Vancomycin - Peripheral Brain

Kullar Nomogram, 2011 – initial screening tool designed for trough values of 15-20 mg/L
Only for patients < 110kg and CrCl > 40 ml/min (via Cockroft-Gault)

<table>
<thead>
<tr>
<th>Wgt (kg)</th>
<th>CrCl 40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>90-99</th>
<th>&gt;100</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-54 kg</td>
<td>500mg q12h</td>
<td>750mg q12h</td>
<td>1000mg q12h</td>
<td>750mg q8h</td>
<td>1000mg q8h</td>
<td>1000 mg q8h</td>
<td>1250 q8h</td>
</tr>
<tr>
<td>55-64 kg</td>
<td>750mg q12h</td>
<td>1000mg q12h</td>
<td>1250mg q12h</td>
<td>750mg q8h</td>
<td>1000mg q8h</td>
<td>1500 mg q8h</td>
<td>1500 q8h</td>
</tr>
<tr>
<td>60-69 kg</td>
<td>750mg q12h</td>
<td>1250mg q12h</td>
<td>1250mg q12h</td>
<td>1000mg q8h</td>
<td>1250mg q8h</td>
<td>1750 mg q8h</td>
<td>1750 q8h</td>
</tr>
<tr>
<td>70-74 kg</td>
<td>750mg q12h</td>
<td>1250mg q12h</td>
<td>1000mg q8h</td>
<td>1000mg q8h</td>
<td>1500 mg q8h</td>
<td>2000 mg q8h</td>
<td>2000 q8h</td>
</tr>
<tr>
<td>75-79 kg</td>
<td>1000mg q12h</td>
<td>1250mg q12h</td>
<td>1000mg q8h</td>
<td>1000mg q8h</td>
<td>1750 mg q8h</td>
<td>2250 mg q8h</td>
<td>2250 q8h</td>
</tr>
<tr>
<td>80-84 kg</td>
<td>1000mg q12h</td>
<td>1250mg q12h</td>
<td>1250mg q8h</td>
<td>1250mg q8h</td>
<td>2000 mg q8h</td>
<td>2500 mg q8h</td>
<td>2500 q8h</td>
</tr>
<tr>
<td>85-89 kg</td>
<td>1000mg q12h</td>
<td>1250mg q12h</td>
<td>1500mg q8h</td>
<td>1250mg q8h</td>
<td>2250 mg q8h</td>
<td>2750 mg q8h</td>
<td>2750 q8h</td>
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<tr>
<td>90-94 kg</td>
<td>1000mg q12h</td>
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<td>1500mg q8h</td>
<td>1500mg q8h</td>
<td>3000 mg q8h</td>
<td>3250 mg q8h</td>
<td>3250 q8h</td>
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<tr>
<td>95-99 kg</td>
<td>1250mg q12h</td>
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<td>1500mg q8h</td>
<td>1500mg q8h</td>
<td>3500 mg q8h</td>
<td>3750 mg q8h</td>
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<tr>
<td>100-104 kg</td>
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<td>1500mg q8h</td>
<td>1500mg q8h</td>
<td>4000 mg q8h</td>
<td>4250 mg q8h</td>
<td>4250 q8h</td>
</tr>
<tr>
<td>105-109 kg</td>
<td>1250mg q12h</td>
<td>1500mg q12h</td>
<td>1500mg q8h</td>
<td>1500mg q8h</td>
<td>4500 mg q8h</td>
<td>4750 mg q8h</td>
<td>4750 q8h</td>
</tr>
<tr>
<td>&gt;110 kg</td>
<td>1250mg q12h</td>
<td>1500mg q12h</td>
<td>1500mg q8h</td>
<td>1500mg q8h</td>
<td>5000 mg q8h</td>
<td>5250 mg q8h</td>
<td>5250 q8h</td>
</tr>
</tbody>
</table>

ASHP/IDSA recommendations 2009:
- **Maintenance dose:** 15-20 mg/kg (as actual body weight) given every 8-12 hours for “most patients with normal renal function”.
- **Loading dose:** in seriously ill patients, a loading dose of 25-30 mg/kg (based on actual body weight) can be used.
- Please note that these recommendations do not include specific dosing recommendations for patients who do not have normal renal function (including unstable renal function, or patients with clinical states which may alter serum creatinine concentrations), obese patients, and children, nor do they include any method to determine the dosing interval.

