GUIDELINE

Febrile Neutropenia: Paediatric Empiric Guidelines

Scope (Staff): Clinical Staff – Medical, Nursing, Pharmacy
Scope (Area): Perth Children’s Hospital (PCH)

This document should be read in conjunction with this DISCLAIMER

Aim
To provide a guideline for the management of presumed bacteraemia/sepsis in an immunocompromised child greater than one month of age.

Definitions:
Fever: Temperature ≥ 38.5°C or Temp ≥ 38.0°C on two sequential occasions in a 12 hour period
Neutropenia: Absolute Neutrophil Count (ANC) < 0.5 x 10⁹/L OR 0.5-1 x 10⁹/L and likely to fall further in next 48h

High risk patients:
- Haematopoietic Stem Cell Transplantation (HSCT) pre-engraftment or with significant myelo/immunosuppression
- Acute Myeloid Leukaemia (AML)
- Relapsed Acute Lymphocytic Leukaemia (ALL) on re-induction chemotherapy
- Infant ALL during intensive chemotherapy

Systemic compromise:
- Haemodynamic compromise
- Significant tachypnoea, increased work of breathing or oxygen saturation <90% on room air
- Confusion or decreased consciousness
- End organ dysfunction including renal or hepatic dysfunction, coagulopathy
**Febrile Neutropenia**

<table>
<thead>
<tr>
<th>CLINICAL SCENARIO</th>
<th>DRUGS/DOSES</th>
<th>Known or Suspected MRSA&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Penicillin allergy&lt;sup&gt;b&lt;/sup&gt; Delayed</th>
<th>Penicillin allergy&lt;sup&gt;b&lt;/sup&gt; Immediate</th>
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<tbody>
<tr>
<td><strong>Standard Protocol</strong></td>
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<tr>
<td>Febrile – not neutropenic</td>
<td>IV <strong>piperacillin/tazobactam</strong> 100mg/kg (to a maximum of 4 grams piperacillin component) 6 hourly</td>
<td><strong>piperacillin/tazobactam</strong>&lt;sup&gt;c&lt;/sup&gt; <strong>AND consider vancomycin</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td><strong>cefepime</strong>&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Discuss with ID or Microbiology service</td>
</tr>
<tr>
<td>Febrile neutropenia - standard risk patient</td>
<td>IV <strong>piperacillin/tazobactam</strong> 100mg/kg (to a maximum of 4 grams piperacillin component) 6 hourly</td>
<td><strong>piperacillin/tazobactam</strong>&lt;sup&gt;c&lt;/sup&gt; <strong>AND consider vancomycin</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td><strong>cefepime</strong>&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Discuss with ID or Microbiology service</td>
</tr>
<tr>
<td>High risk Patient (see definitions above)</td>
<td>IV <strong>piperacillin/tazobactam</strong> 100mg/kg (to a maximum of 4 grams piperacillin component) 6 hourly</td>
<td>As per standard protocol</td>
<td><strong>cefepime</strong>&lt;sup&gt;e&lt;/sup&gt; <strong>AND vancomycin</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Discuss with ID or Microbiology service</td>
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<tr>
<td>Skin infection or erythema over CVAD or fever/rigors following accessing CVAD</td>
<td>IV <strong>vancomycin</strong> 15mg/kg (to a maximum initial dose of 750mg) 6 hourly</td>
<td>As per standard protocol</td>
<td><strong>cefepime</strong>&lt;sup&gt;e&lt;/sup&gt; <strong>AND vancomycin</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Discuss with ID or Microbiology service</td>
</tr>
<tr>
<td>Febrile neutropaenia with sepsis&lt;sup&gt;h&lt;/sup&gt; or septic shock&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Stat dose of IV <strong>gentamicin</strong>&lt;sup&gt;f&lt;/sup&gt; 7.5mg/kg daily (to a maximum of 480mg) <strong>AND</strong> IV <strong>piperacillin/tazobactam</strong> 100mg/kg (to a maximum of 4 grams piperacillin component) 6 hourly <strong>AND</strong> IV <strong>vancomycin</strong> 15mg/kg (to a maximum initial dose of 750mg) 6 hourly</td>
<td>As per standard protocol</td>
<td><strong>gentamicin</strong>&lt;sup&gt;f&lt;/sup&gt; <strong>AND cefepime</strong>&lt;sup&gt;e&lt;/sup&gt; <strong>AND vancomycin</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Discuss with ID or Microbiology service</td>
</tr>
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</table>

Antimicrobial therapy should not be altered without first discussing with the responsible consultant.

