Aminoglycoside Adult, Pediatric, and Neonatal Conventional Initial Dosing Guidelines
HSHS St. John's Hospital, Springfield, IL

ADULT CONVENTIONAL DOSING:

I. PATIENT SELECTION

a. Pharmacy will be automatically consulted for all adult patients receiving aminoglycosides. Exceptions include:
   i. Infectious Disease consult
   ii. One time doses in ED
   iii. Surgical prophylaxis
b. Once-daily dosing algorithm is preferred method of aminoglycoside dosing in adults.
c. Conventional dosing preferred for gram positive synergy, endocarditis, hemodialysis, CrCl < 30 mL/min, ascites, burns, pregnancy

II. CALCULATE DOSE

a. Use **Actual Body Weight** for dosing calculation unless the patient is obese (BMI ≥ 30 kg/m^2). Use Adjusted Body Weight if obese.
b. Round all doses to nearest 10 mg.

Gentamicin / Tobramycin		Amikacin	
Infection	**Dose**	**Infection**	**Dose**
Life Threatening, Pulmonary, or other	2 mg/kg/dose	Life Threatening	7.5 mg/kg/dose
Urinary Tract Infection	1.5 mg/kg/dose		
Gram positive synergy	1 mg/kg/dose		

c. **NOTE:** Gentamicin recommended for gram positive synergy
d. **NOTE:** Amikacin recommended for infections caused by *Pseudomonas aeruginosa*

III. CALCULATE INTERVAL

Gentamicin / Tobramycin	
Estimated CrCl	**Dosing Interval**
≥ 60 ml/min	q 8 h
40 – 60 ml/min	q 12 h
20 – 40 ml/min	q 24 h
< 20 ml/min or dialysis	Give initial dose and base subsequent doses on serum levels

Amikacin	
Estimated CrCl	**Dosing Interval**
≥ 60 ml/min	7.5 mg/kg q12h
40 – 60 ml/min	5 mg/kg q12h
20 – 40 ml/min	5 mg/kg q24h
< 20 ml/min or dialysis	Give initial dose and base subsequent doses on serum levels

IV. ADMINISTRATION

a. To minimize the possibility of neuromuscular blockade, doses should be infused over at least 30 minutes.

V. PATIENT MONITORING

a. General Monitoring:
   i. Daily: medication profile, signs for efficacy and toxicity, clinical status
   ii. Every other day: renal function (SCr, BUN, Intake/Output's) – if rapidly changing, monitor daily
   iii. Every 3 days: CBC w/differential
   iv. Pharmacist may order CBC and BMP as clinically indicated to ensure appropriate monitoring. Please notify physician via text page/Doc Halo/EMR message that order is being placed.

b. Peak and Trough Monitoring:
   i. Peak and trough levels should be drawn around **third dose**. The trough should be ordered 30 minutes before the next dose. The peak should be drawn 60 minutes after start of infusion. Exact times must be placed. Subsequent dosages are adjusted based on these levels.
   ii. Pharmacist may make dose adjustments based off of drug level results.

Goal peak for Gentamicin / Tobramycin:

Serious infections		**Mild infection**		**Synergy (gentamicin recommended)**	
Bacteremia	6 – 8 mcg/ml	*Pyelonephritis*	4 – 6 mcg/ml	*G. positive synergy*	3 – 5 mcg/ml
Intra-abdominal	8 mcg/ml	UTI	4 – 6 mcg/ml		
Neutropenic Fever	8 mcg/ml				
Pulmonary	8 – 10 mcg/ml				
Sepsis	8 – 10 mcg/ml				

Goal trough for Gentamicin / Tobramycin:
Troughs: < 2 mcg/ml
For gram positive synergy: trough < 1 mcg/ml

Goal peak for Amikacin:

Life threatening infections	25 – 40 mcg/ml	**Serious infections**	20 – 25 mcg/ml	**Urinary tract infections**	15 – 20 mcg/ml

