Antimicrobial Stewardship Strategy: Therapeutic drug monitoring (with feedback)

Measurement and interpretation of serum drug concentrations to maximize efficacy and minimize toxicity.

Description

This is an overview and not intended to be an all-inclusive summary. As a general principle, patients must be monitored by the health care team after changes to therapy resulting from recommendations made by the antimicrobial stewardship team.

Optimizing antimicrobial use through therapeutic drug monitoring can maximize efficacy and minimize toxicity for individual patients. It involves the measurement and interpretation of serum drug concentrations drawn at specific times relative to dose administration. The assessment of serum levels and subsequent dosing recommendations requires an understanding of a drug’s pharmacokinetics; the timing of samples; the infection being treated; and the patient’s clinical status, comorbidities and concomitant drug therapy. Pharmacists are best trained to perform this function.

The most extensive literature on and experience with anti-infective therapeutic drug monitoring involves aminoglycosides (e.g., gentamicin, tobramycin, amikacin) and vancomycin. There are definite associations between toxicity and aminoglycoside trough serum levels and between therapeutic efficacy and peak serum levels. Patients on aminoglycoside therapy should have serum levels assessed and be monitored for adverse effects (e.g., renal and ototoxicity).

The monitoring of vancomycin trough levels is somewhat controversial, but may be considered in patients at higher risk of toxicity or therapeutic failure, with serious infections and/or with unpredictable pharmacokinetics.
Many hospitals offer pharmacist consultation for patients on aminoglycosides and vancomycin, either automatically or by request; some use formalized programs. Such consultation ensures appropriate initial dosing; optimal timing of serum levels; timely and appropriate interpretation of levels and subsequent dosing recommendations; and adequate patient monitoring. Medical directives may be considered so that pharmacists can request serum levels and laboratory tests, and make dosing recommendations without a physician’s approval. Documentation in the patient’s chart is essential.

Software/calculator programs are available to assess aminoglycoside pharmacokinetics and calculate individualized dosing regimens. A number of vancomycin nomograms are also available to aid in initial and subsequent dosing.

Institutions that cannot measure levels onsite may experience delays in access to information (slow turn-around time), and this can negatively affect patient care. Efforts to minimize such barriers are necessary.

Therapeutic drug monitoring has typically been used for antimicrobials with a narrow therapeutic range, but increasing pharmacokinetic investigations in different patient groups (e.g., the critically ill, patients with extreme body size, patients with variable renal function) and rising antimicrobial resistance have led to a growing interest in monitoring other agents, such as beta-lactam antibiotics and select antifungal agents. However, the lack of availability of appropriate drug assays limits our ability to monitor many of these antimicrobials.

Advantages

- Important practice to reduce the risk of significant toxicity and adverse events.
- Maximizes pharmacokinetic and pharmacodynamic parameters to improve successful treatment of infection.
- Improves the use of laboratory resources (e.g., aminoglycoside/vancomycin levels).

Disadvantages

- Requires training to ensure adequate understanding of the antimicrobial’s pharmacokinetics, interpretation of levels, patient monitoring and standardized pharmacist practice.
- Some institutions may encounter barriers to timely results (e.g., tests not performed onsite) and interpretation of levels (e.g., lack of knowledge/experience).

Requirements

- Trained personnel (to interpret results).
- Education on the importance of appropriate sampling time.
- Adequate and timely access to laboratory resources.
- Expertise to develop procedures and medical directives, if applicable.

Associated Metrics

- Proportion of patients with a therapeutic level.
- Average time to reach a therapeutic level.
• Number of patients with a 50 per cent increase in serum creatinine from baseline (before and after implementation of a therapeutic drug monitoring program and/or to reflect the effectiveness of a specific process).

References


Additional Useful References

Select articles to provide supplemental information and insight into the strategy described and/or examples of how the strategy was applied; not a comprehensive reference list. URLs are provided when materials are freely available on the Internet.


Tools and Resources


Guidelines for the dosing and monitoring of aminoglycosides (conventional and high dose, extended interval) and vancomycin.


Guidance documents for the use of vancomycin and gentamicin.
Information and online calculators.

Guidance for both intermittent (pulsed) and continuous infusion of vancomycin.
Hartford and Greater Glasgow and Clyde nomograms, as well as administration and monitoring charts for gentamicin.
Samples/Examples (updated June 2016)

- **Example 1:** Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines
- **Example 2:** Markham Stouffville Hospital Corporation - Vancomycin Guidelines
- **Example 3:** Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines
- **Example 4:** Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record
- **Example 5:** Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record
- **Example 6:** Sunnybrook Health Sciences Centre - Monitoring for Aminoglycoside Induced Ototoxicity
- **Example 7:** Sunnybrook Health Sciences Centre - Patient Information Sheet - Aminoglycoside Treatment

*These documents have been generously shared by various health care institutions to help others develop and build their antimicrobial stewardship programs. We recommend crediting an institution when adopting a specific tool/form/pathway in its original form.*

*Examples that contain clinical or therapeutic recommendations may not necessarily be consistent with published guidelines, or be appropriate or directly applicable to other institutions. All examples should be considered in the context of the institution’s population, setting and local antibiogram.*

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**Links with Other Strategies**

- **Dose optimization**
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Citation


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For further information


Email: asp@oahpp.ca
Example 1: Vancouver Coastal Health and Providence Health Care, BC - 
Vancomycin Empiric Dosing Guidelines

Pharmacy
VANCOMYCIN EMPIRIC DOSING GUIDELINES
April 2016, 3rd edition

For more information, please contact Pharmacy
Or visit: www.vhpharmsci.com

KEY
1. Establish patient age, weight, and serum creatinine.
2. Using Table 1, identify initial loading dose and maintenance dose per interval according to patient weight and target pre-vancomycin level.
3. Using Table 2, determine target pre-vancomycin level based on clinical indication.
4. Using Tables 3 or 4, identify initial dosing interval according to target pre-vancomycin level, age, and serum creatinine.
5. Using Table 5, determine dialysis dosing.

