VANCOMYCIN DOSING

1. Determine dose using Total Body Weight (TBW) – 15- 20 mg/kg IV, round to nearest 250mg, at dosing interval recommended for creatinine clearance (CrCl).
A loading dose of 25-30mg/kg of TBW may be considered for severely ill or ICU patients.
Maximum 2g/dose.

2. Calculate Creatinine Clearance (CrCl) to determine frequency
CrCl (mL/min) = [(140 – age) x weight x 1.2] / sCr
*Females: x 0.85
Using Ideal Body Weight (IBW) or Adjusted Body Weight (ABW) if patient is obese (i.e. TBW > 30% over IBW)

IBW (male) = 50kg + 2.3kg (each inch > 5 ft)
IBW (female) = 45.5 + 2.3kg (each inch > 5 ft)
Adjusted Body Weight (ABW) = IBW + 0.4 (TBW - IBW)

CrCl	Dosing Interval
> 50	Q12H (consider q8h clearance > 100ml/min, if young [<30yrs] , cystic fibrosis)
30 – 49	Q24H
15 - 29	Q48H, consult pharmacist to optimize dosing
< 15 Peritoneal Dialysis	Initial loading dose of 15mg/kg; check level after 48 hrs and re-dose with 15mg/kg when serum level ≤ 15mg/L or when ≤ 20mg/L in severe MRSA infections (e.g. meningitis, endocarditis). This also determines the dosing interval for subsequent doses. Consult pharmacist to optimize dosing
Hemodialysis	< 70 kg: 1000mg IV x 1, then 500mg post-dialysis 70 – 100kg: 1250mg IV x 1, then 750mg post-dialysis > 100 kg: 1500mg IV x 1, then 1000mg post-dialysis *Further dosing to be based on levels drawn pre-dialysis.* *Consult pharmacist to optimize dosing*
CRRT	Q12 – 24H

3. Monitoring – Trough Levels
WHO:
- receiving high doses, to maintain trough 15-20 mg/L
- unstable renal function or at high risk of developing nephrotoxicity (i.e. on concomitant nephrotoxins)
- anticipated duration of therapy > 72 hours

WHEN:
- **30 minutes prior to 4th dose** of a new regimen (or earlier in patients with impaired renal function with the caveat that serum concentration would not be at steady state)

- Routine monitoring can then be discussed with clinical pharmacist once stable renal function and desired trough are achieved. Suggested frequency is once weekly if ongoing therapy (serum creatinine can be done two-three times weekly)
*Random levels or peak levels are not routinely performed
Random levels may be ordered in patients with acute and changing renal dysfunction or if receiving renal replacement therapy

WHAT TARGETS
Dosing and trough levels are dependent upon the infecting organism, consult pharmacist to optimize dosing
- 15 – 20mg/L: severe MRSA infections (meningitis, endocarditis, osteomyelitis, bacteremia , HAP)
- 10 -15 mg/L: uncomplicated MRSA infections (e.g. skin and soft tissue infections, UTI) organisms other than MRSA (e.g. CoNS, Enterococcus, Streptococcus species)
*Please note that studies suggesting trough concentrations of < 10mg/L may be associated with therapeutic failure and potential for resistance were only demonstrated in treatment of *S.aureus* infections

4. Dose Adjustment

- Vancomycin displays linear pharmacokinetics in adults (i.e. if you double the dose, then your levels should be doubled)
- Always check that the trough was drawn appropriately and no previous doses were held
- If a trough is just slightly above the reference range (i.e. < 25mg/L), rather than holding dose—start the new regimen at a reduced dose to prevent subtherapeutic levels.
If > 25mg/L – hold dose, repeat level (usually in 12-24 hour intervals to determine when to restart and appropriate dosing interval). Do not use the same dose and frequency that resulted in the high levels.

5. **Administration – general rule is to run 1 gram over 1 hour**
- Slow infusion rate if patient experiences Red Man's Syndrome (not an allergic reaction; characterized by hypotension, maculopapular rash on face, neck, trunk, or upper extremities). Can pre-treat with anti-histamines

AMINOGLYCOSIDE DOSING

Once Daily Dosing (ODD)
Should be used in most clinical situations.
Exceptions when to consider multiple daily dosing:

- Renal impairment (CrCl < 20ml/min)
- Synergy in gram positive endocarditis
- Pregnancy
- Significant ascites
- Burns affecting > 20% BSA
- Septic shock

1. **Determine patient's dosing weight**
   - Use ideal body weight (IBW) unless total body weight (TBW) is less, then use TBW; use adjusted body weight (ABW) in obesity (e.g. TBW $\geq$ 30% over IBW)

2. **Estimate creatinine clearance** using equation (if CrCl < 20 mL/min – use multiple daily dosing, or MDD)

   CrCl (mL/min) = [(140 – age) x weight x 1.2] / sCr
   *Females: x 0.85
   Using Ideal Body Weight (IBW) or Adjusted Body Weight (ABW) if patient is obese (i.e. TBW > 30% over IBW)

   IBW (male) = 50kg + 2.3kg (each inch > 5 ft)
   IBW (female) = 45.5 + 2.3kg (each inch > 5 ft)
   Adjusted Body Weight (ABW) = IBW + 0.4 (TBW - IBW)