Goal trough for Amikacin: < 10 mcg/ml

VI. HEMODIALYSIS DOSING AND MONITORING

a. **<u>Gentamicin / Tobramycin</u>**
   i. Dosing: 1.5 – 2 mg/kg after every HD session
   ii. Monitoring (post-dialysis option): Check peaks and troughs at initiation of therapy and then periodically to avoid accumulation. Draw trough 2 hours <u>post-dialysis</u>. Draw peak 60 minutes after start of infusion.
      1. Redose when:
         a. Trough < 2 mg/L (severe GNR infection)
         b. Trough < 1 mg/L (UTI and synergy)
   iii. Monitoring (pre-dialysis option): <u>Pre-dialysis</u> random levels can also be used in place of troughs to assess for accumulation
      1. Redose when:
         a. Level < 3 – 5 mg/L (severe GNR infection)

b. Level < 2 – 3 mg/L (moderate-severe UTI)
c. Level < 1 mg/L (mild UTI and synergy)

b. **Amikacin** = 5 – 7.5 mg/kg after every HD session
   i. Redose when pre-HD < 10 mg/L or post-HD < 6 – 8 mg/L
   ii. Peak levels can be obtained 60 minutes after start of infusion.
c. Pharmacist may make dose adjustments based off of drug level results.

VII. CONTINOUS RENAL REPLACEMENT THERAPY (CRRT) DOSING AND MONITORING

a. Drug removal and dosing varies depending on CRRT techniques and therefore frequent monitoring is required
b. Check serum concentrations at initiation of therapy and then periodically to avoid accumulation
   i. Obtain a trough before next dose to ensure clearance
   ii. Peak levels can be obtained 60 minutes after start of infusion
c. **Gentamicin / Tobramycin**
   i. Loading dose of 2 – 3 mg/kg once daily, followed by
      1. UTI/Synergy: 1 mg/kg every 24 – 36 hours
         a. Redose when trough < 1 mg/L
      2. Moderate to severe infection: 1 – 1.5 mg/kg every 24 – 36 hours
         a. Redose when trough < 1.5 – 2 mg/L
      3. Systemic infection: 1.5 – 2 mg/kg every 24 – 48 hours
         a. Redose when trough < 2 – 3 mg/L
d. **Amikacin**
   i. Loading dose of 10 mg/kg followed by 7.5 mg/kg every 24 – 48 hours
   ii. Redose when trough < 10 mg/L
e. Pharmacist may make dose adjustments based off of drug level results.

VIII. **EQUATIONS**

a. **IBW:** Males: IBW = 50 kg + (2.3 kg for each inch over 5 feet)
b. **IBW:** Females: IBW = 45.5 kg + (2.3 kg for each inch over 5 feet)
c. **Adjusted Body Weight** = IBW + 0.4(actual weight – IBW)
d. **CrCl:** [(140 – age) x (Wt in kg)] / (72 x Serum Cr) x 0.85 if female

NEONATAL CONVENTIONAL DOSING:

I. CALCULATE DOSE & INTERVAL

a. Pharmacy will be automatically consulted for all patients receiving aminoglycosides for > 72 hours.

b. Use **actual body weight**

c. PMA (post-menstrual age): time between the first day of the last menstrual period and birth (gestational age), plus the time elapsed after birth (chronological age).

i. Usually described in number of weeks and most frequently applied during the perinatal period beginning after the day of birth

Gentamicin / Tobramycin			
PMA (weeks)	**Postnatal (days)**	**Dose (mg/kg)**	**Interval (hours)**
≤ 29*	0 to 7	5	48
	8 to 28	4	36
	≥ 29	4	24
30 to 34	0 to 7	4.5	36
	≥ 8	4	24
≥ 35	ALL	4	24

*or significant asphyxia, PDA, or treatment with indomethacin

Amikacin			
PMA (weeks)	**Postnatal (days)**	**Dose (mg/kg)**	**Interval (hours)**
≤ 29*	0 to 7	18	48
	8 to 28	15	36
	≥ 29	15	24
30 to 34	0 to 7	18	36
	≥ 8	15	24
≥ 35	ALL	15	24

*or significant asphyxia, PDA, or treatment with indomethacin

II. ADMINISTRATION

a. To minimize the possibility of neuromuscular blockade, doses should be infused over at least 30 minutes.