For information regarding escalation of antimicrobial cover – see second table

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<sup>a</sup> MRSA: Methicillin-resistant Staphylococcus aureus

<sup>b</sup> Penicillin allergy: Individuals with a history of anaphylaxis or severe allergic reaction to penicillin.

<sup>c</sup> Penicillin/tazobactam: A combination of penicillin and the beta-lactamase inhibitor tazobactam.

<sup>d</sup> Vancomycin: An antibiotic effective against many Gram-positive bacteria.

<sup>e</sup> Cefepime: A cephalosporin antibiotic.

<sup>f</sup> Gentamicin: An aminoglycoside antibiotic.

<sup>h</sup> Sepsis: An inflammatory response to an infection.

<sup>i</sup> Septic shock: A life-threatening condition characterized by low blood pressure due to overwhelming infection.
**Escalation of Antimicrobial cover**

<table>
<thead>
<tr>
<th>Gram negative bacteria identified on blood culture</th>
<th>ADD a stat dose of gentamicin(^1) to standard therapy and contact infectious diseases or clinical microbiology for urgent advice regarding the need for additional cover.</th>
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<tbody>
<tr>
<td>Gram positive bacteria identified on blood culture</td>
<td>ADD vancomycin(^4) to standard therapy, if already on vancomycin empirically, continue same. Contact infectious diseases or clinical microbiology for urgent advice regarding the need for additional cover.</td>
</tr>
<tr>
<td>Negative blood culture at 48 - 72 hours AND persistent fever AND clinical improvement or no deterioration</td>
<td>Stop vancomycin and continue beta-lactam.</td>
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<tr>
<td>Negative culture to date AND persistent fever AND deterioration at any time.</td>
<td>Contact infectious diseases or clinical microbiology for urgent advice regarding the need for additional cover. Consider the addition of vancomycin(^4) or change from piperacillin/tazobactam to meropenem(^9).</td>
</tr>
<tr>
<td>Negative blood culture and persistent fever despite 96 to 144 hours of antibacterial therapy</td>
<td>Consider scanning and testing galactomannan titre prior to the addition of antifungal therapy</td>
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</table>

a. Children known or suspected to be colonised with MRSA may need to have their therapy/prophylaxis modified. Children suspected of having MRSA include:

(i) Children previously colonised with MRSA

(ii) Household contacts of MRSA colonised individuals

(iii) In children who reside in regions with higher MRSA rates (e.g. Kimberley and the Pilbara) a lower threshold for suspected MRSA should be given

(iv) Children with recurrent skin infections or those unresponsive to ≥ 48 of beta-lactam therapy. For further advice, discuss with Microbiology or ID service

b. An immediate (IgE mediated) reaction is characterised by the development of urticaria, angioedema, bronchospasm or anaphylaxis within 1 to 2 hours of drug administration. Delayed reactions including maculopapular or morbilliform rashes, drug fever and cytopenias and are more in keeping with other forms of immunological reactivity. Isolated diarrhoea is not usually immune-mediated and does NOT contraindicate the future use of an antibiotic

c. IV **piperacillin/tazobactam 100mg/kg** (to a maximum of 4 grams piperacillin component) 6 hourly

d. IV **vancomycin 15mg/kg/dose** (to a maximum initial dose of 750mg) 6 hourly. Therapeutic drug monitoring required.

e. IV **cefpime 50mg/kg/dose** (to a maximum of 2 grams) 8 hourly

f. IV **gentamicin 7.5mg/kg/dose** (to a maximum of 480mg) once daily. Therapeutic drug monitoring required for all patients.

g. IV **meropenen 20mg/kg/dose** (to a maximum of 1 gram) 8 hourly.

h. Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
i. Septic shock is a subset of sepsis in which circulatory and cellular/metabolic abnormalities are profound and substantially increase mortality. It is characterised clinically by hypotension requiring vasopressor support and an elevated serum lactate level despite adequate volume resuscitation.

Related internal policies, procedures and guidelines

- Antimicrobial Stewardship Policy
- ChAMP Empiric Guidelines

References

2. Expert opinion – Paediatric Infectious Diseases Physicians

This document can be made available in alternative formats on request for a person with a disability.