TABLE 1 INITIAL DOSE PER INTERVAL

<table>
<thead>
<tr>
<th>TOTAL BODY WEIGHT</th>
<th>LOADING DOSE (suggested maximum 2500 mg/dose)</th>
<th>MAINTENANCE DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TARGET PRE-LEVEL</td>
<td>10-15 mg/L (20 mg/kg)</td>
</tr>
<tr>
<td>kg</td>
<td>40-50</td>
<td>1000 mg</td>
</tr>
<tr>
<td></td>
<td>51-60</td>
<td>1250 mg</td>
</tr>
<tr>
<td></td>
<td>61-70</td>
<td>1250 mg</td>
</tr>
<tr>
<td></td>
<td>71-80</td>
<td>1500 mg</td>
</tr>
<tr>
<td></td>
<td>81-90</td>
<td>1750 mg</td>
</tr>
<tr>
<td></td>
<td>91-100</td>
<td>2000 mg</td>
</tr>
</tbody>
</table>

Available online from:

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Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines (continued)

**TABLE 2 SUGGESTED TARGET PRE-VANCOMYCIN LEVELS BASED ON INDICATION**

<table>
<thead>
<tr>
<th>Pre-vancomycin Level 10-15 mg/L</th>
<th>Pre-vancomycin Level 15-20 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Skin and soft tissue infection</td>
<td></td>
</tr>
<tr>
<td>* Urinary tract infection (UTI) (if catheter-associated; rule out bacteremia)</td>
<td></td>
</tr>
<tr>
<td>* Catheter-associated bacteremia</td>
<td></td>
</tr>
<tr>
<td>* Central nervous system infection</td>
<td></td>
</tr>
<tr>
<td>* Deep-seated or sequestered infection (e.g. abscess)</td>
<td></td>
</tr>
<tr>
<td>* Endocarditis</td>
<td></td>
</tr>
<tr>
<td>* Osteomyelitis</td>
<td></td>
</tr>
<tr>
<td>* MRSA bacteremia or pneumonia</td>
<td></td>
</tr>
<tr>
<td>* MSSA bacteremia (penicillin allergic patient)</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 3 FOR SKIN AND SOFT TISSUE INFECTION & UTI LOW-TARGET 10-15 mg/L INITIAL DOSING INTERVAL (hours)**

<table>
<thead>
<tr>
<th>SCr (mmol/L)</th>
<th>Age Group (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td></td>
</tr>
<tr>
<td>60-69*</td>
<td></td>
</tr>
<tr>
<td>70-79*</td>
<td></td>
</tr>
<tr>
<td>40-60</td>
<td>8</td>
</tr>
<tr>
<td>61-80</td>
<td>8</td>
</tr>
<tr>
<td>81-100</td>
<td>12</td>
</tr>
<tr>
<td>101-120</td>
<td>12</td>
</tr>
<tr>
<td>121-140</td>
<td>12</td>
</tr>
<tr>
<td>141-160</td>
<td>18</td>
</tr>
<tr>
<td>161-180</td>
<td>24</td>
</tr>
<tr>
<td>181-200</td>
<td>24</td>
</tr>
<tr>
<td>Dialysis</td>
<td>See TABLE 5 (back of card)</td>
</tr>
</tbody>
</table>

**TABLE 4 FOR ALL OTHER INDICATIONS (COMPLICATED INFECTIONS) HIGH-TARGET 15-20 mg/L INITIAL DOSING INTERVAL (hours)**

<table>
<thead>
<tr>
<th>SCr (mmol/L)</th>
<th>Age Group (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td></td>
</tr>
<tr>
<td>60-69*</td>
<td></td>
</tr>
<tr>
<td>70-79*</td>
<td></td>
</tr>
<tr>
<td>80-89*</td>
<td></td>
</tr>
<tr>
<td>40-60</td>
<td>6</td>
</tr>
<tr>
<td>61-80</td>
<td>8</td>
</tr>
<tr>
<td>81-100</td>
<td>12</td>
</tr>
<tr>
<td>101-120</td>
<td>12</td>
</tr>
<tr>
<td>121-140</td>
<td>12</td>
</tr>
<tr>
<td>141-160</td>
<td>18</td>
</tr>
<tr>
<td>161-180</td>
<td>18</td>
</tr>
<tr>
<td>Above 180</td>
<td>Dialysis</td>
</tr>
</tbody>
</table>

Dialysis: See TABLE 5 (back of card)

*In elderly patients with low muscle mass, use clinical judgment as SCr may not reflect renal function accurately.*

*If more aggressive therapy is desired, select more frequent dosing interval.*

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Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines (continued)

TABLE 5 DIALYSIS DOSING

<table>
<thead>
<tr>
<th></th>
<th>Hemodialysis (HD)</th>
<th>Continuous Ambulatory Peritoneal Dialysis (CAPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loading Dose</strong></td>
<td>25 mg/kg</td>
<td>Intrapercutaneous (IP): 30 mg/kg OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intravenous (IV): 20 mg/kg</td>
</tr>
<tr>
<td><strong>Maintenance Dose</strong></td>
<td></td>
<td>weight &lt; 70 kg: 500 mg QHD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>weight ≥ 70 kg: 750 mg QHD</td>
</tr>
<tr>
<td><strong>When To Draw Level</strong></td>
<td></td>
<td>IP: 30 mg/kg every 5-7 days OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV: 20 mg/kg every 4-7 days</td>
</tr>
<tr>
<td><strong>Target Vancomycin Level</strong></td>
<td></td>
<td>Pre-second maintenance dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-4 days after first dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-HD level: 15-20 mg/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trough level: 15-20 mg/L</td>
</tr>
</tbody>
</table>

**THERAPEUTIC DRUG MONITORING**

Vancomycin serum levels should be ordered in the following situations:

1. Pre-vancomycin level on 3rd or 4th dose (within 48 hours) if:
   - a higher level of 15-20 mg/L is desired OR
   - patient is at risk for accumulation (e.g. Q6-BH interval) OR
   - patient is receiving other nephrotoxic agents OR
   - serum creatinine is above normal, renal function is changing or uncertain OR
   - patient is obese (>125% IBW), pregnant, pediatric or hypermetabolic (e.g. burn patient, cystic fibrosis)
   Repeat at least weekly to ensure pre-vancomycin level is within desired therapeutic range

2. Pre-vancomycin level after 7 days of therapy (for prolonged course) if aiming for levels < 15 mg/L AND no other risk factors as per above

3. Pre-vancomycin level if patient is not responding to therapy

4. Pre- and 3 hour post-vancomycin level (target 20-40 mg/L) if calculation of precise kinetic parameters are necessary (e.g. in a case when a target pre-vancomycin level of 15-20 mg/L cannot be achieved while on prolonged therapy, or in an obese, pregnant or pediatric patient, especially when aggressive dosing is required)

Revised April 2016

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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines

INTERDISCIPLINARY MANUAL

AUTHOR: Pharmacist

FOLDER: Medication Guidelines & Protocols

APPROVED BY: Drugs & Therapeutics Committee

REVIEW FREQUENCY: 3 years

ELECTRONIC RESPONSIBILITY: Director of Pharmacy

ORIGINAL APPROVAL DATE: 03/11/05

POLICY HISTORY/ NUMBER CHANGES: REVIEWED/ REVISED DATE: 29/01/09 25/05/13

290.914.916.190 VANCOMYCIN GUIDELINES

Expected Outcome:
Patients will receive Vancomycin for appropriate indications in a sufficient dose to achieve desired trough Vancomycin levels to promote efficacy and avoid development of resistance.

