Antibiotic regimens for suspected hospital-acquired infection (HAI) outside the Paediatric Intensive Care Unit at Red Cross War Memorial Children’s Hospital (RCWMCH)

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Introduction

These recommendations were approved for use by the Pharmaceutical and Therapeutics Committee, RCWMCH on 1 February 2017.

This document replaces empiric antibiotic recommendations for suspected HAI in the 2012 RCWMCH Antimicrobial Recommendations

Excluded from this guideline are antibiotic recommendations for patients with cystic fibrosis and febrile neutropaenia as Drug and Therapeutics Committee antibiotic recommendations exist for these two conditions

Definitions

- Hospital acquired infection (HAI): onset of infection >48 hours after admission or within 30 days of discharge
- Carbapenems: include ertapenem, meropenem, imipenem
- Estimated glomerular filtration rate (eGFR): eGFR = \( \frac{\text{Height (cm)} \times 40}{\text{Creatinine (µmol/L)}} \)

Recommendations

1. All patients suspected of having HAI require a detailed history and clinical examination to identify the likely site(s) of infection. If empiric antibiotics are necessary, appropriate cultures (e.g. urine, blood\(^1\), CSF, peritoneal fluid) should be sent before commencing antibiotics. Complete the ‘infection episode’ details on the antibiotic prescription chart and calculate the eGFR

2. Recommended empiric antibiotics:
   - eGFR >50 ml/minute/1.73 m\(^2\): piperacillin/tazobactam plus amikacin
   - eGFR ≤50 ml/minute/1.73 m\(^2\) (please document the eGFR on the antibiotic prescription chart): meropenem (refer below to renal dose-adjusted recommendations)
   - If eGFR is not known: piperacillin/tazobactam plus amikacin until GFR has been estimated, then follow one of the above two bullet points
   - Suspected hospital-acquired meningitis, an unusual infection in the medical (B) wards: meropenem
- For neurosurgical patients with suspected hospital-acquired meningitis: vancomycin ± meropenem
- Suspected hospital-acquired central-line sepsis: If the patient is stable initiate vancomycin alone or in combination with piperacillin/tazobactam; if the patient is unstable commence vancomycin plus ertapenem (If the eGFR ≤ 50 ml/minute/1.73 m² meropenem should be used instead of ertapenem; refer below to renal dose-adjusted recommendations)
- For suspected ascending cholangitis without prior colonisation initiate piperacillin/tazobactam plus amikacin.
- For suspected ascending cholangitis in a patient known to be colonised, empiric antibiotics depend on the antibiotic susceptibility of the colonising isolate
- If significant renal failure (eGFR ≤50) persists beyond 24 hours the renal unit should be consulted.

3. The empiric antibiotic(s) should be prescribed for a period of 48 hours. Once the microbiology results are known (including 48-hour cultures) the antibiotic prescription MUST be reviewed.
   a. If cultures yield a pathogen that is sensitive to a narrower spectrum antibiotic and it is appropriate to de-escalate antibiotic therapy, then the patient must be de-escalated to the most appropriate antibiotic / antibiotic combination. If there is uncertainty as to de-escalation, the ID service or Microbiology should be consulted.
   b. If culture results show no growth at 48 hours then one of three options should be considered:
      i. all antibiotics should be discontinued if there is no evidence for a bacterial infection,
      ii. if a bacterial infection is still strongly suspected and the child is responding to treatment, antibiotics should be prescribed as follows:
         • If bloodstream infection is suspected, piperacillin-tazobactam plus amikacin for a total of 5 days,
         • If pneumonia is suspected, piperacillin-tazabactam plus amikacin for a total of 5 days,
         • If urinary tract infection is suspected, an aminoglycoside or ciprofloxacin may be administered for a total of 7-10 days,
         • If hospital-acquired meningitis cannot be excluded in a neurosurgical patient, vancomycin ± meropenem should be administered for a total of 14-21 days,
         • If central-line sepsis is suspected, empiric antibiotic regimen for ≤5 days if stable, or 7-10 days if initially clinically unstable, and the feasibility of removing the central line should be reviewed, and
         • If ascending cholangitis is suspected administer the empiric regimen for 10 - 14 days

Furthermore, a detailed explanation for continuing antibiotic therapy should be documented in the patient folder, or
iii. if bacterial infection is suspected and the child is not responding to the prescribed antibiotic regimen, the ID service should be consulted.

c. Monitoring of antibiotic levels

i. Amikacin: Trough levels should be obtained 48-72 hours after commencement of therapy immediately prior to the next dose. Aim for a trough level <1 mg/l. If the trough level is >1 mg/l, increase the dosing interval. A peak level should be measured after the second dose and obtained one hour after a bolus IV, or one hour after an IV infusion is commenced. Aim for a peak level >30 mg/l. If the peak level is <30 mg/l, increase the dose. Once an adequate peak level has been achieved only trough levels need to be monitored (usually twice a week) provided the patient remains stable.

