Stanford Hospital & Clinics Aminoglycoside Dosing Guidelines 2013

I. DETERMINING DOSE AND CREATININE CLEARANCE:

1. 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). For obese patients (total body weight > 20% over Ideal body weight), dosage requirement may best be estimated using an adjusted body weight (ABW) of: IBW + 0.4 (TBW - IBW)

   IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)
   IBW (female) = 45 kg + (2.3 x height inches > 60 inches)

2. 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

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

II. AMINOGLYCOSIDE DOSING STRATEGIES

A. High-dose Extended-Interval Therapy (Once daily dosing)

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. The **Hartford nomogram** method utilizes high-dose, once daily dosing to optimize the peak/MIC ratio in the majority of clinical situations by administering a dose of **7mg/kg** of either gentamicin or tobramycin. The second method of extended-interval therapy utilizes **5 mg/kg** of gentamicin or tobramycin in patients without renal dysfunction.

Exclusion Criteria for High-Dose Extended Interval Therapy:

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

B. Conventional / 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.

C. 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

III. EMPIRIC DOSING

A. Gentamicin & Tobramycin Initial Dosing

CrCL (mL/min)	High-Dose Extended-Interval* (Gentamicin/Tobramycin)	Conventional / Traditional (Gentamicin/Tobramycin)	Synergy** (Gentamicin/Tobramycin)
> 60	4 – 7 mg/kg Q24H	1.7 mg/kg Q8H	1 mg/kg Q8H
40-59	4 – 7 mg/kg Q36H	1.7 mg/kg Q12H	1 mg/kg Q12H
30-39	4 – 7 mg/kg Q48H	1.7 mg/kg Q24H	1 mg/kg Q24H
20-29	Not recommended	1.7 mg/kg Q24H	1 mg/kg Q24H
<20	Not recommended	2 mg/kg load, then dose by level	1 mg/kg load, then dose by level
Hemodialysis	Not recommended	2 mg/kg load, then 1.5 mg/kg post-HD; Redose for post-HD Cp < 1 mg/L or pre-HD ▪ Cp < 1 mg/L (mild UTI) ▪ Cp < 2–3 mg/L (moderate-severe UTI) ▪ Cp < 3–5 mg/L (severe GNR infection)	1 mg/kg q48-72H; Redose for pre-HD or post-HD Cp <1mg/L
CRRT	Not recommended	1.5 – 2.5 mg/kg Q24-48H	1 mg/kg Q24H, then by level

*See Hartford nomogram for monitoring of once-daily dosing regimens
**Alternative for synergy: 3mg/kg Q24H for Streptococci and *Streptococcus bovis* endocarditis

B. Amikacin Initial Dosing

CrCL (mL/min)	High-Dose Extended-Interval* (Amikacin)	Conventional / Traditional (Amikacin)
> 60	15 – 20 mg/kg Q24H	5 – 7.5 mg/kg Q8H
40-59	15 mg/kg Q36H	5 – 7.5 mg/kg Q12H
30-39	15 mg/kg Q48H	5 – 7.5 mg/kg Q24H
20-29	Not recommended	5 – 7.5 mg/kg Q24H
<20	Not recommended	5 mg/kg load, then dose by level
Hemodialysis	Not recommended	5 – 7.5 mg/kg post-HD
CRRT	Not recommended	10 mg/kg load, then 7.5 mg/kg Q24-48H

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

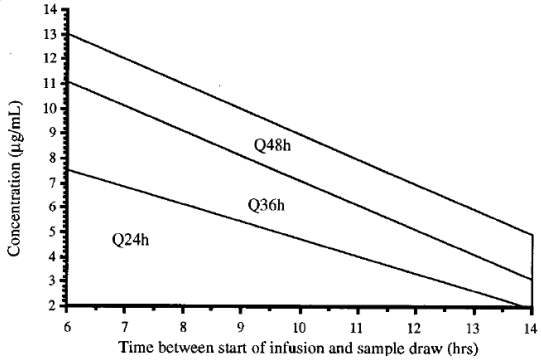
IV. MONITORING

A. TIMING OF LEVELS

High-Dose Extended-Interval

A. **Initial level testing**: Single level drawn 8-12 hours after the first dose (Only applicable for **7 mg/kg** – plotting doses lower or higher than 7 mg/kg may under or overestimate clearance)

- Gentamicin/tobramycin (7 mg/kg/dose): Plot level on graph
- Amikacin (15 mg/kg/dose): Divide level in half, then plot on graph



B. **Follow up trough level testing**

- Trough monitoring (30-60 minutes prior to 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

Conventional / Traditional

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

Gram-Positive Synergy

	Q8H	Q12H	Q24-48H	Hemodialysis	CRRT
TROUGH	30-60 minutes before the 4th dose	30-60 minutes before the 3rd dose	30-60 minutes before the 2nd dose	Immediately *before* HD; Redose for pre-HD or post-HD level: Cp < 1 mg/L	30-60 minutes before 3rd dose

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

B. TARGET LEVELS

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

*7 mg/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

References:

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11. Whitehead A, Conway SP, Etherington C, Caldwell NA, Setchfield N, Bogle S. Once-daily tobramycin in the treatment of adult patients with cystic fibrosis. *Eur Respir J.* Feb 2002;19(2):303-309.