Appropriate Use:
- Treatment of serious infections suspected or documented to be caused by β-lactam resistant gram-positive microorganisms (e.g. ampicillin-resistant Enterococci, methicillin-resistant Staphylococcus aureus (MRSA) or coagulase-negative Staphylococcus)
- Treatment or surgical/procedure prophylaxis of gram-positive infections in patients with severe β-lactam allergy
- Empiric therapy for meningitis until culture and sensitivity results are available
- First-line oral treatment of severe or recurrent Clostridium difficile infection (CDI) or second-line therapy for non-severe cases in patients who have failed to tolerate or respond to oral metronidazole (for oral dosing guidelines for CDI, see Appendix B of policy # 040.912.040 Clostridium Difficile Infection (CDI) – Guidelines for the Diagnosis, Management and Treatment of Symptomatic Patients)

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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

**Situations in which Vancomycin use should be discouraged:**
- Routine surgical prophylaxis other than patient with serious allergy to β-lactam antibiotics
- Empiric antimicrobial therapy for febrile neutropenic patient unless strong suspicion for β-lactam resistant gram-positive organism
- Treatment in response to a single blood culture positive for coagulase negative Staphylococcus if other blood cultures taken during same time frame are negative (contamination likely)
- Continued empiric use for presumed infections in patients whose cultures fail to show evidence of β-lactam resistant gram-positive microorganisms
- Eradication of MRSA colonization
- Treatment of infections caused by β-lactam sensitive gram-positive organisms
- Systemic or local prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters

**IV Dosing Guidelines:**
- Usual Dosage = 15-20 mg/kg q8-12h in patients with normal renal function
- With impaired renal function, the frequency is based on the estimate of creatinine clearance (CrCl). Use Cockcroft-Gault equation** to calculate estimated CrCl.
- Dose is based on actual body weight, even in the setting of obesity. Avoid doses larger than 2 g; instead consider shorter dosing interval
- Consider more aggressive dosing in serious, invasive infections where a trough level target of 15-20 mcg/mL is desired (see Monitoring section)
- In seriously ill patients, consider a **loading dose** of 25-30 mg/kg to facilitate rapid attainment of target trough concentrations. Infuse at a rate of 500 mg/h. Do NOT adjust loading dose for renal dysfunction.
- See the following tables for suggested dosing:

<table>
<thead>
<tr>
<th>Actual Body Weight (kg)</th>
<th>Empiric Initial Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>750</td>
</tr>
<tr>
<td>50-64</td>
<td>1000</td>
</tr>
<tr>
<td>65-74</td>
<td>1250</td>
</tr>
<tr>
<td>75-89</td>
<td>1500</td>
</tr>
<tr>
<td>90-114</td>
<td>1750</td>
</tr>
<tr>
<td>115-130</td>
<td>2000</td>
</tr>
<tr>
<td>Greater than 130</td>
<td>Consider alternate dosing strategy</td>
</tr>
</tbody>
</table>

---

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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

Table 2: Empiric Dosing Interval Based on Creatinine Clearance

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Empiric Initial Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than or = 60</td>
<td>q12h</td>
</tr>
<tr>
<td>41-59</td>
<td>q24h</td>
</tr>
<tr>
<td>31-40</td>
<td>q36h</td>
</tr>
<tr>
<td>16-30</td>
<td>q48h</td>
</tr>
<tr>
<td>10-15</td>
<td>q72h</td>
</tr>
<tr>
<td>Less than 10 or hemodialysis</td>
<td>Order random level and repeat every 1 to 2 days. Repeat dose when level less than 20 mcg/mL.</td>
</tr>
<tr>
<td>CRRT</td>
<td>500 mg q24-48h. Adjust based on levels.</td>
</tr>
</tbody>
</table>

- Pharmacist may adjust the dose based on renal function and patient weight. See policy # 290.914.916.115 Pharmacist Medication Dosing Service.

**Monitoring:**
- Vancomycin therapeutic drug monitoring is used to determine individualized patient pharmacokinetics. The results may be used to guide dosing, enhance safety and efficacy, and to reduce the risk of resistance.
- Peak levels have not been shown to correlate well with toxicity or efficacy and adequate peak levels (20 – 80 mcg/mL) are achieved with recommended doses.
- Trough concentrations should always be maintained above 10 mcg/mL to avoid development of resistance.
- **Target trough range of 15-20 mcg/mL is recommended in select patients with:**
  - bacteremia, endocarditis, meningitis, hospital acquired pneumonia or osteomyelitis caused by S. aureus
- Trough levels greater than 20 mcg/mL may be associated with an increased risk of nephrotoxicity.
- Trough levels should be ordered in patients:
  - expected to remain on vancomycin for longer than 3 days
  - with rapidly changing renal function
  - receiving other nephrotoxic drugs (e.g. gentamicin, tobramycin, amphotericin)
  - receiving aggressive dosing
  - with severely altered volumes of distribution (e.g. burn patients, morbidly obese, compartment syndrome)
- Trough levels should be performed once weekly for patients requiring long term treatment (ie 4-6 weeks). Levels should be done more frequently in hemodynamically unstable patients or suspicion of subtherapeutic level.
- Anuric patients should have a random level drawn and repeated every 1 to 2 days until level is less than 20 mcg/mL. A repeat vancomycin dose is given at this time.
- Initial trough levels should be obtained no earlier than at steady state (before 4th dose in patients with normal renal function)

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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

- Trough levels should be performed 30 minutes or less before scheduled dose. If peak levels are used to assess vancomycin pharmacokinetics, they should be done 1 hour after the end of the infusion.
- Serum creatinine, BUN should be checked at least twice weekly while on vancomycin or more frequently if renal function is unstable, on concomitant nephrotoxic agents or targeting higher trough concentrations. If signs of renal impairment develop, assess risk versus benefit of vancomycin therapy.
- Pharmacist may order vancomycin levels, serum creatinine and BUN as needed and adjust dose or interval according to above recommendations. See policy # 290.914.916.115 Pharmacist Medication Dosing Service. See the following table for suggested dose and interval adjustments.