3. **Select a dose and frequency. Please consult pharmacist to optimize dosing**

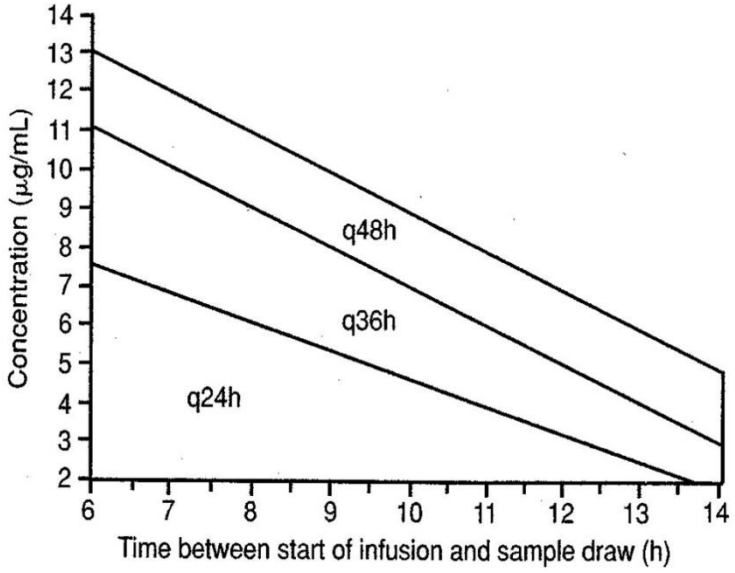
CrCl	Tobramycin / Gentamicin dose (round to nearest 20mg)	Amikacin dose (round to nearest 50mg)
$\geq$ 60 mL/min	5-7mg/kg IV q24h	15mg/kg IV q24h
40 – 59 mL/min	5-7mg/kg IV q36h	15mg/kg IV q36h
20-39 mL/min	5-7mg/kg q48h	15mg/kg IV q48 h
< 20 ml/min	Use multiple daily dosing	Use multiple daily dosing

4. **Monitoring**
   Nephrotoxicity
   Nephrotoxicity associated with elevated trough levels, is usually reversible.
   - Serum creatinine to be checked at least twice weekly and levels at least once weekly or more frequent with renal function changes

A. Use the Hartford nomogram below:

- Check a random level 6-14 hours after start of 1st dose (please note for Amikacin: divide levels in half and then plot on graph). Tobramycin and gentamicin based on a dose of 7mg/kg, if using a dose of 5mg/kg, adjust accordingly.
- Plot level and time on graph. The point may fall into one of these 5 areas:
    - Below nomogram (< 2mg/L): give dose q 24 hrs
    - Q24h, q36h, or q48h: give dose at indicated interval
    - Above nomogram: discontinue ODD and switch to MDD if an aminoglycoside is still warranted

Hartford Nomogram



- B. Alternatively, obtain a trough level within 30 minutes before SECOND DOSE trough should be < 1mg/L for gentamicin / tobramycin and < 4mg/L for amikacin. If level greater than indicated, contact pharmacist to assist with dosing.

*For multidrug resistant organisms requiring aminoglycoside therapy, please consult ID/ASP pharmacist.**Ototoxicity**

- Aminoglycosides may adversely affect cochlear and/or vestibular function. Ototoxicity can occur with normal drug levels and often is not reversible. Consider daily assessment of hearing and balance in patients who are alert. Consider hearing test if on prolonged therapy.

Neuromuscular Blockade
-rare and self-limiting
-contraindicated in myasthenia gravis
MULTIPLE DAILY DOSING (MDD)

1. **Determine patient's dosing weight** as above
2. **Estimate creatinine clearance** using equation above
3. **Select a dose and frequency:**

CrCl (ml/min)	Tobramycin / Gentamicin dose (round to nearest 20mg)	Amikacin dose (round to nearest 25mg)
≥ 60	2mg/kg IV q8h	7.5mg/kg IV q12h
40 – 59	2mg/kg IV q12h	
20-39	2mg/kg IV q24h	7.5mg/kg IV q24h
< 20	2mg/kg loading dose then by level	7.5mg/kg IV x 1 then dose by level
HD	2mg/kg then 1 mg/kg post HD	7.5mg/kg IV post HD
PD	1.5-2mg/kg IV q48h	7.5mg/kg IV q48h
CRRT	2mg/kg IV q24-48h	7.5mg/kg IV q24-48h

4. **Monitoring:**

- Serum creatinine at least twice weekly while on therapy (please always reassess need for aminoglycosides if there is a significant decline in renal function)
- Trough level just prior to **THIRD DOSE**; peak level 30 minutes after completion of **THIRD DOSE**

	Peak (mg/L)	Trough (mg/L)
Gentamicin	4 – 10	< 2
Tobramycin	4 – 10	< 2
Amikacin	15 - 30	< 8

*peaks are general guides and are often dependant on causative organism and type of infection

When gentamicin is used in the setting of endocarditis for synergy with a beta-lactam or vancomycin against gram positive organisms (e.g. enterococcus, staphylococcus, streptococcus): Dose is 1 mg/kg at interval determined by CrCl (see MDD dosing table). Desired target peaks should be 3-5mg/L with trough < 1mg/L.