III. PATIENT MONITORING

a. Renal function (BUN, SCr, UOP) should be monitored in all patients on aminoglycosides if treating for more than 72 hours.

i. BUN and SCr should be monitored twice weekly

ii. UOP should be monitored daily

iii. Pharmacist may order CBC and BMP as clinically indicated to ensure appropriate monitoring. Please notify physician via text page/Doc Halo/EMR message that order is being placed.

b. Measure serum concentrations when treating for more than 72 hours.

i. Draw peak 60 minutes after start of infusion for the listed indications:

1. Confirmed meningitis
2. Confirmed bacteremia
3. Poor renal function
4. Treating physician discretion

ii. Draw trough 30 minutes before the next dose.

iii. Does not apply to inhaled aminoglycosides.
iv. Pharmacist may make dose adjustments based off of drug level results.

c. **Please discuss all labs that need to be ordered with NICU NP prior to ordering. This is to avoid unnecessary blood draws and needle sticks. The phone number for the NP is 217-725-0938.**
d. If patient on aminoglycoside for ≥ 10 days, obtain SCr 1 week after treatment complete. If patient is to be discharged before this time, remind consulting physician to order SCr at follow-up visit.

	Goal peak	**Goal trough**
Gentamicin / Tobramycin	5 – 15 mcg/mL	0.5 – 1 mcg/mL
Amikacin	20 – 30 mcg/mL	2 – 5 mcg/mL

e. If patient has significantly changing fluid or renal status, consider drawing random level 24 hours post dose and use chart below for suggested dosing interval.

Gentamicin / Tobramycin: Dose Adjustments		
Concentrations at 24 hrs (mcg/mL)	**Half-life (hours)**	**Suggested Dosing Interval (hours)**
≤ 1	~ 8	24
1.1 – 2.3	~ 12	36
2.4 – 3.2	~ 15	48
≥ 3.3	---	Hold dose & measure level in 24 hours

Amikacin: Dose Adjustments		
Concentrations at 24 hrs (mcg/mL)	**Half-life (hours)**	**Suggested Dosing Interval (hours)**
≤ 5	~ 9	24
5.1 – 8	~ 12	36
8.1 – 10.5	~ 16	48
≥ 10.6	---	Hold dose & measure level in 24 hours

IV. **EQUATIONS**

a. **Schwartz equation**: eGFR (mL/min) = (k x length in cm) / (SCr in mg/dL)

Age	**K**
Low birth weight ≤1 year	0.33
Full term ≤1 year	0.45
>1 year – 12 years	0.55
> 12 years female	0.55
> 12 years male	0.7

INFANTS & CHILDREN (age > 30 days) CONVENTIONAL DOSING:

I. PATIENT SELECTION

a. Pharmacy will be automatically consulted for all pediatric patients receiving aminoglycosides. Exceptions include:
   i. One time doses in ED
   ii. Surgical prophylaxis

b. Once-daily dosing algorithm is preferred method of aminoglycoside dosing.

c. Conventional dosing preferred for tularemia, gram positive synergy, endocarditis, hemodialysis, renal insufficiency, ascites, burns, pregnancy, and ages not included in the dosing chart.

d. Neonates: see Conventional Dosing Policy on page 4.

II. CALCULATE DOSE & INTERVAL

a. Use actual body weight

b. **Gentamicin / Tobramycin**: 2.5 mg/kg/dose IV q8h

c. **Gentamicin synergy**: 1 – 2 mg/kg/dose IV q8h

d. **Amikacin**: 5 – 7.5 mg/kg/dose IV q8h

e. **NOTE**: gentamicin recommended for gram positive synergy

f. **NOTE**: tobramycin recommended for infections in patients with cystic fibrosis

III. **ADMINISTRATION**

a. To minimize the possibility of neuromuscular blockade, doses should be infused over at least 30 minutes.

IV. **PATIENT MONITORING**

a. Renal function (BUN, SCr, UOP) should be monitored in all patients on aminoglycosides.
   i. BUN and SCr should be monitored twice weekly
   ii. UOP should be monitored daily
   iii. Pharmacist may order CBC and BMP as clinically indicated to ensure appropriate monitoring. Please notify physician via text page/Doc Halo/EMR message that order is being placed.

b. Peaks and troughs should be drawn if therapy continues for greater than 48 hours
   i. Draw peak 60 minutes after start of infusion.
   ii. Draw trough 30 minutes prior to next dose.
   iii. Does not apply to inhaled aminoglycosides.

c. Pharmacist may make dose adjustments based off of drug level results.

d. For patients on prolonged IV aminoglycoside therapy, peaks and troughs should be drawn twice weekly.

e. If patient on aminoglycoside for ≥ 10 days, obtain SCr 1 week after treatment complete. If patient is to be discharged before this time, remind consulting physician to order SCr at follow-up visit.

f. If patient on aminoglycoside for ≥ 2 weeks, remind consulting physician to order audiology exam.