Table 3: Dosage Adjustments Based on Trough Levels

<table>
<thead>
<tr>
<th>Trough less than 10 mcg/mL</th>
<th>Trough 10-13 mcg/mL</th>
<th>Trough 13.1-20 mcg/mL</th>
<th>Trough 20.1-40 mg/mL</th>
<th>Trough greater than 40 mcg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>If dose already given, order peak level (1 hour after end of infusion) and determine patient’s pharmacokinetics. While level pending, <strong>either</strong> increase dose by 250-500 mg <strong>OR</strong> decrease dosing interval.</td>
<td>Keep same dose and interval.</td>
<td>Keep same dose and interval.</td>
<td>Decrease dose by proportion <strong>OR</strong> increase dosing interval.</td>
<td>Hold vancomycin. Order 2 random levels separated by 24 hrs and determine patient’s pharmacokinetics.</td>
</tr>
</tbody>
</table>

**Adverse Effects:**

**Red person syndrome**
Histamine mediated reaction characterized by erythematous flushing, tingling and pruritis involving face, neck and upper torso most often occurring during vancomycin infusion. Associated hypotension may also occur. Management should include extending the duration of infusion to 90-120 minutes with or without premedication with an antihistamine. This does not preclude further use of vancomycin.

**Nephrotoxicity**
Nephrotoxicity due to vancomycin monotherapy is uncommon and often reversible. Vancomycin induced nephrotoxicity is defined as an increase in

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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

- serum creatinine concentration of 45 μmol/L or 50% increase from baseline (whichever is greater) in at least 2-3 consecutive measurements after several days of vancomycin therapy in the absence of an alternate explanation. The incidence of nephrotoxicity increases when vancomycin is combined with aminoglycosides or other nephrotoxic drugs; or when the duration of therapy is prolonged (greater than 21 days).

**Otoxicity**
Severe ototoxicity induced by vancomycin is rare. Case reports are confounded by concurrent use of other ototoxic agents and early reports (1950-60s) felt to be related to impurities in the formulation. The occurrence of ototoxicity does not appear to correlate with excessive peak or trough vancomycin concentrations. Recommendations are to discontinue vancomycin if patient loses ability to hear high frequency sounds or tinnitus occurs.

**Other**
Thrombophlebitis and/or pain, tingling at injection site, neutropenia, thrombocytopenia, rash, hypersensitivity and very rare reports of cardiac arrest related to rapid IV injection

**Administration:**
- Less than or = 500 mg in 100 mL NS or D5W
- Greater than 500 to 1250 mg in 250 mL NS or D5W
- Greater than 1250 mg in 500 mL NS or D5W
- Infuse doses less than or equal to 1000 mg over at least 1 hour, 1100-1500 mg over 90 minutes and greater than 1500 mg over 2 hours
- Adjust doses in increments of 250 mg

**Cockcroft-Gault equation:**

Creatinine clearance (CrCl) = \((140 \text{-age}) \times \text{weight (kg)}\) multiply by 1.2 if male
Serum creatinine (μmol/L)

**References:**
1. CDC. Recommendations for preventing the spread of vancomycin resistance recommendations of the hospital infection control practices advisory committee; Sept. 22, 1995.

ENDORSEMENT(S):
Antibiotic Stewardship Subcommittee
Drugs & Therapeutics Committee

PREVIOUS REVIEWED/REVISED DATE(S):
29/01/09

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines

INTERDISCIPLINARY MANUAL

AUTHOR: Director of Pharmacy

FOLDER: Medication Guidelines & Protocols

APPROVED BY: Drugs and Therapeutics Committee

REVIEW FREQUENCY: 3 years

RESPONSIBILITY: Director of Pharmacy

ORIGINAL APPROVAL DATE: 03/11/2005

POLICY HISTORY/NUMBER CHANGES: REVISED/REVIEWED DATE: 12/09/2013

290.914.916.025 AMINOGLYCOSIDE DOSING IN ADULTS

POLICY:

High dose “once daily” aminoglycoside regimen or Conventional Multiple daily dosing regimen will be used for aminoglycoside dosing in adults. The pharmacist will determine the appropriate regimen based on baseline clinical data, creatinine clearance and assessment parameters, see policy # 290.914.916.115 Pharmacist Medication Dosing Service.

GUIDELINES:

1. COLLECTION OF BASELINE CLINICAL DATA:

   a) Obtain the following baseline clinical data:

      - differential diagnosis, site and severity of infection
      - height (Ht), weight (Wt), ideal body weight (IBW), lean body weight (LBW), and dosing body weight (DBW)
      - age, sex
      - serum creatinine (SCr), BUN, urinary output
      - WBC and differential
      - temperature
      - concurrent disease states or conditions which may affect the pharmacokinetics of aminoglycosides, e.g. cystic fibrosis, burns, obesity, ascites

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

2. DETERMINATION OF DOSSING BODY WEIGHT AND CREATININE CLEARANCE:

a) Determination of DBW
Select the most appropriate value for the DBW. This value is determined by considering the patient’s actual weight (ABW), IBW, LBW, or estimation of ABW. Use the equations below or Micromedex to calculate IBW and DBW.

Female:  
IBW = 45.5 kg + (2.3 X inches over 5')
LBW = 1.07 X Wt(kg) - 146 X (Wt(kg)^2/ (Ht(cm)^2)

Male:  
IBW = 50 kg + (2.3 X inches over 5')
LBW = 1.10 X Wt(kg) - 128 X (Wt(kg)^2/ (Ht(cm)^2)

- If ABW greater than IBW (but not more than 30% over IBW), use DBW = IBW
- If ABW greater than IBW (more than 30% over IBW), use DBW = IBW + 0.4 (ABW - IBW)
- If ABW less than IBW, use ABW or LBW, as appropriate

b) Calculation of Creatinine Clearance:
Calculate creatinine clearance (CrCl) using the Crockcroft-Gault equation below or Micromedex.