Important formulas:
- \( C_2 = C_1 \times e^{-kt} \)  
  \( C \) = concentration \( t \) = time elapsed from \( C_1 \) to \( C_2 \) in the same dosing interval

- \( C_{ss} = \frac{Dose}{T} \left( 1 - e^{-kt} \right) (e^{-kt'}) \)  
  \( C_{ss} \) = concentration at any time in a dosing interval at steady state  
  \( T \) = infusion time  
  \( t' = t - T \) = point of time when level is expected – calculate from end of infusion  
  \( \tau \) = tau, dosing interval

- \( AUC_{24} = \frac{Dose}{[(CrCl x 0.79) + 15.4] x 0.06} \)  
  \( Dose = dose \ per \ day \ (mg) \)  
  \( CrCl \ (ml/min) \)  
  \( AUC_{24} \ (mg \ * \ hr/L) \)

Population Parameters:
- **Elimination:** 2 or 3 compartment; 1º unchanged by glomerular filtration, some tubular secretion (no adjustment in hepatic impairment)  
  Initial phase half-life: ~7 min  
  Second phase half-life: ~0.5-1 hour (prolonged in patients with poor renal function)  
  Terminal phase half-life: ~3-9 hours in adults with normal renal function  
  \( Ke \ (hr^{-1}) = 0.00083 \ (ClCr \ ml/min) + 0.0044 \) – not a great correlation  
  Ke hemodialysis: highly dependent on type of filter, rate, length of dialysis, etc.  
  Ke peritoneal dialysis: highly dependent on peritonitis, dialysis type, etc.

- **Volume of distribution:**  
<table>
<thead>
<tr>
<th>Population</th>
<th>Value (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm Neonates (≤ 4 weeks)</td>
<td>0.47 ± 0.21</td>
</tr>
<tr>
<td>Full Term Neonates</td>
<td>0.69 L/kg</td>
</tr>
<tr>
<td>Infants (&gt; 4 weeks – 1 year)</td>
<td>0.69 ± 0.17 L/kg</td>
</tr>
<tr>
<td>Children (&gt;1 - ≤ 16 years)</td>
<td>0.70 ± 0.12 L/kg</td>
</tr>
<tr>
<td>Adults (≥ 16 years - &lt; 65 yrs)</td>
<td>0.62 ± 0.15 L/kg</td>
</tr>
<tr>
<td>Obese Adults (&gt; 30% over IBW)</td>
<td>0.56 ± 0.18 L/kg</td>
</tr>
<tr>
<td>Geriatrics (&gt; 65 years)</td>
<td>0.76 ± 0.06 L/kg</td>
</tr>
</tbody>
</table>

Weight Used: Total Body Weight
**Information about levels:**

**Evaluation**
- Are the levels at steady state? If so, a peak and trough can be drawn “around” a single dose and be assumed to be the same at all dosing intervals. At SS all peaks and troughs are considered equal.
- Have the previous doses been given at the appropriate times?
- What time are the levels drawn in relationship to the dose?
- How long was the infusion?
- Peaks should be drawn 1.5-2.5 hours after a 1 hour infusion in most patients. In patients with renal failure the peak should be drawn at least 2 hours after a 1 hour infusion to ensure the level is drawn after the distribution phase.
- EMIT assay and newer FPIA assays are preferred for patients with renal failure (others may be falsely elevated)

**Goal**
- **Peak**
  - Conventional dosing is designed for achieving peaks of 20-40mg/L
  - Not highly associated with either toxicity or efficacy
  - Ototoxicity has been implicated with peaks > 25-50 BUT this is NOT well-documented in the literature
  - Peak levels reported in the literature are confounded by the timing (often during the distribution phase)
- **Trough:**
  - Associated theoretically with cure: 10-20 mg/L; 15-20 mg/L bacteremia, endocarditis, osteomyelitis, meningitis, pneumonia
  - AUC/MIC ≥ 400 associated with cure. MIC for most organisms is far <4 mg/L (for most patients, w/ MIC = 1 mg/L, minimum trough levels of 15 mg/L would be required to achieve these ratios)
  - NOT highly associated with toxicity
    - Ototoxicity has been implicated with troughs > 13-32 BUT this is NOT well-documented in the literature
    - Nephrotoxicity has been implicated with troughs > 10 BUT this is NOT well-documented in the literature
- AUC_{24}-MIC > 400 (studied most in pneumonia)