ii. Vancomycin: monitoring of serum trough levels is indicated for all patients. Trough levels should be obtained before the third dose if eGFR >40, before the second dose if GFR 25-40, after 3 days before the second dose if GFR <25 or patient receiving dialysis. It is not necessary to measure peak levels routinely. The target trough level is 10-15 mg/l. If trough <10 mg/l, increase the dose. If trough >15 mg/l increase the dosing interval. For complicated S. aureus infections including bacteraemia, endocarditis) or infections with staphylococci with higher Minimal Inhibitory Concentrations (MICs) (>1 mcg/ml), a trough level of 15-20 mg/l is preferred.

d. Carbapenems should be prescribed or continued in patients with microbiological proof of a previous or current multi-drug resistant organism for which a carbapenem is indicated. The recommended duration of antibiotic therapy is:

- Bloodstream infection: 7 days if relatively stable, or 10 - 14 days if initially clinically unstable
- Pneumonia: 5 - 7 days
- Urinary tract infection: 7 – 10 days
- Meningitis: 14 - 21 days
- Central-line sepsis: ≤5 days if stable, or 7-10 days if initially clinically unstable
- Ascending cholangitis: 10 - 14 days
- Septic arthritis: 21 days
- Osteomyelitis: 4 – 6 weeks

4. Children initiated on carbapenems in the PICU and then transferred to another ward: The PICU registrar / consultant must review the prescription prior to transfer, indicate the duration consistent with guidance given in point 3d. If the ward doctor requires continuation, then ID should be consulted.
### Dosing instructions

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Paediatric dose</th>
<th>Maximum dose</th>
<th>Dose adjustment if significant renal impairment is present (eGFR &lt;50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>IV 100 mg/kg/dose 8 hourly (refers to piperacillin). In immunocompromised or neutropaenic children &lt;50 kg: IV 80 mg/kg/dose 6 hourly</td>
<td>Piperacillin 4 g / Tazobactam 0.5 g per dose 6 - 8 hourly</td>
<td>Yes</td>
</tr>
<tr>
<td>Amikacin</td>
<td>15 mg/kg once daily</td>
<td>1.5 g daily</td>
<td>Avoid drug</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>IV 15 mg/kg/dose 12 hourly</td>
<td>500 mg 12 hourly</td>
<td>Avoid drug</td>
</tr>
<tr>
<td>Meropenem</td>
<td>IV 40 mg/kg/dose 8 hourly</td>
<td>2 g 8 hourly</td>
<td>Yes</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>IV or IM 100 mg/kg/dose once daily or in 2 divided doses</td>
<td>2 g 12 hourly</td>
<td>No</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>IV 15 mg/kg/dose 6 hourly</td>
<td>Not applicable</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**NB:** Dosing instructions for neonates and preterm infants and for children may differ from the above recommendations

### Renal dose-adjustment recommendations (modified from reference 3)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Renal dose adjustment based on eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>eGFR &gt;40: no dose adjustment required&lt;br&gt;eGFR 20–40: 70%†, same dosing interval&lt;br&gt;eGFR &lt;20: 70%†, infused 12 hourly over 4 hours</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>There are no clear recommendations for using ertapenem in children with renal failure. Hence try to avoid this drug if the eGFR is &lt;50. Alternative carbapenems that can be used in renal failure are meropenem or imipenem. If imipenem is advised please consult ID or the renal unit for guidance on adjusting the dose according to the eGFR</td>
</tr>
<tr>
<td>Meropenem</td>
<td>There are no clear recommendations for neonates &lt;7 days old with renal failure. For children &gt;7 days of age:&lt;br&gt;eGFR 10–50: same dose administered 12 hourly&lt;br&gt;eGFR &lt;10: same dose administered every 24 hours</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>eGFR 70-89: same dose administered 8 hourly&lt;br&gt;eGFR 46-69: same dose administered 12 hourly&lt;br&gt;eGFR 30-45: same dose administered every 18 hours&lt;br&gt;eGFR 15-29: same dose administered every 24 hours&lt;br&gt;eGFR &lt;15: Measure trough levels to determine when to dose</td>
</tr>
</tbody>
</table>

†This percentage change indicates that X% of the original dose should be administered
**Carbapenem-containing antibiotic protocols approved by the Pharmaceutical & Therapeutics Committee**

1. Antimicrobial protocols for treating Cystic Fibrosis-related infections at RCWMCH (approved 2016)
2. Rational antimicrobial prescribing policy document for neutropaenic patients (approved 1 February 2017)

**References**

1. RCWMCH Blood culture procedure: [http://www.paediatrics.uct.ac.za/sites/default/files/image_tool/images/38/1.5.11%20BLOOD%20CULTURE%20GUIDELINE%20RCWMCH.pdf](http://www.paediatrics.uct.ac.za/sites/default/files/image_tool/images/38/1.5.11%20BLOOD%20CULTURE%20GUIDELINE%20RCWMCH.pdf)