Note: Conversion factor for serum creatinine: mg/dL = umol/L * 88.4

Males:  
Clcr = \frac{IBW (kg) * (140-age) * X 1.2}{(mL/min) * Scr (umol/L)}

Females:  
0.85 X Clcr (for males - as above)

3. ASSESSMENT - DETERMINATION OF HIGH DOSE OR MULTIPLE DAILY DOSSING:
Assess patient for appropriateness for either the high dose (‘once daily’) aminoglycoside dosing regimen or the conventional multiple daily dose regimen. Patients are initiated on the high dose regimen unless one of the following exclusion criteria is met:
- Pregnancy
- Neonatal or paediatric age
- Endocarditis (except strep viridans endocarditis)
- Ascites, burns
- Cystic fibrosis
- Dialysis

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

- CrCl less than 20 mL/min
- Surgical prophylaxis
- Post-partum less than 7 days
- Use with caution in patients greater than 60 years old
- Amputation

Patients who meet one or more of the above criteria must have therapy initiated with the conventional multiple daily dosing regimen with monitoring of pre and post aminoglycoside levels.

4. HIGH DOSE “ONCE DAILY” AMINOGLYCOSIDE REGIMEN:

RATIONALE AND BACKGROUND:
Pharmacokinetic Properties of Aminoglycosides:

Concentration-dependent killing:
It has been demonstrated that achievement of high peak serum concentration of aminoglycosides relative to the minimum inhibitory concentration of the microorganism is the major determinant of the clinical response to aminoglycosides. This is best achieved with high dose regimens, which result in high peak concentrations of drug.

Post antibiotic effect:
Post antibiotic effect is defined as a period of time after complete removal of the antibiotic from the body during which there is no growth of the target organism. Use of high dose aminoglycosides may result in a period of up to 12 hours of antibiotic effect during which there is no detectable serum concentration of the drug. This property of the aminoglycoside allows for daily dosing without compromising therapeutic efficacy. The higher the concentration of drug, the longer the duration of the post antibiotic effect.

Toxicity:
A major determinant of aminoglycoside induced renal toxicity and ototoxicity is the accumulation of these agents within the renal cortex and perilymph of the inner ear. The accumulation follows saturable kinetics so even though the peak serum drug concentration is higher with high dose aminoglycosides, the kidney does not accumulate more drug. Conversely, it allows for back diffusion of the drug from the kidney and inner ear to flow back out, reducing drug exposure and limiting toxicity.

Clinical Efficacy:
Many studies have been published comparing high dose aminoglycoside regimens (once daily) to conventional multiple daily dosing regimens. In all these studies, high dose aminoglycosides were as effective, and not more toxic, than multiple daily dosing of the drug.

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

**DOSING GUIDELINES:**

**Dose:**
Gentamicin and Tobramycin
- 5 mg/kg DBW (use increments of 20 mg)
- 3 mg/kg DBW (Gentamicin only, for strep viridans endocarditis)

Amikacin
- 15 mg/kg DBW (use increments of 25 mg)

**Interval:**

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>mL/min</td>
<td></td>
</tr>
<tr>
<td>greater than 60</td>
<td>Q24h</td>
</tr>
<tr>
<td>40 – 59</td>
<td>Q36h</td>
</tr>
<tr>
<td>20 – 39</td>
<td>Q48h</td>
</tr>
<tr>
<td>less than 20</td>
<td>Use conventional multiple daily dosing</td>
</tr>
</tbody>
</table>

**Administration:**

- Dilute in 100 mL D5W or NS and infuse over 30 minutes

**Monitoring:**

1. **DO NOT DRAW ROUTINE PEAK AND TROUGH LEVELS.**
   
   Exceptions:
   - significant changes in renal function
   - infections involving highly resistant organisms

   **Desired Trough and Peak Levels**

<table>
<thead>
<tr>
<th></th>
<th>Trough</th>
<th>Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin*/Tobramycin</td>
<td>Less than 0.5 mg/L</td>
<td>20 mg/L</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Less than 2.5 mg/L</td>
<td>60 mg/L</td>
</tr>
</tbody>
</table>

- a. Draw ONE trough level 30 min before the second to fourth dose
  - If level is greater than desired trough extend the dosing interval by 12 hours and repeat level (or use conventional dosing and monitoring methods).

  **OR**

- b. Draw a trough level 30 min before and a peak level 30 min after the second to fourth dose. If peak or trough levels are outside of desired range adjust further doses using pharmacokinetic principles (see section on Dosage Adjustment Form Serum Drug Levels).

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

Note: Amikacin blood samples are sent out of the hospital for processing so a delay in reporting is to be expected.

2. Repeat trough levels if therapy is greater than 7 days and reassess weekly thereafter and with any significant changes in renal function.
3. Monitor serum creatinine pre dose and then 3 x a week.
4. Do not use high dose aminoglycosides for greater than 14 days due to an increased risk of nephrotoxicity/ototoxicity. Consider alternative therapy.
5. Baseline audiometry should be performed for patients on long-term treatment.

* There are no specific guidelines for drug concentration monitoring of gentamicin 3 mg/kg q24h for streptococci endocarditis. A target trough of less than 0.5 mg/L, as with other dosing regimens, is reasonable.

Orders and Documentation:

1. Pharmacist will order the dose, route and frequency.
2. Indicate time for the next dose and order trough level.
3. Pharmacist will document on the electronic record.

References:


5. CONVENTIONAL MULTIPLE DAILY DOSING REGIMEN:
   a) Initial Calculation of Dose and Interval:

   **Method 1:**
   Computer software – Selinger Kinetics or Abbott Kinetics

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Method II:

**Dose:** General Guidelines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>1 – 2 mg/kg/dose (based on DBW)</td>
</tr>
<tr>
<td>Tobramycin</td>
<td></td>
</tr>
<tr>
<td>Netilmicin</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>5 – 7.5 mg/kg/dose (based on DBW)</td>
</tr>
</tbody>
</table>

Select dose based on the severity and site of infection according to the following:

<table>
<thead>
<tr>
<th>Indication/Site of Infection</th>
<th>Gentamicin/Tobramycin</th>
<th>Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synergy (gentamicin)</td>
<td>1 mg/kg</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>1 mg/kg</td>
<td>5 mg/kg</td>
</tr>
<tr>
<td>Gram neg sepsis, other</td>
<td>1.5-2 mg/kg</td>
<td>7.5 mg/kg</td>
</tr>
<tr>
<td>serious infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pneumonia</td>
<td>2 mg/kg</td>
<td>7.5 mg/kg</td>
</tr>
</tbody>
</table>

**Interval**

Choice of the dosing interval is based on the patient's renal function. The patient's urinary output should be considered in addition to the serum creatinine concentration.