Gentamicin / Tobramycin		
	Goal peak	**Goal trough**
CNS, CF, pulmonary, life-threatening infection	8 – 10 mcg/mL	< 2 mcg/mL

Gram negative infections	6 – 10 mcg/mL	< 2 mcg/mL
Gram positive synergy	3 – 4 mcg/mL	< 1 mcg/mL

Amikacin		
	Goal peak	**Goal trough**
CNS, CF, pulmonary, life-threatening infections	25 – 30 mcg/mL	< 5 mcg/mL
Gram negative infections	20 – 30 mcg/mL	< 5 mcg/mL

V. RENAL IMPAIRMENT DOSING

a. Dosing:

Gentamicin / Tobramycin	
eGFR in mL/min/1.73m^2	**Dose**
30 – 50	2.5 mg/kg IV q12h
10 – 29	2.5 mg/kg IV q24h
< 10	2.5 mg/kg x 1, then check levels every 12 – 24 hours until level ≤ 1 mcg/mL
HD	2 mg/kg IV x 1, redose when level ≤ 1 mcg/mL
CRRT	2.5 mg/kg IV q12h

Amikacin	
eGFR in mL/min/1.73m^2	**Dose**
30 – 50	7.5 mg/kg IV q12h
10 – 29	7.5 mg/kg IV q24h
< 10	7.5 mg/kg x 1, then check levels every 24 hours until level ≤ 5 mcg/mL
HD	5 mg/kg IV, redose when level ≤ 5 mcg/mL
CRRT	7.5 mg/kg IV q12h

b. Monitoring:
   i. Monitor patient as described in Section IV: Patient Monitoring.
   ii. Hemodialysis:
      1. Check random levels before HD
      2. Redose after HD when:
         a. Gentamicin/tobramycin level ≤ 1 mcg/mL
         b. Amikacin level ≤ 5 mcg/mL
   iii. CRRT:
      1. Monitor patient as described in Section IV: Patient Monitoring.

VI. EQUATIONS

a. **Schwartz equation**: eGFR (mL/min) = (k x length in cm) / (SCr in mg/dL)

Age	K
Low birth weight ≤1 year	0.33
Full term ≤1 year	0.45
>1 year – 12 years	0.55
> 12 years female	0.55
> 12 years male	0.7

b. **Bedside Schwartz equation**: eGFR (mL/min): = (0.413 x Ht in cm) / (SCr in mg/dL)
   i. Preferred in patients age 1 – 16 years
c. **Cockcroft – Gault CrCl:** [(140 – age) x (Wt in kg)] / (72 x Serum Cr) x 0.85 if female
   i. Consider for adult-sized adolescents or teenagers
d. **IBW in kg (males)** = 50 + (2.3 x inches over 60)
e. **IBW in kg (females)** = 45.5 + (2.3 x inches over 60)

****CONTACT ID/AMS PHARMACIST FOR ASSISTANCE WITH DOSING****

References:

1. Gilbert DN, Leggett JE. Aminoglycosides. In: Mandell GL, Bennett JE, Dolin R. Principles and practice of infectious diseases. 8th ed. Philadelphia: Churchill Livingstone Elsevier; 2015: 310-321.
2. Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Accessed May 26, 2017.
3. Pediatric & Neonatal Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Accessed July 6, 2017.
4. Heintz BH, Matzke GR, Dager WE. Antimicrobial Dosing Concepts and Recommendations for Critically Ill Adult Patients Receiving Continuous Renal Replacement Therapy or Intermittent Hemodialysis. Pharmacotherapy.2009;29(5):562-577.
5. NeoFax® [Internet Database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed: June 29, 2017.
6. Siberry GK. Amikacin. Johns Hopkins Antibiotic Guide. Updated January 30, 2017. Accessed July 6, 2017.
7. Siberry GK. Gentamicin. Johns Hopkins Antibiotic Guide. Updated April 5, 2017. Accessed July 6, 2017.
8. Siberry GK. Tobramycin. Johns Hopkins antibiotic Guide. Updated November 5, 2015. Accessed July 6, 2017.
9. Baltimore RS, Gewitz M, Baddour LM, et al. Infective endocarditis in childhood: 2015 update. *Circulation*. 2015;132:1487-1515.