A. Background

Vancomycin exhibits bactericidal activity in a time-dependant fashion. Penetration of vancomycin in the CNS is limited by its hydrophilicity, relatively large molecular weight (1485) and in part because it crosses the blood-brain barrier by paracellular pathways. Peak concentrations of vancomycin in the CNS are delayed compared to serum levels, and the elimination half-life of vancomycin in the CNS is longer than in the serum. These factors have led to the preferential dosing of vancomycin by continuous infusion in cases of meningitis. Potential advantages of vancomycin dosed by continuous infusion are improved efficacy, safety and decreased cost.

Dosing of vancomycin in meningitis can be particularly challenging as a combination of CNS concentrations and time to target CNS concentrations are critical to decrease neurological sequelae and mortality. Traditional dosing for meningitis administers an intermittent intravenous infusion over 60 or 90 minutes. The continuous infusion of vancomycin has shown that target concentrations are achieved more rapidly with a reduction in dose modifications. Further, continuous infusion of vancomycin has demonstrated higher CNS to serum ratios than intermittent dosing.

B. Appropriate Indications for Use

Meningitis caused by documented or highly suspected Gram-positive organisms and VP shunt infections in the Neurology ICU, Neurology unit and by Infectious Diseases request only. Not intended for empiric therapy of community-acquired pneumococcal meningitis.

C. Dosing

1.0 Loading dose: Administer a 15 mg/kg loading dose

1.1 Use actual body weight (ABW) unless patient is obese (BMI ≥ 30 kg/m²)
1.1.1 For obese males, use dosing weight (DW) of $\text{DW} = \text{IBW} + 0.4(\text{ABW} – \text{IBW})$

$\text{IBW (ideal body weight)} = 50 \text{ kg} + (\text{height in inches} – 60) \times 2.3 \text{ kg}$

1.1.2 For obese females, use dosing weight of $\text{DW} = \text{IBW} + 0.4(\text{ABW} – \text{IBW})$

$\text{IBW (ideal body weight)} = 45.5 \text{ kg} + (\text{height in inches} – 60) \times 2.3 \text{ kg}$

1.2 Continuous infusion: dose based on creatinine clearance

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Loading Dose</th>
<th>Continuous infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90 mL/min</td>
<td>15 mg/kg</td>
<td>45 mg/kg/24 hours</td>
</tr>
<tr>
<td>75-89 mL/min</td>
<td>15 mg/kg</td>
<td>35 mg/kg/24 hours</td>
</tr>
<tr>
<td>60-74 mL/min</td>
<td>15 mg/kg</td>
<td>30 mg/kg/24 hours</td>
</tr>
<tr>
<td>45-59 mL/min</td>
<td>15 mg/kg</td>
<td>25 mg/kg/24 hours</td>
</tr>
<tr>
<td>&lt;45</td>
<td></td>
<td>Intermittent traditional dosing is preferred</td>
</tr>
</tbody>
</table>

D. Dilution and Administration

1.0 Begin continuous infusion 2 hours after end of loading dose administration.

2.0 Vancomycin infusion should be prepared in 0.9% sodium chloride.

3.0 The calculated 24-hour dose should be added to a 500-mL or 1000-mL bag of normal saline and the infusion rate calculated from the total volume of antibiotic plus diluent divided by 24 hours. Final concentration of product should not exceed 5 mg/mL if administered through a peripheral line.

4.0 Keep in mind that a 1000-ml bag of 0.9% normal saline contains 1050ml PLUS the addition of vancomycin. Likewise, a 500-ml bag of 0.9% normal saline contains 525ml PLUS the additional volume of the added vancomycin. Nurses are to take the total volume, labeled on the bag, and run it over 24 hours.

E. Target Concentrations and Dose Adjustments

1.0 Serum drug concentrations are not recommended until at least 48 hours after the continuous infusion has begun or 36-48 hours after dose adjustments.

2.0 Target steady-state, or trough, concentrations for continuous infusion vancomycin for meningitis are 20-28.

3.0 Dose adjustments should be made in 250 mg/day intervals. Once steady-state is attained, further serum concentration monitoring likely will not be necessary unless there are significant changes in creatinine clearance or body weight.

F. Recommended dose adjustments

1.0 Vancomycin half lives for patients within the nomogram may range from 5-14 hours.

2.0 If vancomycin plateau levels are above 30, the continuous infusion daily dose will need to be modified and the infusion held temporarily.
<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Vancomycin plateau 30-32</th>
<th>Vancomycin plateau 33-36</th>
<th>Vancomycin plateau 37-40</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90 mL/min</td>
<td>Hold infusion for 2 hours; decrease daily dose by 20%</td>
<td>Hold infusion for 3 hours; decrease daily dose by 25%</td>
<td>Hold infusion for 4 hours, decrease daily dose by 35%</td>
</tr>
<tr>
<td>75-89 mL/min</td>
<td>Hold infusion for 4 hours; decrease daily dose by 20%</td>
<td>Hold infusion for 5 hours; decrease daily dose by 25%</td>
<td>Hold infusion for 6 hours; decrease daily dose by 35%</td>
</tr>
<tr>
<td>60-74 mL/min</td>
<td>Hold infusion for 6 hours; decrease dose by 20%</td>
<td>Hold infusion for 8 hours; decrease daily dose by 25%</td>
<td>Hold infusion 10 hours; decrease daily dose by 35%</td>
</tr>
<tr>
<td>45-59 mL/min</td>
<td>Hold infusion for 8 hours; decrease dose by 20%</td>
<td>Hold infusion for 10 hours; decrease daily dose by 25%</td>
<td>Hold infusion for 12 hours; decrease dose by 35%</td>
</tr>
</tbody>
</table>

**G. References**