Select the appropriate dosing interval as follows:

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 70</td>
<td>q8h</td>
</tr>
<tr>
<td>40-69</td>
<td>q12h</td>
</tr>
<tr>
<td>15-39</td>
<td>q24h</td>
</tr>
<tr>
<td>Less than 15</td>
<td>Give a dose and draw levels in 24 hours to determine dosing interval</td>
</tr>
</tbody>
</table>

When selecting the interval, additional consideration should be given to patients with factors, which may alter creatinine production. (i.e. muscle wasting, severe muscle atrophy/dystrophy, hyperthyroidism, paralysis, chronic glucocorticoid therapy, aging, hepatic diseases, trauma, surgery, sepsis).

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Method III:
Dose: = DBW (kg) X Vd (L/kg) X Cpd (mg/L)

Cpd = desired peak concentration
Vd = volume of distribution (estimated considering hydration status)

<table>
<thead>
<tr>
<th>Hydration Status</th>
<th>Vd (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.20 - 0.25</td>
</tr>
<tr>
<td>Dehydrated</td>
<td>0.15</td>
</tr>
<tr>
<td>Overhydrated</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Interval:

Interval should be selected based on the criteria given in Method II above.

Method IV:
This method should be used for patients whose renal function is very poor or unknown.

Dose:
Use method II or III to determine dose.

Interval:

No interval should be ordered at this time. The interval should be determined based on the results of a post and random level. Refer to “Dosage Adjustments from Serum Drug Levels”.

b) Timing of Serum Drug Levels:

Intravenous Administration: Aminoglycosides are to be administered over 30 minutes. Pre levels should be taken 0 - 15 minutes before the dose. Post levels should be taken 30 minutes after the end of the infusion.

Intramuscular Administration: Pre levels should be taken 0 – 15 minutes before the IM injection. Post levels should be taken 1 hr after the injection.

Aminoglycoside pre and post levels should be taken around the third dose of a dosage regimen (e.g. 3rd 80 mg dose from a regimen of 100 mg loading dose, followed by 80 mg q8h) for q6 - q12h dosing intervals, or around the second dose for intervals greater than q12h. Pre and post levels should be done following the initiation of therapy or a change in dosage regimen. It may be necessary to draw levels at other specified times for patients with variable renal function

c) Desired Serum Drug Levels:
The following are the desired serum concentrations for aminoglycosides:

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

<table>
<thead>
<tr>
<th>Indication/Site of Infection</th>
<th>Gentamicin/Tobramycin</th>
<th>Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trough (mg/L)</td>
<td>Peak (mg/L)</td>
</tr>
<tr>
<td>Synergy (gentamicin)</td>
<td>Less than 1</td>
<td>3-4 mg/L</td>
</tr>
<tr>
<td>UTI</td>
<td></td>
<td>4-5 mg/L</td>
</tr>
<tr>
<td>Gram neg sepsis, other</td>
<td>0.8 – 2 mg/L</td>
<td>5 – 10 mg/L</td>
</tr>
<tr>
<td>serious infections</td>
<td></td>
<td>6-7 mg/L</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7-8 mg/L</td>
<td>25-30 mg/L</td>
</tr>
</tbody>
</table>

**d) Dosage Adjustments from Serum Drug Levels:**
Four methods may be used to make DOSAGE and INTERVAL adjustments.

**Method I:**
Computer software - Selinger or Abbott Kinetics

**Method II:**

**Interval:**

a) Determine half-life based on rough estimate or equation as follows:

\[ t_{1/2} = \frac{0.693}{k} \]

\[ k \text{ = elimination rate constant} \]

\[ = \text{slope of ln concentration VS time curve} \]

b) Calculate the number of t1/2’s between the desired pre and post.

\[ \text{desired post} = 7.5 \text{ mg/L} \]

\[ \text{desired pre} = 1 \text{ mg/L} \]

\[ \text{7.5} \text{---------> 3.75} \text{---------> 1.875} \text{---------> 0.95 (~1) } \]

\[ 1 \text{ t1/2} \quad 2 \text{ t1/2} \quad 3 \text{ t1/2} \]

Three t1/2’s are required for the dosing interval. If the t1/2 = 3.5 hours, 3 X 3.5 hours = 10.5 hours. Choose the closest standard interval (q12h in this case).

**Dose:**
Adjust dose based on proportional difference between pre and post levels.

i.e.

\[ \text{observed pre} = 2.5 \text{ mg/L} \]
\[ \text{desired pre} = 1 \text{ mg/L} \]
\[ \text{observed post} = 5 \text{ mg/L} \]
\[ \text{desired post} = 7 \text{ mg/L} \]
\[ \text{difference} = 2.5 \text{ mg/L} \]
\[ \text{difference} = 6 \text{ mg/L} \]

\[ 60 \text{ mg dose -------> difference} = 2.5 \text{ mg/L} \]
\[ X \text{ mg dose -------> difference} = 6 \text{ mg/L} \]
\[ \therefore \text{new dose} = 144 \text{ mg, round off to 140 mg for new dose} \]

Check validity of new dose by calculating the mg/kg/dose. This new dose will likely be within the 1 - 2.5mg/kg range.

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Method III:

Use Pharmacokinetic Formulas:

\[ V_d = \frac{R(1 - e^{-kt})}{k(C_{max} - C_{min}e^{-kt})} \]

\[ T = \frac{2.303 \log\left(\frac{C_{min}}{C_{max}}\right)}{k} + t \]

\[ R = C_{max}, \text{desired} \times k \times V_d \times \left(\frac{1 - e^{-kT}}{1 - e^{-kt}}\right) \]

Check:

\[ C_{max} = \frac{R(1 - e^{-kt})}{kV_d(1 - e^{-kT})} \]

\[ C_{min} = C_{max}e^{-k(T-t)} \]

\[ V_d = \text{volume of distribution} \]

\[ k = \text{elimination rate constant} \]

\[ t = \text{time for infusion} \]

\[ T = \text{dosing interval} \]

Method IV:

To use this method, two or three drug levels should be taken following the first dose. One level must be a post, and the others are random levels taken at appropriate times following administration.

Dose:
Adjust dose as outlined in method II (observed pre = 0)

Interval:
Determine the t1/2 from the measured serum drug levels, and select the appropriate interval using the approach outlined in method II.

