy
- Synergy for gram-positive infections
- Ascites
- Burns (>20%)

### Traditional Dosing

Tradition dosing includes reduced doses and frequent administration of aminoglycosides using pharmacokinetic parameters to determine dose and frequency to achieve target peak and trough values.

### Gram positive-synergy Dosing

Synergy dosing is a low dose of aminoglycoside in conjunction with an antimicrobial agent that exhibits activity against the cell wall of gram-positive bacteria (i.e. beta-lactams, glycopeptides) for the treatment of gram-positive infections

### Gentamicin & Tobramycin Initial Empiric Dosing

CrCL (mL/min)	Once daily dosing*	Traditional	Synergy**
> 60	7mg/kg Q24H	1.7mg/kg Q8H	1mg/kg Q8H
40-59	7mg/kg Q36H	1.7mg/kg Q12H	1mg/kg Q12H
20-39	7mg/kg Q48H	1.7mg/kg Q24H	1mg/kg Q24H
<20	Not recommended	2mg/kg load, then dose by level	1mg/kg load, then dose by level
Hemodialysis	Not recommended	2mg/kg load, then 1.5-2mg/kg post-HD	1mg/kg load, then 1mg/kg post-HD
CRRT	Not recommended	1.5-2.5mg/kg Q24-48H	1mg/kg Q12H

\*See Hartford nomogram for monitoring of once-daily dosing regimens

\*\*Alternative for synergy: 3mg/kg Q24H for Streptococci and *Streptococcus bovis* endocarditis

### Amikacin Initial Empiric Dosing

CrCL (mL/min)	Once daily dosing*	Traditional
> 60	15mg/kg Q24H	5-7.5mg/kg Q8H
40-59	15mg/kg Q36H	5-7.5mg/kg Q12H
20-39	15mg/kg Q48H	5-7.5mg/kg Q24H
<20	Not recommended	5mg/kg load, then dose by level
Hemodialysis	Not recommended	5-7.5mg/kg post-HD
CRRT	Not recommended	10 mg/kg load, then 7.5mg/kg Q24-48H

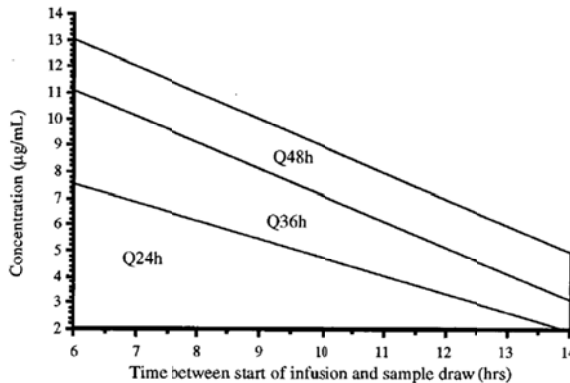
\* See Hartford nomogram for monitoring of once-daily dosing regimens- divide level by half then plot on graph

### Monitoring

#### High Dose Extended Interval (Hartford Nomogram- for once-daily dosing)

A. Initial level testing: Single level drawn 8-12 hours after the first dose

- Gentamicin/tobramycin: Plot level on graph
- Amikacin: Divide level in half, then plot on graph



B. Follow up trough level testing- for traditional and synergy dosing regimens

- Trough monitoring (30-60 minutes prior to next dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure
- Maintenance trough levels should be monitored at least once weekly

#### Traditional Regimens

	Q8H	Q12H	Q24-48H	Hemodialysis	CRRT
<b>Peak</b>	30 minutes after 3 <sup>rd</sup> dose*	30 minutes after 3 <sup>rd</sup> dose*	30 minutes after 2 <sup>nd</sup> dose*	30 minutes after 2 <sup>nd</sup> dose* ▪ target peak Cp post HD ~ 8mg/L (6-10 mg/L)	30 minutes after 2 <sup>nd</sup> dose*
<b>Trough</b>	30-60 minutes before 4 <sup>th</sup> dose	30-60 minutes before 3 <sup>rd</sup> dose	30-60 minutes before 2 <sup>nd</sup> dose	Immediately <i>before</i> HD; Redose for pre-HD: ▪ Cp < 1mg/L (mild UTI and synergy) ▪ Cp < 2-3mg/L (moderate-severe UTI) ▪ Cp < 3-5mg/L (severe GNR infection)	30-60 minutes before 3 <sup>rd</sup> dose

#### Gram-Positive Synergy

	Q8H	Q12H	Q24-48H	Hemodialysis	CRRT
<b>Trough</b>	30-60 minutes before the 4 <sup>th</sup> dose	30-60 minutes before the 3 <sup>rd</sup> dose	30-60 minutes before the 2 <sup>nd</sup> dose	Immediately <i>before</i> HD; Redose for pre-HD: Cp < 1mg/L	30-60 minutes before 3 <sup>rd</sup> dose

\*Peaks are drawn 30 minutes after the end of the infusion; Cp = concentration in plasma

#### Target Levels based on Dosing Regimen

Dose	Gentamicin and Tobramycin				Amikacin		
	1mg/kg	1.5-2mg/kg	7mg/kg*	10 mg/kg**	5-7.5mg/kg	15mg/kg	20 mg/kg**
<b>Usual Interval</b>	Q8H	Q8H	Q24H***	Q24H	Q12H	Q24H***	Q24H***
<b>Peak</b>	3-5	4-8	20-25	20-30	20-35	35-50	40-60
<b>Trough</b>	<1	<1-2	<1	<1	<5-8	<4	<4

\*7mg/kg once daily dosing does not require routine monitoring of target peaks and troughs unless the patient is having fluctuations in renal function or has failed extended interval dosing. Please follow the Hartford nomogram and check an 8-12 hour post-dose level, this can be done after the first dose

\*\*This dose is generally used for cystic fibrosis patients

\*\*\* Extended interval dosing can be Q24H, Q36H, or Q48H

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