Monitoring:

The following parameters should be monitored:

- Temperature - monitor daily
- Weight
- BUN, SCr - monitor 2 to 3 times per week (more frequent monitoring may be necessary for patients with unstable renal function)
- 24 hour urine for CrCl - to be monitored when SCr is not an accurate indication of renal function
- Urinary output (I/O)
- Hydration status
- Culture and sensitivity reports - monitor daily
- Concomitant antibiotics - monitor daily

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Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

Orders and Documentation:

1. Pharmacist will order the dose, route, and frequency.
2. State the time the next dose is due.
3. Specifically order pre, post, or random levels. An order for "gentamicin" levels is not acceptable.
4. State the dose the levels are to be taken around or before, e.g. pre and post gentamicin levels around 1400h dose, or gentamicin pre level before 2200h dose.

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### Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record

**Vancomycin Monitoring Record**

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Age: ___</th>
<th>Sex: ___</th>
<th>Unit: ___</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique #:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Antibiotics:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Target level (mcg/mL)</strong></td>
<td>10-15</td>
<td>15-20</td>
<td></td>
</tr>
<tr>
<td>Allergies:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ht: ___ Wt: ___ IBW: ___</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline CrCl: mL/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doses Given: mg @ h (date)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacist:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orders written (date)</td>
<td>1) Vancomycin ___ mg IV q ___ hr (= ___ mg/kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2) 1st dose: ___ hr ___ (date)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bloodwork</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MICROBIOLOGY**

<table>
<thead>
<tr>
<th>Date</th>
<th>Site</th>
<th>Results</th>
<th>Sensitivities</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Site</th>
<th>Results</th>
<th>Sensitivities</th>
</tr>
</thead>
</table>

**LAB MONITORING**

<table>
<thead>
<tr>
<th>Date</th>
<th>Scr (µmol/L)</th>
<th>Urea (µmol/L)</th>
<th>Ccr (mL/min)</th>
<th>WBC</th>
<th>Neuts (%)</th>
<th>Tmax (°C)</th>
<th>ESR</th>
<th>C-Reactive Protein</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Current Regimen</th>
<th>Trough level Time</th>
<th>New Regimen</th>
<th>(mg/kg/ dose)</th>
<th>Comments</th>
<th>Initial</th>
</tr>
</thead>
</table>

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Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record (continued)

**IV Vancomycin Dosing Guidelines:**

- Usual Dosage = 15-20 mg/kg (actual body weight) q8-12h in patients with normal renal function. Adjust frequency based on estimated CrCl
- Avoid doses larger than 2 g; instead consider shorter dosing interval
- Consider more aggressive dosing in serious, invasive infections where a trough level target of 15-20 mcg/mL is desired (see Monitoring section)
- In seriously ill patients, consider a **loading dose** of 25-30 mg/kg to facilitate rapid attainment of target trough concentrations. Infuse at a rate of 500 mg/h. Do NOT adjust loading dose for renal dysfunction. **Pharmacist to please add note to emar and ordering rate for loading dose.**
- See the following tables for suggested dosing:

<table>
<thead>
<tr>
<th>Actual Body Weight (kg)</th>
<th>Empiric Initial Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>750</td>
</tr>
<tr>
<td>50-64</td>
<td>1000</td>
</tr>
<tr>
<td>65-74</td>
<td>1250</td>
</tr>
<tr>
<td>75-89</td>
<td>1500</td>
</tr>
<tr>
<td>90-114</td>
<td>1750</td>
</tr>
<tr>
<td>115-130</td>
<td>2000</td>
</tr>
<tr>
<td>Greater than 130</td>
<td>Consider alternate dosing strategy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Empiric Initial Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than or = 60</td>
<td>q12h</td>
</tr>
<tr>
<td>41-59</td>
<td>q24h</td>
</tr>
<tr>
<td>31-40</td>
<td>q36h</td>
</tr>
<tr>
<td>16-30</td>
<td>q48h</td>
</tr>
<tr>
<td>10-15</td>
<td>q72h</td>
</tr>
</tbody>
</table>

**Vancomycin Monitoring Guidelines:**

- Trough concentrations should always be maintained above 10 mcg/mL to avoid development of resistance.
- Target trough range of 15-20 mcg/mL is recommended in select patients with bacteremia, endocarditis, meningitis, hospital acquired pneumonia or osteomyelitis caused by S. aureus
- Trough levels should be ordered in patients:
  - expected to remain on vancomycin for longer than 3 days
  - with rapidly changing renal function
  - receiving other nephrotoxic drugs (e.g. gentamicin, tobramycin, amphotericin, acyclovir)
  - receiving aggressive dosing
  - with severely altered volumes of distribution (e.g. burn patients, morbidly obese, compartment syndrome)
- Trough levels should be performed once weekly for patients requiring long term treatment (i.e. 4-6 weeks). Levels should be done more frequently in hemodynamically unstable patients or suspicion of sub therapeutic level.
- Anuric patients should have a random level drawn and repeated every 1 to 2 days until level is less than 20 mcg/mL. A repeat vancomycin dose is given at this time.
- Initial trough levels should be obtained no earlier than at steady state (before 4th dose in patients with normal renal function)

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Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record (continued)

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<thead>
<tr>
<th>Date</th>
<th>Scr (µmol/L)</th>
<th>Urea (µmol/L)</th>
<th>Clcr (mL/min)</th>
<th>WBC</th>
<th>Neuts (%)</th>
<th>Temp (°C)</th>
<th>ESR</th>
<th>C-Reactive Protein</th>
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<thead>
<tr>
<th>Date@time</th>
<th>Current Regimen</th>
<th>Trough level Time</th>
<th>Level</th>
<th>New Regimen (mg/kg/dose)</th>
<th>Comments/Initial</th>
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Example 5: Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record

AMINOGLYCOSIDE MONITORING RECORD

1. PATIENT INFORMATION
   NAME: 
   AGE: ________ SEX: ________ UNIT: ________

DIAGNOSIS: 
OTHER ANTIBIOTICS: 

ALLERGIES: 

MD: 
PHARMACIST: 

2. HT: ________ WT: ________
   Female: IBW = 45.5 kg + (2.3 X inches over 5')
   LBW = 1.07 X WT(kg) - 148 X (WT(kg))2/3 (HT(cm)2)
   Male: IBW = 50 kg + (2.3 X inches over 5')
   LBW = 1.10 X WT(kg) - 128 X (WT(kg))2/3 (HT(cm)2)

If ABW greater than IBW (but not by more than 30% over IBW), use DBW = IBW
If ABW greater than IBW (more than 30% over IBW), use DBW = IBW + 0.4 (ABW - IBW)
If ABW less than IBW, use ABW or LBW, as appropriate

IBW: ________ DBW: ________ LBW: ________

3. DATE:
   Sr CREATIN: ________ umol/L
   CLEARANCE: ________ mL/min

4. REGIMEN ORDERED:
   Gentamicin / Tobramycin / Amikacin ________mg IV q ________h = ________(mg/kg)

Doses Given: 1st mg @ ________h 2nd mg @ ________h 3rd mg @ ________h

5. ASSESSMENT:
   Contraindications to High Dose Extended Interval Dosing
   • Pregnancy
   • Neonatal - Pediatric (less than 18 yr)
   • Entercoccal Endocarditis
   • Ascites, burns

   • Cystic Fibrosis
   • Dialysis
   • CrCl less than 20 mL/min
   • Surgical Prophylaxis (ie x 24 - 48 hr)
   • Post Partum less than 7 days
   • Use with caution in patients over 60 years old

6. DOSE AND FREQUENCY:
   a) High Dose Extended Interval Dosing
      Gentamicin/Tobramycin 5 mg/kg
      Gentamicin for synergy: 3 mg/kg
      Amikacin 15 mg/kg

      DBW: ________ x ________mg/kg = ________mg
      (Increments of 20 mg for Gent/Tobra, 25 mg for Amikacin)

      Interval
      Clearance:
      • over 60 mL/min q 24 h
      • 40 - 60 mL/min q 36 h
      • 20 - 39 mL/min q 48 h
      • less than 20 - use conventional multiple daily dosing

   b) Conventional Multiple Daily Dosing
      Indication/Site of Infection
      Gentamicin/Tobramycin Amikacin
      Synergy (gastroint) 1 mg/kg 1 mg/kg
      UTI 1 mg/kg
      Gram neg sepsis, other serious infections 1.5-2 mg/kg
      Pneumonia 2 mg/kg 5 mg/kg

      DBW: ________ x ________mg/kg = ________mg
      (Increments of 20 mg for Gent/Tobra, 25 mg for Amikacin)

      Interval
      Clearance:
      • over 70 mL/min q 8 h
      • 40-69 mL/min q 12 h
      • 15-39 mL/min q 24 h
      • less than 15 Give a dose and draw levels in 24 hours to determine dosing interval

7. ORDER WRITTEN:
   Gentamicin / Tobramycin / Amikacin ________mg q ________h
   First Dose @ ________h on ________Date

   Levels @ ________h on ________Date Blood Work: ________

Date Discontinued:

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Example 5: Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record (continued)

6. DESIRED LEVELS:
   a) High Dose Extended Interval Dosing
   DO NOT DRAW ROUTINE PEAK AND TROUGH LEVELS. Exceptions:
      • Significant existing renal dysfunction or significant changes in renal function
      • Infections involving highly resistant organisms
      • Patients receiving therapy for more than 7 days, and therapy is likely to continue.
   Options:
      a) draw trough level prior to 2.4\textsuperscript{nd} dose and extend dosing interval by 12 hours if level greater than desired
      b) draw trough and peak level around 2.4\textsuperscript{nd} dose and adjust dose/interval using pharmacokinetic principals

   - **Gentamicin/Tobramycin**
     - Trough
     - Peak
   - **Aminogacn**
     - Trough
     - Peak
     - Under 2.5 mg/L
     - 40 mg/L

b) Conventional Multiple Daily Dosing

<table>
<thead>
<tr>
<th>Infection/Site of Infection</th>
<th>Gentamicin/Tobramycin (mg/L)</th>
<th>Aminogacn (mg/L)</th>
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<tbody>
<tr>
<td>Synergy (p/c)</td>
<td>Trough</td>
<td>Peak</td>
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<td>UTI</td>
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<td>4-6</td>
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<td>6.7</td>
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<td>pneumonia</td>
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<th>Current Regimen</th>
<th>Pre Level (mg/L) Time</th>
<th>Post Level (mg/L) Time</th>
<th>t1/2 (hr)</th>
<th>New Regimen Ordered</th>
<th>mg/kg/dose (DBW)</th>
<th>Comments</th>
<th>Phmst Int'l</th>
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<th>Date</th>
<th>Scr umol/L</th>
<th>Urea (umol/L)</th>
<th>CICr (mL/min)</th>
<th>WBC</th>
<th>Neuts (%)</th>
<th>Temp (°C)</th>
<th>Hydration Status/ Other Comments</th>
<th>Microbiology (Specimen, Culture, Sensitivity)</th>
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Example 6: Sunnybrook Health Sciences Centre - Monitoring for Aminoglycoside Induced Ototoxicity

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Example 7: Sunnybrook Health Sciences Centre - Patient Information Sheet- Aminoglycoside Treatment

PATIENT INFORMATION SHEET
AMINOGLYCOSIDE TREATMENT

You have been prescribed an antibiotic which is called an aminoglycoside. Aminoglycoside antibiotics include drugs such as gentamicin, tobramycin, and amikacin. Aminoglycosides have been available for the treatment of bacterial infections for over 30 years and are highly effective agents. Your doctor has prescribed an aminoglycoside for you because they consider it to be the best option to treat the infection you have, at this time.

Unfortunately, like most medications, there are potential side effects that may occur when aminoglycosides are used. Aminoglycosides may cause reversible kidney damage in 5-10% of patients receiving more than 5 days of treatment with the aminoglycoside. They may also cause irreversible hearing loss or imbalance and dizziness in less than 3% of patients receiving more than 10-14 days of therapy.

- To minimize the risk of kidney damage, your care-givers are monitoring your kidney function weekly, with the use of blood tests.

- To minimize the risk of hearing loss, you should report any symptoms of ringing in the ears, feeling of fullness in the ears, earache, or hearing loss to your care-givers immediately, so that your aminoglycoside therapy can be re-evaluated.

- To minimize the risk of problems with your balance, you should report any symptoms of dizziness, unsteady walking, or loss of balance to your care-givers immediately, so that your aminoglycoside therapy can be re-evaluated.

- If it is necessary to treat your infection for more than 14 days, you will undergo a hearing function test and a test to evaluate your balance. These tests will be done about 2 weeks after aminoglycoside therapy began. A second test will be done 2-3 weeks after the first test. Additional testing will also be done at any time that you report symptoms of hearing or balance problems.

If you have any additional questions about your aminoglycoside therapy, please ask your nurse to arrange for either your pharmacist or physician to come and speak with you about your aminoglycoside therapy.

Pharmacist Name: __________________________
Contact Number: __________________________
Date Counseled: ___________________________

Sunnybrook Antimicrobial Handbook 2013

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